ADVCANCE NUTRITION

M.Sc. - 201

Directorate of Distance Education

SWAMI VIVEKANAND SUBHARTI UNIVERSITY

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UNIT

1

UNDERSTANDING NUTRITION

STRUCTURE

1.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

discuss the discovery of food factors necessary for the prevention of nutritional deficiency diseases and for the promotion of positive health,

analyze the concept and basis of human nutritional requirements,

define basic terminologies in relation to human nutritional requirements such as minimum requirements, maintenance allowance, and recommended allowances,

explain the different methods of determining human nutrition requirements, and

describe the national and international recommended dietary allowances of human nutritional requirements and learn to apply them for planning and evaluating diets for health and disease. .

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1.2 INTRODUCTION

This unit covers the scope of advanced nutrition. It begins with some definitions and basic concepts and briefly traces the history of nutritional sciences. It will make you familiar with tenninologies in nutritional requirements such as minimum requirements, recommended dietary intakes (RDIs) and dietary reference intake (DRIs), terms that you will come across frequently in the other units as well. The understanding of these concepts would help you to analyze critically the various methods that are employed to study and estimate nutrient requirements. Based on considerable research, different National and International organizations have made recommendations concerning human nutrient requirements. You will learn about these and their application in different settings in the final section of this unit.

1.3 NUTRITION SCIENCE: BASIC CONCEPTS

Food is the very basis of our life, The food we eat, through the process of digestion, we know, is converted into nutrients, and these nutrients are absorbed, transported to different parts of the body, and utilized for the clay-to-day functioning, at the end of which they are disposed off by further metabolism and transformation into the end products. We need to consume a variety of foods in order to remain healthy. A simple groups concept is useful in getting a balanced diet that helps us to remain healthy. These basic seven food groups are: 1) cereals and cereal products 2) pulses (also meat and meat products) 3) milk and milk products 4) vegetables and fillits 5) nuts and oil seeds 6) fats and oils, and 7) sugars.

An easy way to understand the balanced consuinption of these seven food groups is represented as four steps to a healthy diet as shown in Figure 1.1. Our daily diets for maintaining good health should be made up of generous amounts of vegetables and fruits, adequate amounts of cereals, pulses, milk and milk products, moderate amounts of meat and flesh foods ancl limited quantities of fats and oils, nuts and ail seeds awl sugars, as shown in the Figure 1.1

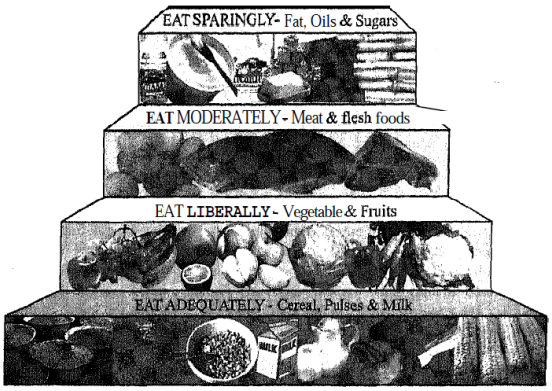

Figure 1.1: Dietary guidelines for Indians: foundation to nutrition and health

Now with this basic understanding, let us gel 10 know what we mean by nutrition science

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What is nutrition science? - A definition

Nutrition science simply defined, the knowledge regarding the role of food maintaining good health, A cotnprehensive definition given by Robinson runs like this

"The science of foods, nutrients and other substances therein; their action, interaction and balance in relation to health and disease; the process by which an organism ingests, digests, absorbs, transports and utilizes nutrients and disposes off their end products ".

Thus, the entire gamut of what foods ate needed for maintaining good health, how they are processed to provide us the wherewith to carry out our daily activities, and how the end products of the foods we ingest are eliminated constitute the science of nutrition.

The next question that you would ask is what parameters can we use to define good health? Can good health, also be referred to as positive health? Does it merely mean freedom from diseases or is it more than that? Let us see.

What constitutes good health?

Positive health has been defined as not merely freedom from diseases but a state of complete physical, mental and spiritual well being. The requirements for positive health are many and these are outlined below.

1) Achievement Qf optimal growth and development during childhood and adolescence, reflecting the full expession of an individual's genetic potential. Growth is defined in terms of physical featules such as height and weight while development includes all aspects of physical and mental clevelopment.

2) Maintaining structural and functional integrity of' body tissues throughout life, allowing thereby to leading an active and productive life. Examples include moist, bright and sparkling eyes for good vision, smooth and soft skin that will prevent the entry of infections through the body surl'aees, and similarly maintaining the integrity of internal organs like the gastrointestinal tract and the liver for proper digestion and assimilation of foods and removal of toxic waste products.

3) `Ability to perform mental tasks efficiently and mental well-being. Good nutrition is essential for children to develop cognitive skills. learn school-oriented tasks well and perform optiinnlly and stay on in school. Similarly good nutrition is impoi-tant in sustaining attention and memory in adults as well.

4) Ability to withstand the inevitable process of ageing with minimal disability.

5) Ability to combat diseases and resist infections, and to minimize the effects of environmental pollutants.

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To maintain positive health, it is essential that we combine and consume a variety of foods in such a way that the nutrient needs for the above functions are all provided. Understanding nutritional needs and translating this into practical diets is no longer a simple process, but requires a sound knowledge of nutrition, First we need to review what are the nutritional components of the foods that we eat. The following paragraph will focus on this aspect.

What are the nutritional components of the foods we consume?

The foods that we consume are composed of varying quantities of the following nutritionally important components:

1) Carbohydrates
2) Proteins
3) Lipids
4) Water
5) Minerals
6) Vitamins
7) Fibre
8) Phytochemicals and anti-oxidants
9) Detoxifying agents

If these nutritional components are consumed daily in the amounts and proportion required, then the chances are that we will maintaina good health. Therefore, a good knowledge and understanding of the food sources of these various nutritional components, their metabolism, and their requirements for different age and physiological groups is an essential prerequisite for maintaining good health. This course is an attempt to provide this knowledge and skills.

The last three decades has seen a tremendous progress in nutrition. Although the importance of nutrition in growth, development and the prevention of nutritional deficiency diseases was well recognized since the 19th century, it is only in the last three decades that the frontiers of nutritional science has expanded to include newer and more dimensions of health such as prevention of chronic degenerative diseases, retardation of ageing and promotion of mental well being.

Human beings require a large number of nutrients, about 40, for many of which the requirements are well established. In addition, recent advances have shown that the diet components like carotenoid pigments, phenolic compounds, flavonoids, anthocyanins, lignins and indoles are bioactive compounds with a potential role in the prevention of degenerative diseases and in detoxification.

The earlier dictum that if the diet provided adequate energy to meet our requirements, then it is likely to be adequate in other respects, is no longer uue. We have to make conscious efforts to have a healthy diet. If you are a nutrition professional or a dietitian, then you also 'have the responsibility of planning diets for others both for health and in diseases and in addition, you will be counseling a large number of people on appropriate diets. This unit will help you to do that by providing a basic understanding of nutritional requirements.

We begin our study of advance nutrition with a review of the history of nutrition and the discovery of food factors. Nutrition scenario in the Indian context is also highlighted in the next section.

1.4 HISTORY OF NUTRITION

Knowledge of human nutritional needs and relationship between diet and health was placed on a modern scientific footing only since the 19th century, after Lavosier established that the body obtained energy through oxidation of foodstuffs and Magendie recognized that protein was essential in the diet for survival. Respiration chambers for estimating energy requirements were developed by mid 19th century. Nitrogen balance studies that measured nitrogen retention reasonably accurately made it possible for the first time to estimate energy and protein requirements with some precision. Some of these experimental evidences and contributions are highlighted in Box 1.1 for your reference. The first dietary standards were proposed, based on these experiments, in the year 1860 that an adult human required a daily intake of food to provide 3000 kilocalories and 80 g of protein. During the next 50 years, several recommendations were made for energy and protein requirements, most of them based on the usual intakes of healthy individuals.

Box 1.1 The Experimental Evidences and Contributions

James Lind in 1747 performed controlled experiments on sailors who developed scurvy. He divided them into different groups. The group receiving 2 oranges and 1 lemon everyday showed dramatic improvements, the first demonstration that scurvy was a disease caused by dietary deficiency. The group receiving cyder everyday showed some improvement, other goups did not show much improvement. Lavoisier's contributions demonstrated that biological oxidation of foods within the body was very similar to combustion of foods outside, both processes utilizing O, and producing COT He introduced the concept of 'Respiratory Quotient', effect of food and exercise on metabolism. The effects of fasting, a post prandial contribution etc. were performed by Seguin and Lavoisier and was published in 1789. Lavoisier is considered as father of modern nutrition. Unfortunately, during the French Revolution, he was executed.

Another scientist, William Stark pelfonned experiments with simple diets on himself. He used water and bread diet; found that it was not even providing

enough energy. Addition of milk, sugar, olive oil was found to contribute to better health but left him still with nutritional deficiencies providing an indication that the science of nutrition was still in an early stage and all necessary dietary constituents for health were not known.

In the 19th century, the energy contributions by carbohydrates, proteins and fats were identified. A controversy developed whether the body can convert carbohydrates into fat which was resolved subsequently. It was further established that carbohydrates and fats are preferred fuels, both at rest and during exercise. The body shifts from one fuel 10 the other depending upon the availabilily of nutrients. By 20th century, the role of minerals and vitamins were established by Lunin, Hopkins, and Eijkman and Funk. The term 'vitamin' was coined by Funk by combining vital and amine.

Let us review the discovery of essential food factors and the expanding frontiers of nutrition next.

1.4.1 Identification of Food Factors and Discovery of Water Soluble Vitamins

Nutritional deficiency diseases such as beriberi, pellagra, and scurvy were all known and described much before the food factors responsible for these illnesses were discovered. Beriberi is reported 10 be mentioned in the Chinese medical book dating back to 2697 B.C., but it was only in 1926 A.D., it was established that this illness was due to the deficiency of a dietary factor present in rice bran. Later, this dietary factor was identified as thiamin (vitamin B,). Similarly, pellagra and scurvy were råmpant in the 18th and 19th century but the deficient food factors responsible for these diseases, namely, niacin and ascorbic acid, were identified only in the 1930s.

Pellagra was first described in 1930 by Casal in poor peasants consuming maize diet, Where they associated it with in cereal during fermentation. But later studies showed that it is niacin deficiency which led to pellagra. The discovery of scurvy was well documented in sea voyages and that it can be cured by consumption of fresh fruits was well established by the experiments of James.

The four decades from 1910 to 1940, were the golden era of vitamins when thiamin, niacin and ascorbic acid were isolated from food sources and were shown to result in complete recovery from the then widely prevalent diseases of beriberi, pellagra and scurvy. Today these diseases are no longer a public health problem anywhere in the world.

Dietary recommendations made through the 1920s and the early 30s were based on limited quantitative information, but it was already recognized by the League of Nations Health Organization, as well as, the US Department of Agriculture that scientific knowledge of human requirements for essential nutrients was needed to provide a reliable base for practical nutrition programmes. The Food and Nutrition Board of the National Research Council/National Academy of Sciences (NRC/NAS)

of USA prepared a set of dietary standards for adequate intakes of nine nutrients in the year 1941, which was formally adopted at a National Nutrition Conference in the same year. These were the first set of recommended dietary allowances.

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1.4.2 Discovery of other Essential Nutrients

Following the identification of the food factors involved in beriberi, pellagra and scurvy, the search was on for other water-soluble vitamins. During the years that followed, we witnessed an expansion in the list of essential nutrients, which currently stand at about 40 . These include the major energy giving food components, namely, carbohydrates, proteins and fats (also known as the proximate principles), the water and fat-soluble vitamins, and the minerals including the trace and ultra trace minerals. The list of currently known essential nutrients is shown in Table 1.1.

Table 1.1: Currently known essential nutrients and nutritionally relevant compounds

1.	Proteins and amino acids*	21.	Ribloflavin*
2	Carbohydrates	22.	Nicotinic acid*
3.	Lipids*	23.	Vjtcunilf
4.	Water	24.	Pantothenic acid"'
5.	Sodium	25.	Biotin"'
6.	Potassium	26.	Fokic acid*
7.	Calcium*	27.	Vitamin B
8.	Phosphorous	28.	Vitamin C*
9.	Magnesium"'	29.	Choline
10.	Iron*	30.	Carnitine
11.	Zinc*	31.	Inositol
12.	Copper	32.	Taurine
13.	Selenium*	33.	Arsenic
14.	Lodinetli	34.	Boron
15.	Chromium	35.	Manganese
16.	Vitamin A*	36.	Molybdenum
17.	Vitamin D'	37.	Nickel
18.	Vitamin E*	38.	Silicon
19.	Vitamin K*	39.	Vanadium
20.	Thiamin*	40.	Fluorine

* RDAs established for these by the Joint FAO/WHO Expen Consultation.

1.4.3 Expanding Frontiers of Nutrition

While the essential nutrients mentioned in Table 1.1 are indispensable and our diets need to provide them all in adequate quantities, it has become clear that for healthy living they are not by themselves enough. Other dietary constituents, such as the phyto-chemicals and anti oxidant substances, are equally important. A deficiency of these may not produce overt recognizable symptoms but they ale nevertheless known to play an important role in prevention of degenerative diseases, delaying the adverse and often considered as inevitable consequefices of ageing like cataracts, blunted memory and in the detoxification of waste nlatérials or environmental pollutants. The present data is sufficient to include these as essential dietary components but what is lacking is the information conceming the amounts of these compounds that we need to consume in our daily diet.

While on the topic of history of nutrition and expanding frontiers of nutrition, let us also look at the developments in the nutrition scenario in India.

1.4.4 The Indian Nutrition Scenario

Nutrition research in India was pioneered by Dr. Robert Mc Carrison. His works on beriberi and gained attention on the interlinks between nutrition and health. Further 'Nutrition Research L,aboratorys' (NRLs) were established in Coonoor in Southetm India in 1929, a time when the three nutritional deficiency diseases mainly Beriberi, Scurvy and Pellagra were occupying the attention of nutlition scientists every where. Notable British scientists such as Dr. Passmore made significant contributions in the initial 10 years. Dr. Wallace Aykryod as the director of these laboratries contributed meaningful research for improving the nutritional status of ullnerable groups in India. Infromation on Nutritive Value of Indian Foods was first published in 1937 by Dr. Aykroyd. This booklet popularly known as Health Bulletin No, 23 has undergone several revisions and currently is the best known resource to nutrition scientists as far as the nutritive value of Indian Foods are concerned. Following this an excpllent tradition of nutrition research primarily focused on finding solutions to our major nutritional problems has been developed and passed on to the present generation by stalverts like D" V.N. Patwardhan, D: C. Gopalan, Dr. V Ranzalingaswamy, and Dt: S.G Srikantia to name a few. The NRL was shifted to Hyderabad in 1966 and was renamed as 'National Institute of Nutrition', (NIN), an apex body administered by the ICMR that coordinates nutrition resealch in India.

Recent advances in cellular and molecular biology have opened new avenues for research in nutrition. Various interactive fields have been developed between nutrition on one hand and immunology, neurosciences, genetics ete. on the other as the major thrust areas for understanding the major nutritional problems of the country, and contributing to meaningful research. Thus, NIN along with other research institutions is developing locally relevant solutions to combat various nutritional disorders in the country. Major contributions have been on iron deficiency

anaemia, vitamin A control programme, fluorosis, lathyrism, iodine deficiency disorders (IDD). To combat for Inuior losses, fortification programmes are being developed. This has been achieved because of the major understanding about the physiological role of a nutrient and its metabolic influences on health.

The history of nutrition reviewed above is summarized herewith under points to remember. Do read them carefully.

POINTS TO REMEMBER

History of Nutrition

The first recommendations for energy and protein requirements were made in the year 1826. The yews 1910 to 1940 witnessed the discovery of thiamin, niacin ascorbic acid and several other water soluble vitamins and led to the dietary prevention of beriberi, scurvy and pellagra. The last three decades of the 20th century has ushered in a new era of expanding frontiers of nutrition, with a major focus on diet as the sheet anchor of prevention of age and life style related chronic degenerative diseases.

With this basic review of history' of nutrition we shall now tum our attention towards understanding the basic concepts of human nutritional requirements.

1.5 NUTRITIONAL REQUIREMENTS

Nutritional requirements are defined as 'intake levels of nutrients that meet specified criteria of adequacy such as normal growth, prevention of deficiency signs, and maintenance of tissue pools of nutrients, and at the same time, preventing the risk qf deficiency or excess. ' The concepts In relation to human nutritional requirements are defined next in this section.

1.5.1 Definition of Concepts in Relation to Human Nutritional Requirements

In this sub-section we will understand a few basic concepts that are related to nutritional requirements. Go through these carefully and understand the concept, as you proceed further.

A) Probability concept of requirements vs risk deficient and excess intake Figure 1.2 best illustrates the concept of a requirement for an essential nutrient. The relationship between the level of intakes and the probability that the intake is deficient or excess, is portrayed in this Figure. As you may have noticed, the estimated average requirement (EAR) is the intake at which the risk of the inadequacy is 0.5 (50 percent) to an individual. The intake at which the risk of inadequacy is judged to be essentially zero is taken as the requirement for that nutrient. As the intake rises above this

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level, a point is reached when risk of excess exceeds zero. The range between the intake level at which risk of deficiency is zero and the point at which the risk of excess rises above zero is taken as the 'safe range intakes'. This concept is utilized in deriving the recommended dietary intakes (RDAs) and the upper intake level (UL) for all the nutrients except energy. Why this concept is not used in deriving energy requirements is discussed in Unit 2 on

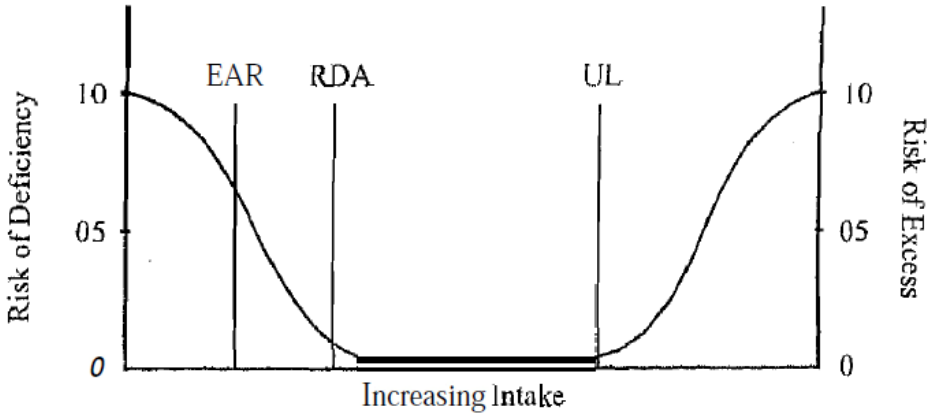

Figure 1.2: Relation between level of dietary intake of an essential nutrient and probability that intake is inadequate or excess

Having understood the probablity concept of requirements, let us now turn our attention to other factors that are determinants of nutrient requirements.

B) Age, sex and body weight are the determinants of nutrient requirements Age sex, and the body weight influence nutrient requirements. Let us see how.

Age: Requirements change with increasing age between bilth and maturity. Nutrient requirements per unit body weight are higher during growth and they decrease •after growth has ceased. For e.g., the energy requirement of an infant is 103 Kcal per kg body weight, while for a sedentary adult male it is only 38 Kcal per kg body weight. Similarly, the protein requirement for an infant 9- 12 mths is 1.5 g per kg, while that of an adult is lg per kg body weight. Requirements increase during pregnancy as the foetus grows. In lactation, the requirements increase in proportion to the amount of milk secreted. At ages of 40 and beyond, there is a decline in the lean body tissue and a decline in activities, both of which result in a decline in the energy requirements. However, this is not accompanied by a reduction in the nutrient requirements due to a reduced efficiency of gastrointestinal function with ageing. We will learn more about these issues later in this course.

Sex: There are some differences in requirements between the two sexes. However, except for iron, these are apparent rather than real, as the differences disappear when the requirements are expressed per unit of

body weight. In the case of iron, between menarche and menopause, the iron requirements of females are more than that of' males due to menstrual losses of blood in women.

Body weight: Requirements are considered to be a function of body weight for. individuals who are not overweight. However, for some nutrients, requirements are not propoftional to body weight. The general procedure for those who deviate from the normal weight is to adjust the requirements to their actual body weights. For overweight and obese individuals lean body weight may be used instead of the total body weight. Related to the concept of requirements being a function of body weight is the concept of defining a reference man and a woman.

Reference man and reference woman: The reference man and woman are defined as points of reference only. For Indians, a reference man is defined as 'a man between 20-39 years of age, with a body weight of 60 kg, free from disease and physically fit for active work. On each working day, he is engaged for 8 hours in an occupation that involves moderate activities. While not at work, he spends 4-6 hours sitting and moving about, 2 hours in active recreation and 8 hours in sleep'. A reference woman is defined as a healthy woman of 20- 39 years, with a body weight of 50 kg, engaged for 8 hours in an occupation involving moderate activities, and while not at work spends 4-6 hours sitting and moving about, 2 hours in active recreation and 8 hours in sleep. Nutrient requirements are defined for the reference man and woman, and for those who deviate from the reference man and woman, adjustments are made for the different body weights. Table 1.2 presents the RDA for different nutrients for Indians. Study these requirements closely.

Besides age, sex and body weight there are other factor which influences the requirement, which are highlighted next.

C) Individual variability requirements

Nutritional requirements, like many other biological characteristics, vary for different individuals', arising due to inherent diffe ences between individuals. Two adult men with the same body weight can have different requirements for energy and other nutrients. The distribution of requirement for proteins of adults is illustrated in Figure 1.3. This distribution is called 'Gaussian 'or 'normal distribution'. We have only limited data on the distribution of nutrient requirements, Therefore, it cannot be said that all requirement distributions follow the normal distribution as illustrated in Figure 1.3. Iron requirements for females, for example, are a highly negatively skewed distribution (portraying the likelihood that a given level of usual intake is inadequate to meet the true needs) as shown in Figure 1.4. However, in the absence of adequate data for many nutrients about the requirement distribution, an assuinption is made that for all nutrients except iron, the requirements are normally distributed i.e. they follow a Gaussian distribution.

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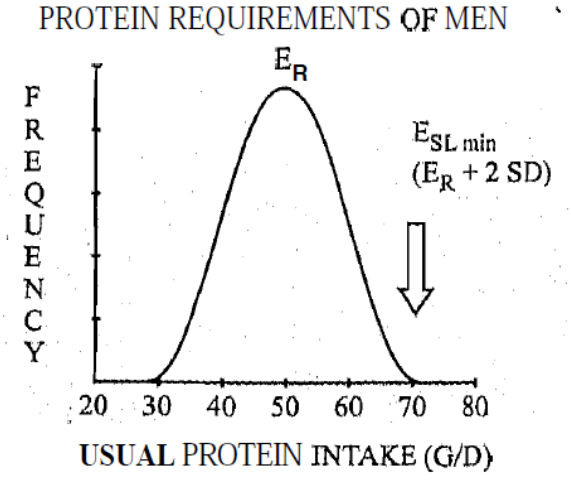

Figure 1.3: Protein requirement for men

Group	Category/Age	Body Weight (kg)	Vitamin A (µg/d)		Thiamine (mg/d)	Riboflavin (mg/d)	Niacin Equivalent (mg/d)	Vitamin B_6 (mg/d)	Ascorbic Acid (mg/d)	Dietary Folate (µg/d)	Vitamin B_{12} (µg/d)
			Retinol	B-carotene							
Men	Sedentary work	60	600	4800	1.2	1.4	16	2.0	40	200	1.0
	Moderate work				1.4	1.6	18				
	Heavy work				1.7	2.1	21				
Women	Sedentary work	55	600	4800	1.0	1.1	12	2.0	40	200	1.0
	Moderate work				1.1	1.3	14				
	Heavy work				1.4	1.7	16				
	Pregnant		800	6400	+0.2	+0.3	+2	2.5	60	500	1.2
	Lactating 0-6 m		950	7600	+0.3	+0.4	+4	2.5	80	300	1.5
	6-12 m				+0.2	+0.3	+3	2.5			
Infants	0 - 6 months	5.4	350	----	0.2	0.3	710 µg/kg	0.1	25	25	0.2
	6 - 12 months	8.4		2800	0.3	0.4	650 µg/kg	0.4			
Children	1 - 3 years	12.9	400	3200	0.5	0.6	8	0.9	40	80	0.2 - 1.0
	4 - 6 years	18.0			0.7	0.8	11	0.9		100	
	7 - 9 years	25.1	600	4800	0.8	1.0	13	1.6		120	
Boys	10 - 12 years	34.3	600	4800	1.1	1.3	15	1.6	40	140	0.2 - 1.0
Girls	10 - 12 years	35.0			1.0	1.2	13	1.6			
Boys	13 - 15 years	47.6			1.4	1.6	16	2.0	40	150	0.2 - 1.0
Girls	13 - 15 years	46.6			1.2	1.4	14	2.0			
Boys	16 - 17 years	55.4			1.5	1.8	17	2.0	40	200	0.2 - 1.0
Girls	16 - 17 years	52.1			1.0	1.2	14	2.0			

Figure 1.3: Recoomended RDA For Indian 2010

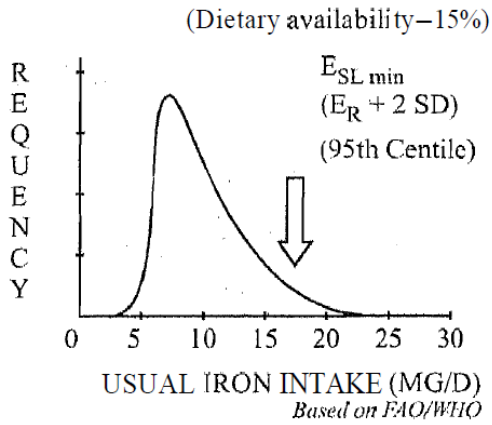

Figure 1.4: Iron requirement for wonicn

When the requirement distribution is normal, the quantitative requirement for a nutrient, for 95% to 99.9% of individuals in a population group, fall between the mean + 2 S.D. and mean +3 SD. Refer to Figure 1.5. As the normal distribution is symmetrical, 50% of individuals in a group will have requirements below the inean and another 50% will have requirements above the mean. Individual variability is often expressed as coefficient of variation (CU, that is, 'standard deviation expressed as a percentage of the mean'. For most biologic variables, including nutrient requirements, CV is about 15%.

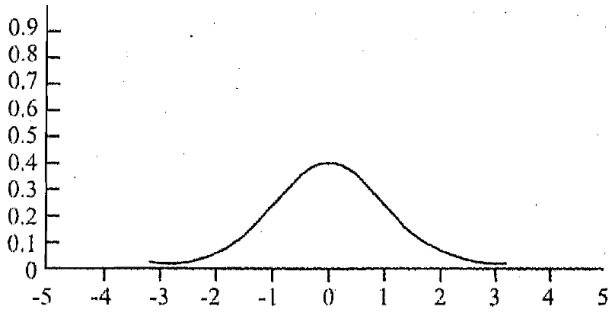

Figure 1.5: Tlie standard normnl distribution

Based on the above properties of the normal distribution, you can see that the quantitative nutrient requirements of prgctically all individuals in a specified life stage and gender group will be covered by the inean + 2 SD. This concept is used in deriving the reconunended dietary allowances and safe levels of requirements. Next, let us study about bioavailability as a factor influencing requirements.

D) Bioavailability of nutrients

The amount of many nutrients needed in the diet depends on the absorption or bioavailability of the nutrients. Bioavailability is defined as 'the percent of the dietary nutrient absorbed and utilized for a specific function by the body'. The percent absorption'varies widely for different nutrients depending on the quantities ingested and the presence of other constituents of the diet. Examples are: iodine absorption is nearly 100%, calcium absorption in a normal adult is about 40% to

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60% while that of iron varies from 1% to 15% , depending on the type of iron and other constituents of the diet.

The concept of bionvailability is best illustrated by iron, Iron is present as inorganic iron in vegetarian foods and as organic iron in meat and flesh foods, The inorganic form of the iron, as you may already be aware, is known as 'non-haem iron' while the organic form is known as haem iron. The 'non-haem iron" absorption is affected by several constituents of the diet while haem iron absorption is relatively independent of these constituents as you would learn later in Unit 10 of this course.

The dietary constituents that inhibit non-haem iron absorption are many: phytates present in the outer layer of cereal grains, tannins in tea, calcium in foods, and oxalates in leafy vegetables, are all inhibitors of iron absorption and reduce the absorption from a vegetarian diet. On the contrary, vitamin C present in fiuits and vegetables and sulphur containing amino acids and a factor in meat and flesh foods enhance iron absorption. The net absorption of iron from a vegetarian diet depends on the relative amounts of the inhibitors and enhancers in the diet. If the diet is predominantly vegetarian and has high amounts of inhibitors, the absorption. of iron may be as low as 1% and if the proportion of enhancers is high, the absorption could rise to 5 t010%.The recommended amounts of nutrients, include a correction for bioavailability wherever relevant. An example is provided in Table 1.3 for iron and zinc.

Having gone through the discussion above we hope the few basic concepts that are related to nutritional requirements must be clear and well understood. Next, we shall review a few basic terminologies that you would come across while studying about nutritional requirements.

1.5.2 Basic in Relation to Nutritional Requirements

By now you would have a good understanding that nutrient requirements are affected by a number of factors and in order to have adequate nutrient intakes these factors have to be taken into consideration for different population groups. You will recall that earlier we defined positive health as not merely freedom from diseases but a state of complete physical and mental health. In a similar manner, nutrient requirements should be such as to promote optimuin health rather then merely to prevent nutritional deficiency disease. There are differences in the level of requirements for prevention of deficiency diseases v/s promotion of positive health. Let us now get familiar with the basic terminologies to describe these.

Minimum Requirement: Minimum nutrient requirement is defined as. the 'lowest amount of the nutrient ji-om the diet that will prevent clinically detectable impairment in function'. For example, it has been established through experimental studies that an intake of 10 mg of ascorbic acid will prevent the occurrence of scurvy in individuals, and therefore the minimum requirement of ascorbic acid is 10 mg per day; however, it is highly undesirable to subsist on minimum requirement on a

continuing basis. We should strive on a daily basis to meet the lowest intakes that would assure positive health rather than merely protect us from frank nutritional disease. In other words, we should strive for the safe level or the RDA rather than the minimum requirement. Maintenance Requirement: This is defined as 'the amount of nutrient that is needed to replace the wear and tear of the tissues within the body in a healthy individual'. This does not take into account the need for growth or for replacement of body tissues in a person recovering from illness.

Safe Requirement: Given the individual variations in nutritional requirements that have been discussed earlier, the lowest continuing intake level of a nutrient to satisfy good health varies from one individual to another. In practice, we want to set up requirements that would meet the needs of most people and will be safe at the same time for all. The lower and upper limit of the range of intake in which the of inadequacy, as well as, the risk of excess is zero is taken as the range of safe requirement.'

Subsistence Allowance: These estimates are also called survival requirements and are of value during emergency or natural calamities such as earthquakes etc. Hence, when there is a crisis and whole population is involved, the people are fed on such.

	Calcium	Magnesium	Selenium	Zinc			Iron (i)				Iodine
	(c)			High bioavail-ability	Moderate bioavail-ability	Low bioavail-ability	15% bioavail-ability	12% bioavail-ability	10% bioavail-ability	5% bioavail-ability	(m)
Age	mg/day	mg/day	mg/day	mg/day	mg/day	mg/day	mg/day	mg/day	mg/day	mg/day	µg/day
Infants											
Premature											30(p) µg/kg/day
0 - 6 months	300 (a) 400 (b)	26 (a) 36 (b)	6	1.1 (e)	2.8 (f)	6.6 (g)	(k)	(k)	(k)	(k)	15 (p) µg/kg/day
7 -11 months	400	53	10	0.8 (e) 2.5 (h)	4.1 (h)	8.3 (h)	[6] (l)	[8] (l)	[9] (l)	[19] (l)	135
Children											
1 - 3 years	500	60	17	2.4	4.1	8.4	4	5	6	13	75
4 - 6 years	600	63	21	3.1	5.1	10.3	4	5	6	13	110
7 - 9 years	700	100	21	3.3	5.6	11.3	6	7	9	18	100
Adolescents											
Males 10 - 18 years	1,300 (d)	250	34	5.7	9.7	19.2	10 (10 - 14yrs) 12 (15 - 18yrs)	12 (10-14yrs) 16 (15-18yrs)	15 (10-14yrs) 19 (15-18yrs)	29 (10-14yrs) 38 (15-18yrs)	135 (10-11yrs) 110 (12 + yrs)
Females 10 - 18 years	1,300 (d)	230	26	4.6	7.8	15.5	9(10 - 14yrs)(m) 22 (10 - 14 yrs) 21 (15 - 18 yrs)	12 (10 - 14yrs) (m) 28 (10 - 14 yrs) 26 (15 - 18 yrs)	14 (10 - 14yrs) (m) 33 (10 - 14 yrs) 31 (15 - 18 yrs)	28 (10-14yrs) (m) 65 (10 - 14 yrs) 62 (15 - 18 yrs)	140 (10 - 11yrs) 100 (12 + yrs)
Adults											
Males											
19 - 65 years	1,000	260	34	4.2	7.0	14.0	9	11	14	27	130
Females											
19 - 65 years (pre-menopausal)	1,000	220	26	3.0	4.9	9.8	20	24	29	59	110
51- 65 years (menopausal)	1,300	220	26	3.0	4.9	9.8	8	9	11	23	110
Older adults											
Males 65 + years	1,300	230	34	4.2	7.0	14.0	9	11	14	27	130
Females 65 + years	1,300	190	26	3.0	4.9	9.8	8	9	11	23	110
Pregnancy											
First trimester		220		3.4	5.5	11.0	(n)	(n)	(n)	(n)	200
Second trimester		220	28	4.2	7.0	14.0	(n)	(n)	(n)	(n)	200
Third trimester	1.200	220	30	6.0	10.0	20.0	(n)	(n)	(n)	(n)	200
Lactation											
0 - 3 months	1,000	270	35	5.8	9.5	19.0	32	40	48	95	200
4 - 6 months	1,000	270	35	5.3	8.8	17.5	32	40	48	95	200
7 - 12 months	1,000	270	42	4.3	7.2	14.4	32	40	48	95	200

Table 1.3: Recommended Nutrient Intakes" Minerals

For the purposes of the composite tables of RNI values, the body weights used were derived from the 50th percentile of NCHS data until adult weight of 55 kg for femalesand 65 kgformales were reached. Theweights used are the following: 0-6mo=6 kg; 7-12mo = 8.9 kg: 1-3 yr = 12. I kg; 4-6yr = 18.2 kg; 7-9yr = 25.2 kg; 10-11 yr M = 33.4kg; 10-11yr F=34.8kg: 12-18yr M-55.1 keg; 12-18yr F=50.6kg; 10-18yr M=55.1 kg•, 10-18yr F=50.6kg; 19-65yr M=65 kg•, 19-65yr F=55 kg-

Inview of the high variability in body weights at these ages the RNIs mentioned body weight/day. allowance. Such an intake allows only minimum movement and is not compatible for long term health and makes no allowance for the energy needed to earn a living or prepare food. Long intake of diets of such value shows deficiency as the minimum requirements are not met, and hence can prove to be fatal.

Recommended Dietary Allowances (RDA): The recommended dietary allowances are defined as the 'daily dietary intake level that is sufficient to meet the nutrient requirenzents of nearly all healthy individuals in a particular life stage and gender group'. The RDA is derived from the statistical distribution of requirements for nutrients. It is generally assumed that nutrient requirements are distributed normally. With this kind of distribution, the requirements of 97 to 98% of individuals in a given population group will be below the mean plus two standard deviations. Thus, mean + 2 SD will cover the requirements of practically all individuals in that population group and is designated as the RDA for that panicular nutrient. This approach is used for deriving the RDA for all nutrients except energy. The RDA is intended for use primarily as a goal for usual intakes. Recommended Nutrient Intakes (RNIs), is another term commonly used to describe nutrient requirements and is equivalent to RDA.

Dietary Reference Intakes: Dietary Reference Intakes (DRIs) are relatively new to the field of nutrition. The DRIS are a set of four nutrient-based reference values, that can be used for planning and evaluation of diets of individuals and population groups and are meant to replace the former RDAs of the US and RNIs of Canada. The DRIS are different from the RDAs and RNIs in three respects. These include:

1) Where specific data on safety and efficacy exist, reduction in the risk of chronic degenerative diseases is included in the formulation of the reference intakes rather than using only the absence of signs of deficiency.

2) Where data are adequate, upper levels of intake to prevent adverse consequences of excess are established i.e. the upper levels will tell you not to exceed these at usual intakes, and

3) Components of food that may not fit the traditional concept of essential nutrient but nevertheless are shown to have beneficial effects for human health are reviewed, and if data permit, DRIS are established for these.

The four nutrient reference values are described below:

a) **The Estimated Average Intake (EAR)** : Considering that the nutrient requirements follow a normal distribution, the EAR is defined as 'the median usual intake that meets the requirement of half of the healthy individuals in a given life stage and gender group.

Note: Earlier RDA has used mean rather than the median.

At this level, the other half of the individuals will not meet their requirements. The EAR is based on specific c iterion of adequacy, derived from a review of the literature. Reduction of disease risk is considered along with other health parameters in the selection of this criterion. EAR is used to calculate RDA.

b) **RDA**: The RDA is the average daily dietary intake that is sufficient to meet the nutrient requirement of nearly all healthy individuals in a particularlife stage and gender group. Under assumption of normality of the distribution of requirements, the RDA can be calculated from the EAR and the standard deviation of requirements as follows:

Recommended Dietary Intake = Estimated Average Intake + 2 SD requirement

The RDA is intended to be used as a goal for usual intakes from the diet. Since RDA is established from EAR, if data are inadequate to estimate the EAR, no RDA can be established, In such cases, the adequate intake (A1), as described next, is used as the goal.

POINTS TO REMEMBER

Concepts and Definitions in Relation to Nutrient Requirements

1) The probability concept describes the relationship between the levels of intake and the probability of risk of inadequate and excess intakes.

2) The range of intake in which there is zero probability of risk of deficiency and risk of excess is known as the safe requirement range.

3) Age, sex and body weight are determinants of nutrient requirements.

4) Nutrient requirements vary for different individuals due to genetic differences. The individual variations are described by the term coefficient of variation which is the standard deviation expressed as a percent of the mean requirement.

5) Mean + 2 SD is the recommended allowance for a nutrient, which meets the needs of 97 to 98% of the individuals in a life stage and gender group. For energy only the mean is taken as the RDA.

6) Bioavailability of nutrients must be taken into account while making recommendations for nutrient requirements.,

7) The basic terms used in relation to nutrient requirements are minimum requirements, safe allowances, recommended dietary allowances, dietary reference intakes.

NOTES

1.6 METHODS FOR STUDYING THE NUTRIENT REQUIREMENTS

Several methods have been used Tor studying the nutrient requirements, They range from observational methods like population survey of dietary intake$ to experimental methods involving nutrient balance and nutrient turn over. These are describedherewith.

1.6.1 Population Survey of Dietary Intakes of Nutrients

The basis of this method rests on the premise that average dietary intake of nutrients by healthy members of a group of individuals at a specific life stage and gender represents the requirement of this group. This was the only method available for a long time to estimate the nutrient needs. All early recommendations were based on this method. The limitations of the method are that since the average is calculated from usual intakes of healthy individuals eating to appetite, the method can both over or underestimate the requirements. The limitation of this method is best illustrated by the early recoinmendations for protein. The first ever recommendation that was formally adopted put the protein requirement of adult man as 80 g per day. Some years later, Chittenden, a German nutrition scientist based on experiments on himself recoinmended that for good health, an adult man required no more than 50 g protein per day.

1.6.2 Growth Studies

Nutrient requirements of infants and young children are estimated by studying the rate of growth of healthy children and the deposition ofnutrients in the body. Estimation of protein needs of children is an example of this method. The weight gain of infants and children apd the nitrogen content of the body at different ages are used in estimating the protein needs of children.

1.6.3 Depletion and Repletion Studies

This is an experimental procedure in which volunteer subjects are kept on a diet devoid of a particular nutrient, until such a time when they develop overt clinical signs of deficiency of the nutrient. The lowest level of the nutrient that reverses the clinical symptoms in all volunteer subjects is the minimum requirement for that nutrient. The minimum requirement for some B vitamins and ascorbic acid has been determined through this method.

1.6.4 Nutrient Balance Studies

The ingested nutrients are metabolically converted into end products that are eliminated from the body through urine, faeces and sweat. Some of the nutrients are extensively catabolized while others may undergo minimal changes. For example, dietary proteins are converted into nitrogenous compounds and

eliminated. The major nitrogenous compound of protein catabolism is urea that is excreted primarily in the urine. The vitamins are converted into incompletely oxidized forms while the minerals like Ca are excreted as such.

We can study the amount of the nutrient ingested and the amount excreted from which the nutrient balance can be calculated as follows:

Amount of Nutrient Ingested — Amount Excreted = Amount Retained

The balance is usually zero in adults and positive in growing children, indicating replacement df wear and tear needs in adults and retention for growth and tissue development in children.

Using this concept we can study the lowest average intake that is necessary to maintain zero balance in adults that will represent the maintenance requirement.

Maintenance of protein requirements have been estimated this way. Calcium balance studies have been performed to arrive at the requirements for calcium.

1.6.5 Use of Isotopically Labeled Nutrients: Nutrient Turnover

Radioactive labeled nutrients are used to know the total body pool and the compartment in which it is stored. The pool that falls below a certain level shows deficiency. These are used ta estimate how much nutrient is lost on a daily basis. Let us consider an example of iron.

Isotopically labeled iron has been used in estimating the iron requirements for different groups. Ingested iron is absorbed and incorporated into red cells; complete incorporation occurring in 15 days time. A small dose of radio labeled iron is mixed with the diet and two measurements made; the basal radioactivity of the blood before ingesting the radio labeled diet and radioactivity of red cells after 15 days of ingesting the diet. From the retained radioactivity, the amount absorbed and requirements are calculated.

1.6.6 Obligatory Losses of Nutrients

Obligatory losses of nutrient are defined as 'the losses that occur when an individual is put on a diet free of that nutrient'. For example, when we are on a protein free diet, we continue to lose protein in the form of urinary' urea and other nitrogenous compounds. Within 5 to 6 days on a protein free diet, the total nitrogen losses as urea and other compounds stabilize to a low and constant value. The amount of dietary protein needed to replace these losses has been experimentally determined. These represent the maintenance requirement for protein in an adult. This method, however, has been discarded as it represents a non-physiological state.

The various methods discussed above are summarized in points to remember herewith.

POINTS TO REMEMBER

Methods for Studying the Nutrient Requirements

1) Population survey of nutrient intakes of healthy individuals is one method of estimating nutrient requirements. The average intake by healthy individuals in a particular life stage and gender group represents the requirement for that group. Currently this method is used only when there is not adequate data on requirement distribution in population groups.

2) For infants and children, growth and body weight gain has been used along with the nutrient composition of body tissues to arrive at the nutrient requirements.

3) Experimental methods such as depletion and repletion of nutrients and nutrient turnover studies have helped in determining the minimum requirements and recommended allowances.

4) Some methods like the obligatory losses which were used at one time for estimating the maintenance requirements of nutrients are no longer in use as they represent a non physiological state.

Now that we have understood about the nutrient requirements and how they are estimated, let us get to know about the national and the international recommendations for the nutrient requirements.

1.7 NATIONAL AND INTERNATIONAL RECOMMENDATIONS FOR NUTRIENT REQUIREMENTS

Various nutrition institutes and research and professional organizations in India and all over world have given recommendations for the nutrient requirements for their population groups and for people of all ages. Let us review some of these recommendations.

1.7.1 Recommendations for Indians by the Indian Council of Medical Research (ICMR)

The Indian Council of Medical Research in its recent "Nutrient Requirements and Recommended Dietary Allowance for Indians"(1990 reprinted in 1998), has made recommendations for energy, protein, fat, two minerals namely caléium (Ca) and iron: one fat soluble vitamin ,Vitamin A, and 7 water soluble vitamins namely thiamin, riboflavin, niacin, ascorbic acid, pyridoxine, folic acid and vitamin B12 These are shown in Table 1.2 earlier. The recommendations are made for different life stages, and gender groups separately.

These RDAs have been derived from average nutrient requirements for each group estimated by one of the methods mentioned under section 1.5. The RDA takes into account the variation that exists between individuals by choosing a level that is 2 standard deviations higher than the average requirement so that the requirements of 97 to 98% of individuals in a given age, sex and physiological

group are met. It thus aims at meeting the requirements of nearly all individuals'in a population group.

This approach, however, is not used for energy requirements. The average requirement for energy is taken as the RDA. The reason for this is that consumption of other nutrients in excess of requirement,to the tune of 2 SD is not associated with any adverse effects whereas consumption of energy even in small excess over requirement for a period of time can lead to overweight and obesity.

The RDA also takes into account nutrient bioavailability as in the case of iron. The bioavailability of iron in Indian diets is approximately 3% and the RDAs for adult men, children and adolescent boys are based on this level of bioavailability. The underlying principle of all RDAs is worth recalling here again. The RDAs are meant to be used as a goal for dietary intakes on a continuing basis, so that practically all individuals in a life stage and gender group will be protected from inadequate intakes of nutrients and thus would be in a position to maintain good health.

The RDAs are not meant to be used as a standard for determining whether an individual requirement has been met. Individuals with intakes lower than the IRDA are not necessarily at risk, if their requirements are less than the RDA, which they are for many.

1.7.2 FAO/WHO Expert Committee Recommendations

The FAO/WHO/UNU joint Expert committee makes recommendations for nutrient requirements periodically, revising them as and when more data becomes available. The most recent recommendations on vitamin, mineral requirement and energy requirements were published in 2002 and 2004, respectively. The Recommended Nutrient Intakes for the minerals such as' calcium, magnesium, selenium, zinc, iron and iodine and for the fat soluble vitamins , A, D, E, and K and the water soluble vitamins, thiamin, riboflavin, niacin, vitamin $B_{„}$ pantothenic acid, biotin, folic acid, vitamin $B_{„„}$ and vitamin C along with some explanatory notes.

We will learn about the energy requirements in the next unit, Along with the WHO/FAO/UNU recommendations, we have also reviewed the dietary reference intake for population groups in US and Canada and provide valuable information on upper intake limits in the next sub-section.

1.7.3 Dietary Reference Intakes for US and Canada

Dietary Reference Intakes has been published by the National Academy Press for the Food and Nutrition Board and the Institute of Medicine, Washington DC, USA. These are meant to be used as goals for intake in North America. Four nutrient based values are defined; these are estimated average intake, recommended dietary allowances, adequate intake and tolerable upper levels as described earlier in sub- section 1.4.2. The EAR and RDA carry the same meaning as the average intake and RDA of the Indian Reference values. Also, the Recommended Nutrient

Intakes of FAO/WHO and RDA of the DRI are similar in concept. Two other values pot included in the Indian recommendations and the FAO/WHO expert committee recommendations are the A1 and the UL.

NOTES

Table 1 4: . Recommended nutrient intakes (mg) - water and fat soluble vitamins*

Age	WATER SOLUBLE VITAMINS								FAT SOLUBLE VITAMINS			
	Thiamin mg/day	Ribo-flavin mg/day	Niacin (a) mg/day	Vit. B6 mg/day	Panto-thenate mg/day	Biotin mg/day	Folate (c) mgDFE/day	Vit. B12 mg/day	Vit. C (d) mg/day	Vit. A mg/day	Vit. D mg/day	Vit. E (Acceptable intakes) (h) mg a-TE/day	Vit. K (l) mg/day
Infants													
0 - 6 months	0.2	0.3	2 (b)	0.1	1.7	5	80	0.4	25	375	5	2.7 (i)	5(m)
7 -11 months	0.3	0.4	4	0.3	1.8	6	80	0.5	30	400	5	2.7 (i)	10
Children													
1 - 3 years	0.5	0.5	6	0.5	2	8	160	0.9	30	400	5	5 (k)	15
4 - 6 years	0.6	0.6	8	0.6	3	12	200	1.2	30	450	5	5 (k)	20
7 - 9 years	0.9	0.9	12	1.0	4	20	300	1.8	35	500	5	7 (k)	25
Adolescents													
10 - 18 years													
Males	1.2	1.3	16	1.3	5	25	400	2.4	40	400	5	10	35-65
Females	1.1	1.0	18	1.2	5	25	400	2.4	40	600	5	7.5	35-55
Adults													
Males													
19 - 65 years	1.2	1.3	16	1.3 (19 - 50yrs) 1.7 (50 + yrs)	5	30	400	2.4	45	600	5 (19-50 yrs) 10 (50+yrs)	10	65
Females													
19 - 65 years	1.1	1.1	14	1.3	5	30	400	2.4	45	500	5	7.5	55
(pre-menopausal)													
50 - 65 years	1.1	1.1	14	1.5	5	30	400	2.4	45	500	10	7.5	55
(menopausal)													
Older adults													
65 + years													
Males	1.2	1.3	16	1.7	5		400	2.4	45	600	15	10	65
Females	1.1	1.1	14	1.5	5		400	2.4	45	600	15	7.5	55
Pregnancy	1.4	1.4	18	1.9	6	30	600	2.6	55	800	5	(j)	55
Lactation	1.5	1.6	17	2.0	7	35	500	2.8	70 (e)	850	5	(j)	55

Points to remember given next summarizes the information presented in this section. So read it carefully.

For further information on these recommendations you may want to look up the following web site:

NOTES

Adequate Intake (AI): If sufficient data are not available to establish an EAR and hence RDA, the A1 is defived instead. The AI is derived from observations of nutrient intakes by a group of apparently healthy individuals who are maintaining a defined nutritional state or criterion of adequacy. Criteria of adequacy include normal growth, maintenance of normal levels of nutrients in plasma or general health. The mean observed intake of this group of healthy individuals of a particular life stage and gender is taken as the AI. While AI can be used as a goal for individual intake, it has only limited use in assessment. As and when more data become available, the AI will be replaced with RDAs.

It must be noted here that AI represents an informed judgment about what appears to be an adequate intake for an individual based on available information. On the other hand, RDA is data-based and is a statistically relevant estimate of the required level of intake of the nutrient for almost all individuals. For this reason, A1 must be used with caution.

d) **The Upper Level (UL)**: The UL is 'the highest continuing level of daily nutrient intake that is likely to pose no risk .of adverse health effects in almost all individuals, in the specified life stage group'.

Note: The UL is not intended to be a recommended level of intake. It serves the

purpose of warning people that levels higher than UL are going to be associated with

adverse health effects and therefore should be avoided.

The concepts discussed above are summarized in the points to remember below. Read them carefully.

POINTS TO REMEMBER

1) The Indian Council of Medical Research has formulated recommended dietary allowances for the following nutrients for different age, sex and physiological groups.

   Energy
   Protein
   Fat
   Calcium
   Iron
   Vitamin A

NOTES

Thiamin
Riboflavin
Niacin
Pyridoxin
Ascorbic acid
Folic acid
Vitamin B_{12}

2) These recommended allowances for all nutrients except energy are the mean requirement +2 SD, keeping in line with the probability approach.

3) The other two sets of recommended allowances described in this section are the ones by the joint FAO/WHO expert group and the dietary reference intakes for USA and Canada.

The nutrient requirements described as RDA serve several purposes and are used by the Food and Agricultural Ministries in different countries quite extensively. As a student you may be looking at these requirements for evaluating intakes at the community or population level but the application of RDA goes beyond this.

We will tell you something about the application of RDA's in the next section.

1.8 GOALS OF NATIONAL AND INTERNATIONAL REQUIREMENT ESTIMATES AND RDAS

One of the goals of the RDAs has been reiterated through this unit. They serve as the guidelines for continuing dietary intakes that healthy people should strive for on a day to day basis, in order to maintain good health. Apart from this, there are other goals. These are:

1) Planning for national food supplies,
2) Planning for •emergency rations,
3) Providing information on food fortification,
4) Evaluation of nutrient adequacy at individual and group level, and
5) Modifying nutrient requirements in clinical management of diseases, Besides nutrient requirements you will come across dietary guidelines published now and then related to specific diseases conditions or for good health, We shall end our study of this unit with a brief review on these dietary guidelines.

1.9 DIETARY GUIDELINES

Dietary Guidelines are becoming increasingly powerful tools to help the general

public to appreciate the role of diet in-prevention of degenerative diseases associated with ageing, affluence and environmental degradation. Unlike the RDAs, which provide infonnation on nutrient requirements in quantitative terms, the dietary guidelines are qualitative and the purpose is not so much to help people to get the nutrients as per RDA but to facilitate people to choose diets that are health promoting and disease preventing. While there is only one set of nutrient requirements and RDAs for each country, there can be several dietary guidelines for people within a country.

Many countries have come up with Food based Dietary Guidelines appropriate to their culture and food habits. In India, there are at least two sets of Dietary Guidelines that have been published to help the general public at large. The first by the National Institute of Nutrition, Hyderabad and the second by the Department of Women and Child Development, of the Ministry of Human Resources. Interested students can obtain these from the respective institutions.

1.10 LET US SUM UP

In this unit, we studied about the historical development of how nutrition, as a science, evolved to the present day, the nutrients were identified and discovered. Nutritional science simply defined is the knowledge regarding the role of food in maintaining good health. Good health is not merely freedom from diseases but is a state of complete physical and mental well being. Then we leamt that human nutritional requirements are quantitative estimates of the amount of nutrients that will meet the needs of 97 to 98% of individuals in a particular life stage and gender group with zero risk of deficiency or excess. The niain concept deriving these nutritional requirements is a statistical probability concept that relates the intakes to risk of deficiency and excess.

Finally, the Recommended Dietary Allowances (RDAs), and the Recommended Nutrient Intakes (RNIs), derived using the probability concept was presented, intended to serve as goals for usual daily dietary intakes. The RDAs for Indians by the Indian Council of Medical Research and the RNIs for the world population by the FAO/ WHO joint consultation are two important reference values that must be remembered.

1.11 GLOSSARY

Nutritional requirements : intakelevels of nutrients that met specified criteria of adequacy such as normal growth, prevention of deficiency signs, maintenance of tissue pools of nutrients and preventing the risk of deficiency or excess.

NOTES

Safe range of intake : the range between the intake level at which risk of deficiency is zero and the point at which the risk of excess rises above zero.

Reference man : a man between 20-39 years of age, with a body weight of 60 kg., free from disease and physically fit for active work. On each working day, he is engaged for 8 hours in an occupation that involves moderate activities. While not at work, he spends 4-6 hours sitting and moving about, 2 hours in active recreation and 8 hours in sleep.

Reference woman : a healthy woman of 20-39 years, with a body weight of 50 kg, engaged for 8 hours in an occupation involving moderate activities, and while not at work spends 4-6 hours sitting and moving about, 2 hours in active recreation and 8 hours in sleep.

Coefficient of variation : Standard deviation expressed as a percentage of mean.

Standard deviation : a statistical measure of the distance, which a quantity is likely to lie from its average value/ a measure of the extent to which numbers are spread around their average.

Bioavailability : the percent of the dietary nutrient absorbed and utilized for a specific function by the body.

Non-haem Iron : the inorganic form of the iron.

Haem-iron : the organic form of the iron.

Minimum nutrient requirement : the lowest amount of nutrient from the diet tha will prevent clinically detectable impairment of function.

Maintenance requirement : the amount of nutrient that is needed to replace the wear and tear of the tissues within- the body in a healthy individual.

Recommended dietary allowance : the daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all healthy individuals in a particular life stage and gender group.

Estimated average intake : the median usual intake that meets the requirements of half of the healthy individuals in a given life stage and gender group.

Upper level : the highest continuing level of daily nutrient intake that is likely to pose no risk of adverse health effects in almost all individuals, in the specified life stage goup.

Obligatory losses : the losses that occur when an individual is put on a diet free of any particular nutrient.

1.12 CHECK YOUR PROGRESS

1) List the major determinants of nutrient requirements.

2) Briefly explain the concept of bioavailability of nutrients.

3)Are the minimum nutrient requirements same as maintenance requirements?

4) What is meant by RDA? How can we calculate it?

5) Write short notes on:

a) Estimated Average Intake

b) Adequate Intake

c) Upper Level

NOTES

UNIT

2

HUMAN ENERGY REQUIREMENTS

STRUCTURE

2.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

define the units of energy and physiological fuel value of foods,

discuss the components of energy requirements,

describe the methods of estimation of energy requirements,

define and explain the basis for formulating the energy requirements of different physiological groups, and critically

analyze the regulation of energy metabolism— problems associatecl with high and low energy intake.

2.2 INTRODUCTION

This unit focuses on the human energy requirements. The nutrient requirement for Indian population, you may recall studying in the last unit, are computed by the Indian Council of Medical Research (ICMR) and published in its regent "Nutrient Requirements and Recommended Dietary Allowance for reprinted in 1998. The energy requirements have been computed on the basis of recommendations made

by a Joint Expert Consultation of the World Health Organization(WHO)/Food and Agricultural Organization (FAO)/United Nations University (UNU) in 1985 and by an Expert Committee constituted in 1988 by ICMR, These data, of course, have to be continuously updated particularly now in the light of the new Food and Agriculture Organization/ World Health Organization/United Nations University (FAO/WHO/UNU) recommendations.

A Joint FAO/WHO/UNU Expert Consultation on Human Energy Requirements, convened in October 2001 at FAO headquarters in Rome, Italy has formulated recommendations for human energy requirements published in 2004. The levels of energy intake recommended by this expert consultation are based on estimates of the requirements of healthy, well-nourished individuals. The recommendations that have resulted from this consultation are important guidelines on energy in human nutrition for the academia, scientists, nutritionists, physicians and other health workers, as well as, for planners and policy-makers in both the agriculture and health sectors throughout the world.

The ICMR is in the process of now updating the earlier recommendations. Till such time the new recommendations are published the old recommendations are being followed in our countsy and have been included in this unit. The new FAO/ WHO/ UNU 2004 recommendations for human energy requirements throughout the life cycle are also presented in this unit on the basis of which our new recommendations for energy may be formulated in course of time.

What are the components of energy requirement? Which are the factors which influence the energy expenditure and requirements of individuals? What are the old and new methods we can use for measuring the energy expenditure and requirement? What are the problems associated with high and low energy intakes? These me some of the issues covered in this unit.

2.3 ENERGY: SOME BASIC CONCEPTS

Energy in simple terms may be defined as the ability, or power, to do work. As a student of dietetics and nutrition, you already know that the physiological sources of energy are carbohydrates, protein, fats — the macronutrients present in food.

Energy is released by the metabolism of food and the potential energy value of foods is expressed in terms of the kilocalorie (Kcal). A kilocalorie is defined as the amount of heat required to raise the temperature of 1 kg of water through 1°Celsius (centigrade). Internationally, you may notice that the unit of energy measurement commonly used is the Joule (J). It expresses the amount of energy expended when 1 kg of a substance is moved 1 meter by a force of 1 newton. The conversion factor for changing kilocalories to kilojoules is 1 kilocalorie = 4.184 kilojoules.

The amount of heat energy (kilocalorie) per gram that can be made available to the body by each of the energy-yielding macronutsients — carbohydrate, protein,

fat — must be known to you.

Yes, 1g of carbohydrates yields 4 Kcal, 1g of fat yields 9 Kcal, and 1g protein yields 4 Kcal. These values are known as the physiological fuel factors.

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Do you know how the energy in various foods is generally measured? The amount of energy available in a food is precisely determined by a laboratory technique known as calorimetry. In this process, a weighed amount of food is placed inside a metal container called a bonzb calorimeter, which is immersed in water. The food is then ignited in the presence of oxygen and burned. The increase in temperature of the surrounding water is measured and used in calculating the number of kilocalories given off by the oxidation of the food,

An alternate method of measuring food energy is to use the macronutrient composition Of foods in the food composition tables and by using the physiological fuel factors referred to earlier. The Indian Council of Medical Research (ICMR), India has published food value tables in a book titled 'Nutritive Value of Indian Foods'. Certainly, as a student of nutrition or dietetics, you may have refened to this book some time or other.

With this basic understanding of the measurement of energy, let us move on to Human Energy studying the energy requirements. But before we move on to the requirements we Requirements must give a definition of what we understand by energy requirements and also know about the components of energy requirements. These are described next.

2.4 DEFINITION AND COMPONENTS OF ENERGY REQUIREMENT

We shall begin our study in this section first understanding what we mean by energy requirement. Energy requirement (ER) is defined as the amount of food energy needed to balance energy expenditure in order to maintain body size, body composition and a level of necessary and desirable physical activity, and also to allow optimal growth and development of children, deposition of tissues during pregnancy, and secretion of milk during lactation, consistent with long-term good health. For healthy, well-nourished adults, it is equivalent to total energy expenditure (TEE). There are additional energy needs to support growth in children and in women during pregnancy, and for milk production during lactation.

Total energy expenditure (TEE), may be defined as the energy spent, on average, in a 24-hour period by an individual or a group individuals. By delinition, it reflects the average amount of energy spent in a typical day, but it is not the exact amount of energy spent each and every day.

The energy needs vary widely among individuals in a group. You will find it impossible to compute an individuals energy need without knowing something

about the personal lifestyle and metabolism. Consider the following situations:

Situation 1: A 30 year old women who bikes, and swims each day, would require more energy than a 30 year old who does a desk job.

Situation 2: In a group of 20 odd people, with similar body weight and activity levels, some individuals may require more energy per day than others.

Why do you think the energy requirements are different in these situations?

Well the requirement is dependent on the ways in which the body spends energy. For example in the first case the intensity of work or voluntary activity i.e. intentional activities (such as cycling, swimming) conducted by voluntary muscles affects the amount of energy used, hence the variation in the requirement. On the other hand, think of all the involuntary activities of our body that are necessary to sustain life, including circulation, respiration, temperature maintenance, hormone secretion, nerve activity, new tissue synthesis etc. All these involuntary activities of the body, which continue day in and day out without our conscious awareness, require energy. Further, as the food is chewed, digested, absorbed, these metabolic response to food increases total energy expenditure. Therefore, the human beings need energy for the following:

- **Basal ntetabolism**. This comprises a series of functions that are essential for life, such as cell function and replacement; the synthesis, secretion and metabolism of enzymes and hormones to transport proteins and other substances and molecules; the maintenance of body temperature; uninterrupted work of cardiac and respiratory muscles; and brain function. The amount of energy used for basal metabolism in a period of time is called the basal metabolic rate (BMR). BMR is measured under standard conditions that include being awake in the supine position after 10 to 12 hours of fasting and eight hours of physical rest, and being in a state of mental relaxation in an ambient environmental temperature that does not elicit heat-generating or heat-dissipating processes, Depending on age and lifestyle, BMR represents 45 to 70 percent of the total daily energy expenditure, and it is determined mainly by the individual's age, gender, as well as, body size and body composition. We will learn more about these factors which influence the BMR in the next section

  BMR is commonly extrapolated to 24 h to be more meaningful, it is then refened to as Basal Energy Expenditure (BEE) and is expressed as Kilocalories per 24 hours. The basal metabolic rate, as defined originally by Boothby and Sandiford was measured in the morning upon awakening, before any physical activity and 12-18 h after a meal. A closely related tenn used now is Resting Metabolic Rate (RMR). RMR is measured with the subject in a supine or sitting position in a comfortable environment several hours after a meal and without any significant activity. RMR is slightly higher than BMR but the difference is small. RMR when extrapolated to 24 hours is the resting energv expenditure (REE).

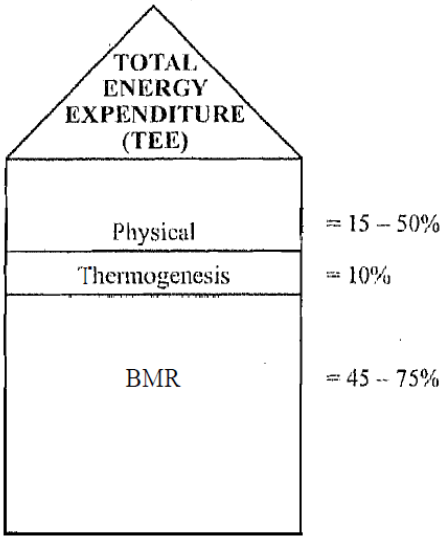
- **Metabolic response to food**. Eating requires energy for the ingestion and digestion of food, and for the absorption, transport, interconversion, oxidation and deposition of nutrients. These metabolic processes increase heal production and oxygen consumption, and are known by terms such as 'dietary-induced thermpgenesis', 'specific dynanzio action of food' and 'thermic effect of feeding' (TEF). The metabolic response to food increases total energy expenditure by about 10 percent of the BMR over a 24-hour petiod in individuals eating a mixed diet.
- **Physical activity**. This is the most variable and, after BMR, the second largest component of daily energy expenditure. Humans perform obligatory and discretionary physical activities. Obligatory activities can seldom be avoided within a given setting, and they are imposed on the individual by economic, cultural or societal demands. The term "occupational" was used earlier in the WHO/FAO[UNU 1985 report but the preferred term now is obligatory as it is more comprehensive. In addition to occupational work, obligatory activities include daily activities such as going to school, attending to the home and family and other demands made on children and adults by their economic, social and cultural environment. Discretionary activities, although not socially or economically essential, are important for health, well-being and a good quality of life in general. They include the regular practice of physical activity for fitness and health, the performance of optional household tasks that may contribute 10 family comfort and well-being; and the engagement in individually and socially desirable activities for personal enjoyment, social interaction and community development. We will dwell further on this aspect later in this unit; however, we need to look at two concepts in the context of physical activity namely physical activity level (PAL) and physical activity ratio (PAR), which find extensive use in calculating the total energy requirement of healthy, well-nourished adults. Physical activity level (PAL) is defined as the total energy required over 24 hours divided by the energy needed for basal metabolism over 24 hours. In simple terms, TEE for 24 hours expressed as a multiple of BMR, and calculated as TEE/BMR for 24 hours. In adult men and non-pregnant, non-lactating women, multplied by PAL is equal to TEE or the daily energy requirement.
- **Physical activity ratio (PAR)**: The energy cost of an activity per unit of time (usually a minute or an hour) expressed as a multiple of It is calculated as energy spent in an activity/BMR, for the selected time unit.
- Growth. The energy cost of growth has two components: l) the energy needed to synthesize growing tissues; and 2) the energy deposited in these tissues. The energy cost of growth is about 35 percent of total energy requirement during the first three months of age, falls rapidly to about 5 percent at 12 months and about 3 percent in the second year, remains at I to 2 percent until mid-adolescence, Pregnancy. During pregnancy, extra energy is needed for the growth of the foetus, placenta and various matemal tissues, such as in the uterus, breasts and Requirements fat stores, as well as, for changes in matemal metabolism and the increase in maternal effort at rest and during

physical activity.

- **Lactation**. The energy cost of lactation has two components: 1) the energy content of the milk secreted, and 2) the energy required to produce that milk. Well-nourished lactating women can derive part of this additional requirement from body fat stores accumulated during pregnancy.

From our discussion above, it is evident that the total energy expenditure over a 24- hour period is the sum of BMR, TEF, and energy for physical activities as also highlighted. in Figure 2.1. For adults, this is equivalent to daily energy requirements. Additional energy for deposition in growing tissues is needed to detemmine energy requirements in infancy, childhood, adolescence and during pregnancy, and for the production and secretion of milk during lactation. Energy balance is achieved when input (i.e. dietary energy intake) is equal to the output (i.e. total energy expenditure), plus the energy cost of growth in childhood and pregnancy, or the energy cost to produce milk during lactation.

When energy balance is maintained over a prolonged period, an individual is considered to be in a steady state.



Figwe 2.1: Componcnts of total energy expenditure

In the next section, we shall review the factors which influencer,thee nergy expenditure and requirements.

2.5 FACTORS AFFECTING ENERGY EXPENDITURE AND REQUIREMENT

As mentioned earlier, the energy needs veuy widely among individuals in a group. Why? A number of factors cause the RMR or more appropriately the REE to vary among individuals. Major determinants are the body size, composition, age, sex, growth etc. Similarly, there are factors affecting the thermic effect of food and

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energy expended in physical activity. A brief review on these factors follows.

2.5.1 Factors Affecting the BMR

Basal metabolic rate, we know, is the largest component of the daily energy demand representing 45 to 70 percent of daily total energy expenditure. It is highly variable and the causes of this variation include factors such as fat free mass (FFM),fat mass (FM), age, sex, hormonal status, growth, disease/infections etc. Let us learn about these factors starting with body size and composition. Body size and composition: Basal and resting energy expenditures are related to body size, being most closely correlated with the size of the fat-free mass (FFM), which is the weight of the body less the weight of its fat muss.

The size of the FFM generally explains about 70 to 80 percent of the variance in RMR' FFM is the metabolicaly active tissue in the body; what we also call as the lean body mass (LBM) and so most of the variation in BMR between people can be accounted for by the variation in their FFM. For example, athletes with greater muscular development have approximately a 5% higher basal metabolism than non-athletic individuals. Thus, exercise can help maintain a higher lean body mass and hence a higher metabolic rate. Similarly, the lower basal metabolic energy requirement of women is primarily related to their generally lower amount of lean muscle tnass (more of fat mass) as compared to men. The decline in BMR with increasing age is also to some extent the consequence of changes in the relative size of organs and tissues. Further larger people (big size) have higher metabolic rates than people of sinaller size. In fact, individuals with greater surface area have higher metabolic rate. To illustrate, if two people of different heights weigh the same, the taller individual with the larger body surface area will have a higher metabolic rate. In adults with higher percentages öf body fat composition, mechanical hindrances C"an also increase the energy expenditure associated with certain types of activity.

Age: The BMR per unit weight also varies with age, being higher in children and lower in the elderly. The loss of FFM with ageing is associated with a decline in the metabolic rate, amounting to about 1-2% decline per decade after early adulthood The REE is highest during the periods of rapid growth, chiefly during the first and second year of life, and reaches a lesser peak through the periods of puberty and adolescence in both sexes.

Gender: We have already emphasized earlier that sex difference in metabolic rates are primarily attributable to difference in body size and composition. Women who have generally more fat in propo tion to muscle than men, have metabolic rates which are 5-10% lower than men of the same weight and height. Thus, differences in BMR between genders are due to the greater level of body fatness in women.

Hormonal Status: Thyroid status may be most important factor and can make differences of up to plus or minus 50% for hyperthyroidism or hypothyroidism, respectively. Hyperthyroidism increases the resting metabolic rate, whereas hypothyroidism decreases the RMR. Stimulation of the sympathetic nervous

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system (e.g. during the period of stress or emotional excitement or fear, anxiety) causes the release of epinephrine, which directly promotes glycogenolysis and increases cellular activity. This too is associated with increased metabolic rate. In adult premenopausal women, the metabolic rate fluctuates with the menstrual cycle. An average of 359 Kcal/ day difference in the BMR has been measured between the low point, about I week before ovulation on day 14, and the high point, just before the onset of menstruation.

Environmental Conditions: Extremes in environmental temperatures also affect the metabolic rate. Energy expenditure will be increased if extra heat production is needed to maintain body temperature in a cold climate. The extent to which the energy metabolism increases in extremely cold environment depends on the insulation available from .body fat and protective clothing. Conversely, there is some evidence that the basal metabolic rate is reduced in hot climates, For example, BMK is on an average lower in Indians than in North Europeans. Further exercise undertaken in temperatures greater than 86^0F also imposes an additional metabolic load of about 5% from increased sweat gland activity.

Besides climatic conditions, altitude too has been shown to affect metabolic rates. oxygen in tissues) of high altitude increases BMR. Hypoxia increases Requirements glucose utilization, which might affect the Inetabolic rate. However, these are temporary effects, which disappear with acclimatization.

Pregnancy and Lactation: These periods of physiological stress also have an impact on the metabolic rate. Earlier, we studied that REE is highest during the periods of rapid growth, i.e. chiefly during the first and second year of life, In pregnancy too, which is the foetal growth period, the metabolic rate increases, particularly later in pregnancy because of uterine, placental and foetal growth and the mother's increased cardiac work load.

Fever/lllness/lnfections/lnjury: Any illness or fever caused by an illness influences the metabolic rate. Fevers increase the Inetabolic rate by about 7% for each degree increase in body temperature above 98.6^0F or in other words 13% for each degree above 37^OC.

During injury or infections there is an increased BMR, and this increase is dependent on the severity of the injury. For example, the BMR may even double with bums of more than 40% of the body sui-face, in severe sepsis, multiple traumas, whereas it may only increase by about 25% in patients with long bone fractures and even less after surgery. But we need to understand that in sick patients who are likely to be in bed, the increase in the BMR due to the stress imposed by the disease Inay be offset by the decrease in physical activity, such that the total daily energy expenditure may not change drastically.

Nutritional status: Undernutrition and starvation are the factors which require consideration. Prolonged undernutrition or starvation causes a reduction of about

10-20% in BMR. In semi-starvation studies, data suggest that the subjects BMR decrease by about 25% when expressed per kilogram of their free fat mass (FFM) (or metabolic active tissue). Reduction in BMR are partly mediated through weight loss itself, in which metabolically demanding tissue of the body (the FFM i.e. the lean body tissue) are reduced in size, and partly through reduction in the metabolic activity of these tissues. We will leai•n more about this aspect later in section 2.6 in this unit.

Other Factors: Smoking is one variable thought to influence the Inetabolic rate. Smoking increases BMR, cessation of smoking lowers BMR. The BMR in sleep is about 5% less than in the basal condition.

Thus, there is an exhaustive list of factors which influence BMR and hence the total energy requirements, under different conditions. Next, we shall move on to the study of the factors affecting the thermic effect of food.

2.5.2 Factors Affecting the Thermic Effect of Food

thermic effect of food, as we learnt earlier, is the increase in energy expenditure associated with the consumption of food and it accounts for approximately 10% of TEE (Total Energy Expenditure). The intensity and duration of meal induced TEF (Thermic effect of food) is, however, determinecl primarily by the amount and composition of the foods consumed. TEF, for example, is greater after consumption of carbohydrate and protein than after fat. The increments in energy expenditure during digestion above baseline rates, divided by the energy content of the food consumed, vary from 5 to 10 percent for carbohydrate, 0 to 5 percent for fat, and 20 to 30 percent för protein.

The high TEF for protein reflects the relatively high metabolic cost involved in processing the amino acids yielded by absorption of dietary protein, for protein synthesis, or for the synthesis of urea and glucose. Activation of the sympathetic nervous system elicited by dietary carbohydrate and by sensory stimulation causes an increase in energy expenditure. Consumption of the usual mixture of nutrients (i.e. a mixed diet) is generally considered to elicit increases in energy expenditure equivalent to 10 percent of the food's energy content. Spicy foods enhance and prolong the effect of TEF. Meals with chili and mustard may increase the metabolic rate as much as 33% more than unspiced meal, and this affect may last for more than 3 hours. Caffeine and nicotine also stimulate TEF.

Next, we shall review the factors influencing the energy expended on physical activity.

2.4.3 Factors Affecting the Energy Expended in Physical Activity

Physical activity as we learnt earlier, is the second largest component of daily energy expenditure, after BMR. However, the energy expended in physical

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activity is most variable as it may range from 10% in a person who is bedridden to as much as 50% of TEE in an athlete. In fact, different Ifestyles have different levels of energy demands. The examples of lifestyles with different levels of energy demands as given by FAO/WHO/UNU 2004 are enumerated herewith.

Sedentary or light activity lifestyles: These people have occupations that do not demand much physical effort, are not required to walk long distances, generally use motor vehicles for transportation, do not exercise or participate in sports regularly, and spend most of their leisure time sitting or standing, with little body displacement (e.g. talking, reading, watching television, listening to the radio, using computers). One example is male/female teachers, office workers (executives, clerks, typists etc.) in urban areas, who only occasionally engage in physically demanding activities during or outside working hours. Another example are housewives living in urban areas with access to energy saving devices and domestic help to carry out most of the manual chores and other moderate energy activities.

Active or moderately active lifestyles: These people have occupations that Are not strenuous in terms of energy demands, but involve more energy expenditure than that described for sedentary lifestyles. Alternatively, they can be people with sedentary occupations who regularly spend a certain amount of ctime in moderate to vigorous physical activities, during either the obligatory or the discretionary part of their daily routine. For example, the daily performance of one hour (either continuous or in several bouts during the day) of moderate to vigorous exercise, such as jogging/running, cycling, aerobic dancing or various sports activities. Other examples of moderately active lifestyles are associated with occupations such as servants, house cleaners, masons and construction workers, or mral women in less developed traditional villages who participate in agricultural chores or walk long distances to fetch water and fuel wood.

Vigorous or vigorously active lifestyles: These people engage regularly in strenuous work or in strenuous leisure activities for several hours. Examples are women with non-sedentary occupations who swim or dance an average of two hours each day, or non-mechanized agricultural labourers who work with a machete, hoe or axe for several hours daily and walk long distances over rugged telTains, often carrying heavy loads. Other examples of vigorously active occupations include rickshaw pullers, mine workers, coolies etc.

Now that we have classified the different lifestyles, it is important to note that the energy expended will vary not only with the different types of activity undertaken an individual (both occupational and discretionary physical activity), but also by time spent in each activity/task and the energy cost of arch activity t a theoretical 24-hour period. The classification of lifestyles in relation to the eaerey cost of each activity or the intensity of habitual physical activity, ot physical acitvity level (PAL) is given in Table 2.1. Physical activity level (PAL), we learff eo lier, is defined as the total energy required over 24 hours clivided the basal m.. KI! olic rate over 24

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hours. In adult men and non-pregnant, non-lactating women, BB IR times PAL is equal to TEE or the daily energy requirement.

Table 2.1: Classification of lifestyles in relation to the intensityof habitual physical activity, Human or PAL Requirements

Category	PAL value
Sedentary or light activity lifestyle	**1.40 - 1.69**
Active or moderately active lifestyle	1.70 - 1.99
Vigorous or vigorously active lifestyle	2.00 - 2.40*

You would realize that the energy expended in physical activity tends to decrease with age, a trend that as you may already be aware is associated with a decline in FFM and an increase in fat mass which influences the energy requirement.

In addition to the immediate energy cost of individual activities, physical activity also affects energy expenditure in the post-exercise period. Excess post-exercise oxygen consumption (EPOC) depends on exercise intensity and duration, as well as, other factors, such as environmental temperatures, state of hydration, and degree of trauma, demonstrable sometimes up to 24 hours after exercise. The increase in daily energy expenditure is somewhat greater, however, because exercise induces an additional small increase in expenditure for some tilne after the exertion itself has been completed. This excess post-exercise oxygen consumption (EPOC), as mentioned above, depends on exercise intensity and duration and has been estimated at some 15 percent of the increment in expenditure that occurs during exertions like walking/jogging.

There may also be chronic changes in energy expenditure associated with regular physical activity as a result of changes in body composition and alterations in the metabolic rate of muscle tissue, neuroendocrine status, and changes in spontaneous physical activity associated with altered levels of fitness. Habitual exercise does not cause a significant prolonged increase in metabolic sate per unit of active tissue, but it does cause an 8-14% higher metabolic rate in men who are moderately and highly active because of their increased fit free mass i.e. lean body tissue.

Since FFM is the major predictor of BMR and RMR, increases in FFM due to increased physical activity would be expected to increase BMR or RMR. The level of fitness also affects the energy expenditure of voluntary activity, probably because of variation in muscle mass.

To conclude, intensity, duration and frequency of the activity, the body mass of the person, efficiency at performing the æäviä.' and age influences the energy expended in physical activity.

Next, we shall move to a review the methods/means to calculate the energy expenditure and/or requirements. But before that let us recapitulate what we

have learnt so far .

2.6 METHODS OF ESTIMATION OF ENERGY EXPENDITURE AND REQUIREMENTS

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There are a variety of methods available to measure human energy expenditure. Knowledge of these methods will help us in calculating the expenditure either in the practical sessions or in the research setting. Some of these methods covered in this section include:

Direct calorimetry

Indirect calorimetry

Factorial estimation

The doubly labelled water (DLW) technique

Heart rate monitoring (HRM)

Let us get to know about these techniques.

2.6.1 Direct Calorimetry

Calorimetry refers to the measurement of the amount of heat evolved or absorbed in a chemical reaction, change of state, or formationof a solution. calorimetry is the method, which monitors the amount of heat produced by a subject placed inside a structure large enough to permit inoderate ainount of activity, These structures are referred to as whole room calorimeters.

This method provides a measure of energy expended in form of heat, but provides no information on the kind of fuel being Human oxidized. Further, this method is limited by the high cost and by the confined nature of the testing conditions i.e. the physical activity within the chamber is limited and therefore not representative of free-living environment.

Another method to be considered is the use of a respiration chamber or of a direct calorimeter. To obtain reliable data with either of these techniques involves an experimental set-up which is both expensive and technically complex. Relatively few of these chambers exist and their usefulness in the present context is restricted to specific basic problems which do not require a natural free-living environment.

2.6.2 Indirect Calorimetry

This method estimates energy expenditure by determining the oxygen consumption and carbon dioxide production of the body or a cell over a given period of time. Data so obtained from this method permits calculation of the respiratory quotient (RQ) which is expressed as:

$$RQ = \frac{\text{moles CO, expired}}{\text{moles O, consumed}}$$

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The RQ indicates the source of metabolic energy. It ranges from 1.0 (carbohydrate oxidation) to 0.7 (fat oxidation). On a mixed diet the RQ is about 0.85.

This determination is converted into kilocalories of heat produced per square meter of body surface area per hour and is extrapolated to energy expenditure in 24 hours.

2.6.3 Double Labeled Water (DLW) Technique

DLW is currently considered the most accurate technique for measuring TEE in free- living individuals. It is the method used to measure the average total energy expenditure of free-living individuals over several days (usually 10 to 14), based on the disappearance of a dose of water enriched with the stable isotopes 21-1 and 180. The use of the doubly labeled water (DLW) (2H,180) technique to calculate total production of carbon dioxide (CO,) over several day's and, from this, total energy expenditure was originally developed for use in stnall mammals and its application was later validated in humans. TEE measured by this method includes basal metabolism, the metabolic response to food, thermoregulatory needs, physical activity costs, and the energy cost to synthesize growing tissues. Consequently, energy requirements are calculated as the sum of TEE plus the energy deposited as protein and at in growing tissues and organs.

2.6.4 Heart Rate Monitoring (HRM) Method

HRM is a method to measure the daily energy expenditure of free-living individuals, based on the relationship of heart rate and oxygen consumption and on minute-by-minute monitoring of heart rate.

Extrapolating from heart rate to energy expenditure is a method which has been widely believed to be valuable and reasonably valid. The technique is fairly practicable, there are several instruments on the market which are not very expensive, and it is probably the method of choice in some population groups, such as young children, old people, and ill people. This is not the place to give a detailed critique of the methodology, other than to say that it must be used with circumspection and an awareness of the variable relationships of heart rate and energy expenditure.

Finally, let us learn about the factorial estimation of total energy expenditure which is most practical and provides a good indication of total requirements.

2.6.5 Factorial Estimation Total Energy Expenditure

The wide variations observed in the physical activity patterns of adults from different

geographic, social and economic groups combined with the variations observed in body size and composition of adults, do not allow the universal application of TEE measured by DLW technique, described above, to be used directly for estimating the energy requirements for adults. Therefore, the factorial estimate is used which combines the time allocated to different habitual activities and the energy cost of these activities expressed in multiples of BMR per unit of time, i.e. either per minute or per hour. Total energy expenditure can, therefore, be estimated by a factorial approach involving summation of all the expected components of energy expenditure, including BMR and taking into account the energy costs of different activities and their durations. Table 2.2 shows examples of these calculations.

To account for differences in body size and composition, the energy cost of activities is calculated as a multiple of BMR per minute also referred to as the physical activity ratio (PAR) (refer to Table 2.2), and the 24-hour energy requirements are expressed as a multiple of BMR per 24 hours by using the PAL value. Together with BMR of the population, PAL when known or when derived using BMR estimated from age and gender- specific predictive equations based on the average body weight of the population provides an estimate of TEE and hence the mean energy requirement Fcy that population.

It must be noted here that the factorial approach should be used only for adults. It should not be used in the case of infants and children.

Table 2.2: Factorial calculations Of total energy expenditure for a population group

Main Daily Activities	Time Allocation Hours	Energy Cost* PAR	Time x Energy Cost	Mean PAL" Multiple of 24-hour BMR
Sedentary or light activity lifestyle				
Sleeping	8	1	8.0	
Personal care (dressing, showering)	I	2.3	2.3	
Eating	1	1.5	1.5	
Cooking	1	2.1	2.1	
Silting (office work, selling produce, tending shop)	8	1.5	12.0	
General household work	1	2.8	2.8	
Driving car to/from work	1	2.0	2.0	
Walking at varying paces without a load	I	3.2	3.2	
Light leisure activities (watching TV, chatting)	2	1.4	2.8	
Total	**24**		36.7	36.7124 = 1.53
Active or **moderately** active lifestyle				
Sleeping	8	1	8.0	
Personal care (dressing, showering)	I	2.3	2.3	
Eating	I	1.5	1.5	
Standing, carrying light loads (waiting on tables, arranging merchandise)'	8	2.2	17.6	
Commuting to/from work on the bus	1	1.2	1.2	
Walking at varying paces without a load	1	3.2	3.2	
Low intensity aerobic exercise	I	4.2	4.2	
Light leisure activities (watching TV, chatting)	3	1.4	4.2	
Total	24		42.2	42.2124 = 1.76

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Vigorous or vigorously active lifestyle				
Sleeping	8	1	8.0	
Personal care (dressing, bathing)	1	2.3	2.3	
Eating	1	1.4	1.4	
Cooking	1	2.1	2.1	
Non-mechanized agricultural work (planting, weeding, gathering)	6	4.1	24.6	
Collecting water/wood	1	4.4	4.4	
Non-mechanized domestic chores (sweeping, washing clothes and dishes by hand)	1	2.3	2.3	
Walking at varying paces without a load	1	3.2	3.2	
Miscellaneous light leisure activities	4	1.4	5.6	
Total	24		53.9	53.9124 = 2.25

Energy costs of activities, expressed as multiples of basal metabolic rate, or PAR, are based cn data presented in Annexure I given at the end of the course.

PAL= physical activity level, cr energy requirement expressed as a multiple of 24-hour BMR,

Composite of the energy cost of standing, walking slowly and serving meals or canying a light load.

Let us understand this calculation with the help of an example. However, we shall first learn about the use of predictive equations to measure BMR.

We already know that BMR constitutes about 45 to 70 percent of TEE in adults, and is determined principally by gender, body size, body composition and age. It can be measured accurately with small intra-individual variation by direct or indirect calorimetry under standard conditions as described above..But, BMR can be measured only under laboratory conditions and in small groups of representative individuals by these methods. There is a need to estimate BMR at the population level when using the factorial approach to estimate TEE from the average BMR and PAL value attributable to that population. I-lence, the alternative has been to estimate a group's mean BMR using predictive equations based on measurements that are easier to obtain, such as body weight and/or height. The report from the 1985 FAO/WHO/UNU expert consultation used a set of equations proposed in 1985 by Schofield derived mostly from studies in Western Europe and North America. Table 2.3 present these equations.

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Table 2.3: Equations for estimating BMR from body weight*

Age *Years*	No.	BMR: MJ/day	see	BMR: Kcal/day	see
Males					
< 3	162	0.249 kg - 0.127	0.292	59.512 kg - 30.4	70
3 - 10	338	0.095 kg + 2.110	0.280	22.706 kg + 504.3	67
10 - 18	734	0.074 kg + 2.754	0.441	17.686 kg + 658.2	105
18 - 30	2879	0.063 kg + 2.896	0.641	15.057 kg + 692.2	153
30 - 60	646	0.048 kg + 3,653	0.700	11.472 kg + 873.1	167
> 60	50	0,049 kg + 2.459	0.686	11.711 kg + 587.7	164
Females					
< 3	137	0.244 kg - 0,130	0.246	58.317 kg - 31.1	59
3 - 10	413	0.085 kg + 2.033	0.292	20.315 kg + 485.9	70
10 - 18	575	0.056 kg + 2.898	0.466	13.384 kg + 692.6	111
18 - 30	829	0.062 kg + 2.036	0.497	14.818 kg + 486.6	119
30 - 60	372	0.034 kg + 3.538	0.465	8.126 kg + 845.6	111
> 60	38	0.038 kg + 2.755	0.451	9,082 kg + 658.5	108

We can use these equations to estimate from body weight. Multiplying the PAL by the BMR then gives the actual energy requirements. The PAL values as given in Table 2.1 for different lifestyles may be considered.

Now, let us understand the factorial calculation of total energy expenditure using the predictive equations to estimate BMR and using the PAL values with the help of an example.

Example: Manju is a female, 25 years of age, with a moderately active lifestyle and a mean body weight of 55 kg. Now let us calculate her energy requirements. Calculations:

- From the Table 2.3, BMR calculated from the predictive equation is: 5.45 MJ/ day (1302 Kcal/day) (i.e. 0.062 x 55 + 2.036 = 5.446 MJ/ 14.818 x 55 + 486.6 = 1301.59).

  PAL from mid-point of the moderately active lifestyle in Table 2.1 is 1.85. TEE or Energy requirement: 5.45 x 1.85 = 10.08 MJ/day (2409 Kcal/day), or 10.08/55 = 183 kJ/kg/day (44 Kcal/kg/day).

We hope that with this example you have understood the factorial estimation of total energy requirement. In this manner, with the help of the BMR predicitve equation and the PAL value you can calculate the total energy expenditure (TEE) which will be the energy requirement for the individual.

Few other examples specific to different lifestyles are presented next, to help you understand the concept better.

Examples:

Sedentary or light activity: If this PAL was from a female population, 30 to 50

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years old, with mean weight of 55 kg and mean BMR of 5.40 MJ/day (1290 Kcal/ day), TEE = 1.53 x 5.40 = 8.26 W (1975 Kcal), or 150 kJ (36 Kcal)/kg/d.

Active or moderately active: If this PAL was from a female population, 20 to 25 years old, with mean weight of 57 kg and mean of 5.60 MJ/day (1338 Kcal/ day), TEE = 1.76 x 5.60 = 9.86 MJ (2355 Kcal or 173 kJ (41 Kcal)/kg/d.

Vigorous or vigorously active: If this PAL was from a male population, 20 to 25 years old, with mean weight of 70 kg and mean BMR of 7.30 MJ/day (1745 Kcal/ day), TEE = 2.25 x 7.30 = 16.42 MJ (3925 Kcal), or 235 kJ (56 Kcal)/kg/d.

Next, let us study about the energy requirements for different age groups.

2.7 ENERGY REQUIREMENTS AND DIETARY ENERGY RECOMMENDATIONS

Energy requirement, as you may recall studying earlier, is the amount of food energy needed to balance energy expenditure in order to maintain body size, body composition and a level of necessary and desirable physical activity consistent with long-terni good health. This includes the energy needed for the optimal growth and development of children, for the deposition of tissues during pregnancy, and for the secretion of milk during lactation consistent with the good health of mother and child. The recommended level (f dietary energy intake for a population group is the mean energy requirement of the healthy, well-nourished individuals who constitute that group.

Energy requirements and recommended levels of intake are often referred to asdaily requirements or recommended daily intakes. These terms are used as. matter of convention and convenience, indicating that the requirement represents an average of energy needs over a certain number of days, and that the recommended energy intake is the amount of energy that should be ingested as a daily average over a certain period of time.There is no implication that this amount of energy must be consumed every day or that the requirement and the recommended intake remain constant day after day. A convenient time frame of one week has been often used in practice for defining the number of days over which the requirement and the recommended energy intake may be averaged, although there is no biological basis for this or any other time frame. Considering that habitual physical activities may vary on some days of the week a seven day period appears reasonable for averaging the requirement and the tecommended intakes.

Remember, estimates of energy requirements are derived from measurements of individuals. Measurements of a collection of individuals of the same gender and similar age, body size and physical activity are grouped together to give the average energy requirement — or recommended level of dietary intake — for a class of people or a population group.

The energy needs for Indian population has been computed on the basis of recommendations made by a Joint Expert Consultation of the World Health Organization (WHO)[Food and Agricultural Organization (FAO)/United Nations University (UNU) in 1985 and by an Expert Committee constituted in 1988 by the Indian Council of Medical Research (ICMR) as already informed earlier in the introduction section. However, recently the Joint FAO/WHO/UNU Expert Consultation on Human Energy Requirements, convened in October 2001 at FAO headquarters in Rome, Italy has formulated recommendations for human energy requirements published in 2004. The ICMR is in the process of now updating the earlier recommendations. Till such time the new recommendations are published the old recommendations ate being followed in our country. A brief review on these recommendations along with the new FAO/ WHO/UNU 2004 recommendations for human energy requirements through out the life cycle is presented herewith.

2.7.1 Energy Requirements of Infants (from Birth to 12 Months)

Energy requirements during infancy are very high because this is one of the periods of very rapid growth. Energy requirement for infants and children of all age group are based on the principle of calculating energy requirements from total energy expenditure (TEE) plus the energy needs for growth. Energy needs for growth have two components: l) the energy used to synthesize growing tissues, which is pmt of the total energy expenditure, and 2) the energy deposited in those tissues, basically as fat and protein, because carbohydrate content is insignificant. This has to be taken into account along with the basal energy needs and energy needs for activity in infants and children.

Available data suggest that energy needs are highest during the first three months and then fall over the next six months when the growth rates are lower. It rises again after nine months as the child becomes physically more active. The RDA for infants drawn by ICMR, as given in Table 2.4 takes this phenomenon inta account. The requirements are categorized into two groups: 0-6 months and 6-12 months, and are calculated as energy units per kilogram of body weight.

Tsble 2.4: RDA for infants and children

	Energy per kg Body Weight	Net Energy (Kcal/d)	Body Weight (kg)
< 6 months	108/kg	583	5.4
6 - 12 months	98/kg	844	8.6

Breastmilk is the best food for infants, and exclusive breastfeeding is strongly recommended during the first six months of life which is sufficient to meet the energy requirements. Thereafter, a combination of breastmilk and complementary foods throughout infancy is recommended to meet the requirements. We will learn more about the requirements and how to meet these requirements later in Unit 14.

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Table 2.5 presents the FAO/WHO/UNU 2004 recommended average energy requirements of infants from one to 12 months of age, combining the needs of breastfed and formula-fed infants. TEE is calculated with the predictive linear equations described later in this section. The sum of TEE and energy deposition is the mean daily energy requirement (in MJ or Kcal). It is calculated as energy units per kilogram of body weight, dividing the daily requirement by the median weight at each month of age.

The TEE is lower among breastfed than formula-fed infants during the first year of life; hence the energy requirements of breastfed infants are also lower, as you may have noticed in Table 2.5.

Table 2.5: Energy requirement of breastfed, formula-fed and all infants

Age	Breast-fed			Formula-fed			All breast&formula-fed		
Months	Boys	Girls	Mean	Boys	Girls	Mean	Boys	Girls	Mean
MJ/kg/d									
1	445	415	430	510	490	500	475	445	400
2	410	395	405	400	455	460	435	420	430
3	380	375	380	420	420	420	395	395	395
4	330	335	330	360	370	365	345	350	345
5	330	330	330	355	365	360	340	345	345
6	325	330	330	350	355	355	335	340	340
7	320	315	320	340	340	340	330	330	330
8	320	320	320	340	340	340	330	330	330
9	325	320	320	340	340	340	330	330	330
10	330	325	325	340	340	340	335	330	335
11	330	325	325	340	340	340	335	330	335
12	330	325	330	345	340	340	335	330	335
Kcal/kg/d									
1	106	99	102	122	117	120	113	107	110
2	98	95	97	110	108	109	104	101	102
3	91	90	90	100	101	100	95	94	95
4	79	80	79	86	89	87	82	84	83
5	79	79	79	85	87	86	81	82	82
6	78	79	78	83	85	84	81	81	81
7	76	76	76	81	81	81	79	78	79
8	77	76	76	81	81	81	81	79	78
9	77	76	77	81	81	81	79	78	79
10	79	77	78	82	81	81	80	79	80
11	79	77	78	82	81	81	80	79	80
12	79	77	78	82	81	81	81	79	80

Compared with the values in the FAO[WHO/UNU 1985 report, energy requirements proposed by FAO/WHO/UNU 2004 consultation are about 12 percent lower in the first three months of life, 17 percent lower from three to nine months, and 20 percent lower from nine to 12 months. The requirements for breastfed infants are 17, 20 and 22 percent lower than the 1985 estimates at ages 0 to three, three to nine and nine to 12 months, respectively.

The equations to predict TEE from body weight of infants are as follows:

Breast-fed:

TEE **(MJ/day)** = – 0.635 + 0.388 kg

TEE (Kcallday) = – 152.0 + 92.8 kg

Formula-fed:

TEE **(MJ/day)** = – 0.122 + 0.346 kg

TEE (Kcallday) = – 29.0 + 82.6 kg

Breast and formula-fed:

TEE **(MJ/kg/day)** = – 0.416 + 0.371 kg

In populations around the world, and particularly in India, we have large numbers of newborns with intrauterine growth retardation, and malnourished children less than one year of age. In addition to proper health, social and emotional support, these infants require special nutritional care for a rapid, catch-up growth that will allow them to attain the expected weight and height of normal children born with adequate size at tenn, and who have never been malnourished.

Therefore, diets for catch-up growth must provide all nutrients and energy sourcesin amounts that are proportionally higher than those required by well-nourished infants of adequate size. However it is difficult to generalize the quantitative energy requirements for catch up growth and it is best done on individual basis. Some tentative estimates as proposed by the FAO/ WHO/UNU expert Consultation of 2001 are given in Table 2.6.

Table 2.6: Increase in energy requirements needed to allow for twice the normal growth rate of children six to 24 months old*

Age (Months)	Average Weight Gain	% Increase Over Energy Requirement
6 - 9	1.83	14.5
9 - 12	1.15	8.5
12 - 18	0.67	5
18 - 24	0.5 1	3.5

It was assumed that the lequilements for normal growth wae 1,5 fimes the theol?tical estimates based on weight gain.

Source: Adapted WHO, 1985.

Next, let us learn about the requirements of older children and adolescents.

2.7.2 Energy Requirement for Children and Adolescent

The preschool years represent the age from approximately 1 to 6 years. Marked variability exists between requirements during the preschool years because of variation in growth and physical activity. Energy needs for growth have two components: 1) the energy used to synthesize growing tissues; and 2) the energy deposited in those tissues, basically as fat and protein, because carbohydrate contentis negligible. Dietary energy recommendations also include recommendations for physical activity compatible with maintenance of health and optimal growth and maturation. The WHO/FAO/ UNU and the ICMR Expert Committee took note of the fact that Indian children are smaller at birth, infancy, childhood and adolescence but suggested that it is desirable that the growth potential of children should be fully expressed and that the estimates of energy and protein requirement should allow for this. However, as the normal Indian children are smaller and they weigh less, the actual energy requirements may be substantially lower. The dietary intakes thus recommended by ICMR for Indian childlen are presented in Table 2.7. You would have noticed that the energy needs for preschoolers is given in two categories: 1-3 years and 4-6 years.

Table 2.7: Energy requirement for Indian children and adolescent

Group	Particulars	Body Weight (kg)	Net Energy (Kcal/d)
Children	1-3 years	12.2	1240
	4-6 years	19.0	1690
	7-9 Years	26.9	1650
Adolescent			
Boys	10-12 years	35.4	2190
Girls	10-12 years	31.5	1970
Boys	13-15 years	47.8	2450
Girls	13-15 years	46.7	2060
Boys	16-18 years	57.1	2640
Girls	16-18 years	49.9	2060

Source: ICMR, 1988.

Marked variability exists 'for boys and girls in the energy requirements after 9 years of age because of variations in growth rate and physical activity levels. Marked gender differences in intensity and duration of the adolescent growth spurt in fat free mass (FFM) dictates higher energy needs in boys than girls. Hence energy requirements are specified separately for boys and girls after the age of 9 years as you can see in Table 2.7

The energy requirements for adolescents are based on estimates of energy expenditure and requirements for growth based on tissue deposition. Dietary

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energy recommendations also include recommendations for physical activity compatible with health, prevention of obesity, and appropriate social and psychological development. In adolescents, growth is relatively slow except around the adolescent growth spurt, which varies considerably in timing and magnitude among individuals between 10 and 19 years. Adolescents gain 30 percent of their adult weight and more than 20 percent of their adult height between 10 and 19 years. Taking into account, the desirability of achieving full potential for growth, ICMR has used NCHS/well-to-do Indian children's body weight for computing RDA for adolescents as given in Table 2.7.

However, children from the poorer segments of the population in India are shorter and weigh less. It is unlikely that any extra food at this stage can accelerate or extend the duration of physical growth. Additional dietary intake at this period can only lead to adolescent obesity. The new ICMR Expert Committee for RDA, which is already working on revising the requirements for Indians, may have to take all these into account and evolve appropriate recommendations for dietary intake in Indian adolescents.

Occupational and recreational activities variably affect energy requirements. The WHO/FAO/UNU 2004 recommendations, have taken this into consideration and energy requirements are calculated for children over five years of age and for adolescents with lifestyles involving three levels of habitual physical activity as enumerated herewith:

Examples of populations with light physical lifestyles, or that are less active than Human Enerw Requirements average, are children and adolescents who every day spend several hours at school or in sedentary occupations; do not practice physical sports regularly; generally use motor vehicles for transportation; and spend most leisure time in activities that require little physical effort, such as watching television, reading, using computers or playing without much body displacement.

Examples of populations with vigorous lifestyles, or that are more active than average, are children and adolescents who walk long distances every day or use bicycles for transportation; engage in high energy-demanding occupations, or perform high energy-demanding chores for several hours each day; and/or practise sports or exercise that demand a high level of physical effort for several hours, several days of the week.

Children and adolescents with habitual physical activity that is more strenuous than the examples given for a light lifestyle, but not as demanding as the examples for vigorous lifestyle, would qualify in the category of average or moderate physically active lifestyles.

Table 2.8 and 2.9 presents the energy requirements for boys and girls (WHO/FAO/UNU 2004) in populations with these three levels of habitual physical activity.

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Table 2.8: Boys energy requirements in populations with three levds of habitual physical activity

Age Years	Weight Kg	Light Phycial Acfivity Daily Energy Requirement				PAL	Moderate Physical Activity Daily Energy Requirement				PAL	Heavy Physical Activity Daily Energy Requirement				PAL
		MJ/d	Kcal/d	K.J/kg/d	Kcal/kg/d		MJW	Kcal/d	K.J/kg/d	Kcal/kg/d		MJ/d	Kcal/d	K.J/kg/d	Kcal/kg/d	
1-2	11.5						4.0	950	345	82	1.45					
2-3	13.5						4.7	1125	350	84	1.45					
3-4	15.7						5.2	1250	335	80	1.45					
4-5	17.7						5.7	1350	320	77	1.50					
5-6	19.7						6.1	1475	310	74	1.55					
6-7	21.7	5.6	1350	260	62	1.30	6.6	1575	305	73	1.55	7.6	1800	350	84	1.80
7-8	24.0	6.0	1450	250	60	1.35	7.1	1700	295	71	1.60	8.2	1950	340	81	1.85
8-9	26.7	6.5	1550	245	59	1.40	7.7	1825	285	69	1.65	8.8	2100	330	79	1.90
9-10	29.7	7.0	1675	235	56	3.40	8.3	1975	280	67	1.65	9.5	2275	320	76	1.90
10-11	33.3	7.7	1825	230	55	1.45	9.0	2150	270	65	1.70	10.4	2475	310	74	1.95
11-12	37.5	8.3	2000	220	53	1.50	9.8	2350	260	62	1.75	11.3	2700	300	72	2.00
12-13	42.3	9.1	2175	215	51	1.55	10.7	2550	250	60	1.80	12.3	2925	290	69	2.05
13-14	47.8	9.8	2350	205	49	1.55	11.6	2775	240	58	1.80	13.3	3175	275	66	2.05
14-15	53.8	10.6	2550	200	48	1.60	12.5	3000	235	56	1.85	14.4	3450	270	65	2.15
15-16	59.5	11.3	2700	190	45	1.60	13.3	3175	225	53	1.85	15.3	3650	260	62	2.15
16-17	64.4	11.8	2825	185	44	1.55	13.9	3325	215	52	1.85	16.0	3825	245	59	2.15
17-18	67.8	12.1	2900	180	43	1.55	14.3	3400	210	50	1.85	16.4	3925	240	57	2.15

Table 2.9 : Girls energy requirement in populations with three levels of habitual physical activity

Age Yenrs	Weight Kg	Light Physical Activity Daily Energy Requirement				PAL	Moderate Physical Activity Daily Energy Requirement				PAL	Heavy Physical Activity Daily Energy Requirement				PAL
		MJ/d	Kcal/d	K.J/kg/d	Kcal/kg/d		MJ/d	Kcal/d	K.J/kg/d	Kcal/kg/d		MJ/d	Kcal/d	K.J/kg/d	Kcal/kg/d	
1-2	10.8						3.6	850	335	80	1.40					
2-3	13.0						4.4	1050	335	81	1.40					
3-4	15.1						4.8	1150	320	77	1.45					
4-5	16.8						5.2	1250	310	74	1.50					
5-6	18.6						5.6	1325	300	72	1.55					
6-7	20.6	5.1	1225	245	59	1.30	6.0	1425	290	69	1.55	6.9	1650	335	80	1.80
7-8	23.3	5.5	1325	235	57	1.35	6.5	1550	280	67	1.60	7.5	1775	320	77	1.85
8-9	26.6	6.0	1450	225	54	1.40	7.1	1700	265	64	1.65	8.2	1950	305	73	1.90
9-10	30.5	6.6	1575	215	52	1.40	7.7	1850	255	61	1.65	8.9	2125	295	70	1.90
10-11	34.7	7.1	1700	205	49	1.45	8.4	2000	240	58	1.70	9.6	2300	275	66	1.95
11-12	39.2	7.6	1825	195	47	1.50	9.0	2150	230	55	1.75	10.3	2475	265	63	2.00
12-13	43.8	8.1	1925	185	44	1.50	9.5	2275	215	52	1.75	11.0	2625	245	60	2.00
13-14	46.3	8.5	2025	175	42	1.50	10.0	2375	205	49	1.75	11.4	2725	235	57	2.00
14-15	52.1	8.7	2075	165	40	1.50	10.2	2450	195	47	1.75	11.8	2825	225	54	2.00
15-16	55.0	8.9	2125	160	39	1.50	10.4	2500	190	45	1.75	12.0	2875	220	52	2.00
16-17	56.4	8.9	2125	160	38	1.50	10.5	2500	185	44	1.75	12.0	2875	215	51	2.00
17-18	56.7	8.9	2125	155	37	1.45	10.5	2500	185	44	1.70	12.0	2875	215	51	1.95

Note:

Body weight at mid-point of age interval (WHO, 1983).
Moderate physical activity, MJ/d = (1.102 + 0,273 kg – 0.0019 kg^2) + 8.6 KJ/g daily weight gain.
Vigorous physical activity: 15%> moderate physical activity.
Number rounded to the doses 0.1 MJ/d, 25 Kcal/d, 5KJ/kg/d, 1 Kcal/MJ/d, 0.05 PAL unit
Light physical activity: 15% < moderate physical activity.
PAL = TEE/(Predicted BMR/d).

Compared with previous estimates (WHO/FAO/UNU 1985), energy requirements thus proposed by this consultation are on average 18 percent lower for boys and 20 percent lower for girls under seven years of age, and 12 and 5 percent lower, respectively, for boys and girls seven to ten years of age. From 12 years onwards, the proposed requirements are an average of 12 percent higher for both boys and girls.

Next, we move on to the energy requirement for the adults.

2.7.3 Energy Requirement of Adults

The energy needs of Indian men and women for different activity levels computed on the basis of recömmendations made by ICMR are shown in Table 2.10.

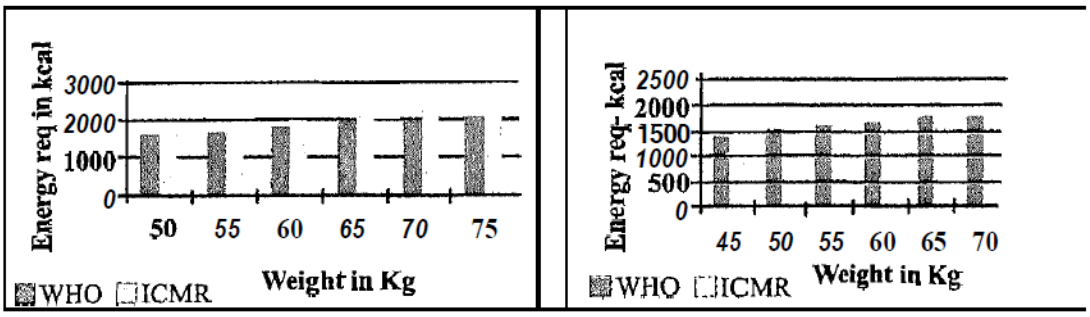
For computing RDA, the ICMR has taken body weight of 'reference man' as 60 kg and that of woman' as 50 kg. Average weight of Indian men, however, is 52 kg and women 44 kg. In view of these, it is likely that the energy requirement of Indians is likely to be substantially lower (about 10-12% lower) than the current ICMR recommendations as highlighted in Table 2.10. The present ICMR recommendations are therefore likely to be revised.

Table 2.10: ICMR's RDA for energy (reference body weight and actual body weight)

Sex	Ref.Body Weight	Actual Body Weight	Energy RDA			
			Acitivity Category	For Ref. Body Weight	For Actual Body Weight	Percent Difference
Man	60.0	52.0	Sedentary	2425	2115	13
			Moderate	2875	2492	13
			Heavy	3800	3293	13
Woman	50.0	44.0	Sedentary	1875	1740	12
			Moderate	2225	1958	12
			Heavy	2925	2594	11

Source: Dr. B.S. Nar inga Rao-Gopalan Oration 2001.

With increasing age, there are metabolic changes and also reduction in physical activity and, as a result, the energy requirement of older adults and elderly is substantially lower than younger adults as highlighted in Figure 2.2(a) and 2.2(b).



(a): Daily average energy requirement of sedentary males > 60 years.

(b): Daily average energy requirement of sedentary females >60 Years

Figure 2.2: Daily average energy requirement of sedentary adults

Source: 10th Five Year Plan (2002-2007), Planning Commission, Govemment (f India. The previous expert consultation (WHO/FAO/UNU, 1985) classified the PAL of adult population groups as light, moderate or heavy, depending on their occupational or other work, and multiplied it by the corresponding BMR to an-ive at requirements. The recent FAO/WHO/UNU 2004 report considered that the 24-hour PAL should not be based only on the physical effort demanded by occupational work, as there are people with light occupations who perform vigorous physical activity in their spare time, and people with heavy work who are quite sedentary the rest of the day. Therefore new recommendations base the factorial estimates of energy requirements on the energy expenditure associated with lifestyles that combine occupational and discretionary physical activities.

Multiplying the PAL value by the BMR gives the actual energy requirements. Table 2.11, 2.12, 2.13 and 2.14 gives the energy requirement as recommended by FAO/WHO[UNU 2004 report for men and women aged 18 to 29.9 years and 30 to 59.5 years, respectively. The consultation also suggested that the average energy cost of activities expressed as a multiple of BMR, or PAR, should be similar for men and women, Further, the report suggests that the energy requirements for older adults and the elderly should be calculated on the basis of PALs, just as they are calculated for younger adults. Allowances must be made for population groups who are more or less active at an advanced age, rather than using age as the single cut-off point to define energy requirements for the elderly. Table 2.15 and 2.16 presents the recommendations for elderly male and female, respectively over 60 years,

The practice of regular physical activity is associated with the maintenance of adequate body weight, cardiovascular and respiratory health, and fitness and a lower risk of developing chronic non communicable diseases associated with diet and lifestyle. Consequently, dietary energy recommendations to satisfy requirements should be accompanied by recommendations to perform adequate amounts of physical activity regularly has been strongly advocated by the WHO/ FAO/UNU 2004 recommendation.

Table 2.11: Daily average energy requirement for men aged 18 to 29.9 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																				Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90 ×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
50	121	29	8.8	175	2100	42	9.7	195	2300	46	10.6	210	2 550	51	11.5	230	2750	55	12.4	250	2950	59	13.3	265	3200	64	1.42	1.54	1.64
55	116	28	9.2	170	2200	40	10.2	185	2450	44	11.1	200	2650	48	12.1	220	2900	53	13.0	235	3100	57	14.0	255	3350	61	1.49	1.62	1.72
60	111	27	9.7	160	2300	39	10.7	180	2550	43	11.7	195	2800	47	12.7	210	3050	51	13.7	230	3250	55	14.7	245	3500	59	1.55	1.69	1:80
65	108	26	10.1	155	2400	37	11.2	170	2650	41	12.2	190	2900	45	13.3	205	3150	49	14.3	220	3450	53	15.4	235	3700	57	1.62	1.76	1.87
70	104	25	10.6	150	2550	36	11.7	165	2800	40	12.8	185	3050	44	13.9	200	3300	47	15.0	215	3600	51	16.1	230	3850	55	1.68	1.83	1.95
75	102	24	11.1	145	2650	35	12.2	165	2900	39	13.3	180	3200	42	14.5	195	3450	46	15.6	210	3750	50	16.8	225	4000	53	1.74	1.89	2.01
80	99	24	11.5	145	2750	34	12.7	160	3050	38	13.9	175	3300	41	15.1	190	3600	45	16.3	205	3900	49	17.5	220	4150	52	1.79	1.95	2.08
85	97	23	12.0	140	2850	34	13.2	155	3150	37	14.4	170	3450	41	15.7	185	3750	44	16.9	200	4050	48	18.2	215	4350	51	1.85	2.01	2.14
90	95	23	12.4	140	2950	33	13.7	150	3300	36	15.0	165	3600	40	16.3	180	3900	43	17.6	195	4200	47	18.8	210	4500	50	1.90	2.07	2.21

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 11.7 MJ(2800 Kcal)/day or 195 KJ(47Kcal)/kg/day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 11.1 to 12.8 MJ(2650 to 3050 Kcal)/day or 185 to 200 KJ(44 to 48 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

NOTES

Table 2.12: Daily average energy requirement for men aged 30 to 59.9 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																						Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90 ×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
50	121	29	8.8	175	2100	42	9.7	195	2300	46	10.6	210	2550	51	11.5	230	2750	55	12.4	250	2950	59	13.3	265	3200	64	1.42	1.54	1.64
55	114	27	9.1	165	2200	40	10.1	185	2400	44	11.0	200	2650	48	12.0	215	2850	52	12.9	235	3100	56	13.8	250	3300	60	1.49	1.62	1.72
60	109	26	9.5	160	2250	38	10.5	175	2500	42	11.4	190	2750	46	12.4	205	2950	49	13.4	225	3200	53	14.4	240	3450	57	1.55	1.69	1.80
65	104	25	9.8	150	2350	36	10.8	165	2600	40	11.9	180	2850	44	12.9	200	3100	47	13.9	215	3300	51	14.9	230	3550	55	1.62	1.76	1.87
70	100	24	10.2	145	2450	35	11.2	160	2700	38	12.3	175	2950	42	13.3	190	3200	45	14.4	205	3450	49	15.4	220	3700	53	1.68	1.83	1.95
75	97	23	10.5	140	2500	34	11.6	155	2750	37	12.7	170	3050	40	13.8	185	3300	44	14.9	200	3550	47	16.0	215	3800	51	1.74	1.89	2.01
80	94	22	10.9	135	2600	32	12.0	150	2850	36	13.1	165	3150	39	14.2	180	3400	43	15.4	190	3650	46	16.5	205	3950	49	1.79	1.95	2.08
85	91	22	11.2	130	2700	32	12.4	145	2950	35	13.5	160	3250	38	14.7	175	3500	41	15.9	185	3800	45	17.0	200	4050	48	1.85	2.01	2.14
90	89	21	11.6	130	2750	31	12.8	140	3050	34	14.0	155	3350	37	15.1	170	3600	40	16.3	180	3900	43	17.5	195	4200	47	1.90	2.07	2.21

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 11.4 MJ(2750 Kcal)/day or 190 KJ(46Kcal)/kg/day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 11.0 to 12.3 MJ(2650 to 2950 Kcal)/day or 175 to 200 KJ(42 to 48 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

Table 2.13: Daily average energy requirement for women aged 18 to 29.9 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																				Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90 ×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
45	107	26	7.0	155	1650	37	7.7	170	1850	41	8.4	190	2000	44	9.2	205	2200	49	9.9	220	2350	52	10.6	235	2550	57	1.34	1.46	1.56
50	103	25	7.4	150	1800	36	8.2	165	1950	39	9.0	180	2150	43	9.8	195	2350	47	10.5	210	2500	50	11.3	225	2700	54	1.42	1.54	1.64
55	99	24	7.9	145	1900	35	8.7	160	2100	38	9.5	175	2300	42	10.3	190	2450	45	11.2	205	2650	48	12.0	220	2850	52	1.49	1.62	1.72
60	96	23	8.3	140	2000	33	9.2	155	2200	37	10.1	170	2400	40	10.9	180	2600	43	11.8	195	2800	47	12.7	210	3050	51	1.55	1.69	1.80
65	93	22	8.8	135	2100	32	9.7	150	2300	35	10.6	165	2550	39	11.5	175	2750	42	12.4	190	2950	45	13.3	205	3200	49	1.62	1.76	1.87
70	91	22	9.2	130	2200	31	10.2	145	2450	35	11.2	160	2650	38	12.1	175	2900	41	13.1	185	3100	44	14.0	200	3350	48	1.68	1.83	1.95
75	89	21	9.7	130	2300	31	10.7	145	2550	34	11.7	155	2800	37	12.7	170	3050	41	13.7	185	3300	44	14.7	195	3500	47	1.74	1.89	2.01
80	87	21	10.1	125	2400	30	11.2	140	2700	34	12.2	155	2950	37	13.3	165	3200	40	14.3	180	3450	43	15.4	190	3700	46	1.79	1.95	2.08
85	86	21	10.6	125	2550	30	11.7	140	2800	33	12.8	150	3050	36	13.9	165	3300	39	15.0	175	3600	42	16.1	190	3850	45	1.85	2.01	2.14

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 10.1 MJ(2400 Kcal)/day or 170 KJ(40Kcal)/kg/day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 9.5 to 11.2 MJ(2300 to 2650 Kcal)/day or 160 to 175 KJ(38 to 42 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

NOTES

Table 2.14: Daily average energy requirement for women aged 30 to 59.9 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																				Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90 ×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
45	113	27	7.3	165	1750	39	8.1	180	1950	43	8.9	195	2100	47	9.6	215	2300	51	10.4	230	2500	56	11.1	250	2650	59	1.34	1.46	1.56
50	105	25	7.6	150	1800	36	8.4	170	2000	40	9.2	185	2200	44	10.0	200	2400	48	10.7	215	2550	51	11.5	230	2750	55	1.42	1.54	1.64
55	98	24	7.8	145	1850	34	8.7	155	2050	37	9.5	170	2250	41	10.3	185	2450	45	11.1	200	2650	48	11.9	215	2850	52	1.49	1.62	1.72
60	93	22	8.1	135	1950	33	8.9	150	2150	36	9.8	165	2350	39	10.6	175	2550	43	11.4	190	2750	46	12.3	205	2950	49	1.55	1.69	1.80
65	88	21	8.3	130	2000	31	9.2	140	2200	34	10.1	155	2400	37	10.9	170	2600	40	11.8	180	2800	43	12.6	295	3000	46	1.62	1.76	1.87
70	85	20	8.6	125	2050	29	9.5	135	2250	32	10.4	150	2500	36	11.2	160	2700	39	12.1	175	2900	41	13.0	185	3100	44	1.68	1.83	1.95
75	81	19	8.8	120	2100	28	9.7	130	2350	31	10.7	140	2550	34	11.6	155	2750	37	12.5	165	3000	40	13.4	180	3200	43	1.74	1.89	2.01
80	78	19	9.1	115	2150	27	10.0	125	2400	30	11.0	135	2600	33	11.9	150	2850	36	12.8	160	3050	38	13.8	170	3300	41	1.79	1.95	2.08
85	76	18	9.3	110	2250	26	10.3	120	2450	29	11.2	130	2700	32	12.2	145	2900	34	13.2	155	3150	37	14.1	165	3400	40	1.85	2.01	2.14

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 9.8 MJ(2350 Kcal)/day or 165 KJ(39 Kcal)/kg/day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 9.5 to 10.4 MJ(2250 to 2500 Kcal)/day or 150 to 170 KJ(36 to 41 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

Table 2.15: Daily average energy requirement for men aged > 60 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																						Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
50	98	23	7.1	140	1700	34	7.9	155	1900	38	8.6	170	2050	41	9.3	185	2250	45	10.1	200	2400	48	10.8	215	2600	52	1.42	1.54	1.64
55	94	22	7.5	135	1800	33	8.2	150	1950	35	9.0	165	2150	39	9.8	180	2350	43	10.6	190	2550	46	11.3	205	2700	49	1.49	1.62	1.72
60	90	22	7.8	130	1850	31	8.6	145	2050	34	9.4	155	2250	38	10.3	170	2450	41	11.1	185	2650	44	11.9	200	2850	48	1.55	1.69	1.80
65	87	21	8.2	125	1950	30	9.0	140	2150	36	9.9	150	2350	36	10.7	165	2550	39	11.6	180	2750	42	12.4	190	2950	45	1.62	1.76	1.87
70	84	20	8.5	120	2050	29	9.4	135	2250	32	10.3	145	2450	35	11.2	160	2650	38	12.1	170	2900	41	13.0	185	3100	44	1.68	1.83	1.95
75	82	20	8.9	120	2150	29	9.8	130	2350	31	10.7	145	2550	34	11.7	155	2800	37	12.6	170	3000	40	13.5	180	3250	43	1.74	1.89	2.01
80	80	19	9.2	115	2200	28	10.2	130	2450	31	11.2	140	2650	33	12.1	150	2900	36	13.1	165	3150	39	14.0	175	3350	42	1.79	1.95	2.08
85	78	19	9.6	115	2300	27	10.6	125	2550	30	11.6	135	2750	32	12.6	150	3000	35	13.6	160	3250	38	14.6	170	3500	41	1.85	2.01	2.14
90	76	18	10.0	110	2400	27	11.0	120	2650	29	12.0	135	2850	32	13.1	145	3100	34	14.1	155	3350	37	15.1	170	3600	40	1.90	2.07	2.21

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 9.4 MJ(2250 Kcal)/day or 155 KJ(38 Kcal)/kg/day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 9.0 to 10.3 MJ(2150 to 2450 Kcal)/day or 145 to 160 KJ(35 to 39 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

NOTES

Table 2.16: Daily average energy requirement for women aged > 60 years*

Mean Weight	BMR per kg[a]		Daily energy requirement according to BMR factor (or PAL) and body weight indicated																						Height (m) for BMI values[b]		
			1.45×BMR				1.60×BMR				1.75×BMR				1.90 ×BMR				2.05×BMR				2.20×BMR						
kg	KJ	Kcal	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	MJ	KJ/kg	Kcal	Kcal/kg	24.9	21.0	18.5
45	99	24	6.5	145	1550	34	7.1	160	1700	38	7.8	175	1850	41	8.5	190	2050	45	9.2	205	2200	49	9.8	220	2350	52	1.34	1.46	1.56
50	93	22	6.7	135	1600	32	7.4	150	1800	36	8.1	165	1950	39	8.8	175	2100	42	9.5	190	2300	46	10.2	205	2450	49	1.42	1.54	1.64
55	88	21	7.0	130	1700	31	7.8	140	1850	34	8.5	155	2050	37	9.2	165	2200	40	9.9	180	2350	43	10.7	195	2550	46	1.49	1.62	1.72
60	84	20	7.3	120	1750	29	8.1	135	1950	32	8.8	145	2100	35	9.6	160	2300	38	10.3	170	2450	41	11.1	185	2650	44	1.55	1.69	1.80
65	80	19	7.6	115	1800	28	8.4	130	2000	31	9.1	140	2200	34	9.9	155	2350	37	10.7	165	2550	39	11.5	175	2750	42	1.62	1.76	1.87
70	77	18	7.9	110	1900	27	8.7	125	2050	30	9.5	135	2250	32	10.3	145	2450	35	11.1	160	2650	38	11.9	170	2850	41	1.68	1.83	1.95
75	75	18	8.1	110	1950	26	9.0	120	2150	29	9.8	130	2350	31	10.6	140	2550	34	11.5	155	2750	37	12.3	165	2950	39	1.74	1.89	2.01
80	72	17	8.4	105	2000	25	9.3	115	2200	28	10.1	125	2400	30	11.0	140	2650	33	11.9	150	2850	35	12.7	160	3050	38	1.79	1.95	2.08
85	70	17	8.7	100	2050	24	9.6	115	2300	27	10.5	125	2500	29	11.4	135	2700	32	12.3	145	2950	34	13.2	155	3150	37	1.85	2.01	2.14

* Values rounded to closest 0.1 MJ/d, 50 Kcal/d, 5 KJ/kg/d, 1 Kcal/kg/d.

[a] BMR calculated for each weight from the equations in Table 2.3. Values of BMR/kg are presented for ease of calculations for those who wish to use different PAL values or different weights.

[b] Height ranges are presented for each mean weight for ease of making dietary energy recommendations to maintain an adequate BMI based on a population's mean height and PAL. For example, the recommended mean energy intake for a male population of this age group with a mean height of 1.70 m and a lifestyle with a mean PAL of 1.75, is about 8.8 MJ(2100 Kcal)/day or 145 KJ(35 Kcal)/kg/ day to maintain an optimun population median of 21.0 (WHO/FAO, 2002), with an indivual range of about 8.5 to 9.5 MJ(2050 to 2250 Kcal)/day or 135 to 155 KJ(32 to 37 Kcal)/kg /day to maintain the individual BMI limits of 18.5 to 24.9 (WHO, 2000).

2.7.4 Energy Requirement During Pregnancy

The energy requirements of pregnancy are those needed for adequate maternal gain to ensure the growth of the foetus, placenta and associated maternal tissues, and to provide for the increased metabolic demands of pregnancy, in addition to the energy needed to maintain adequate matemal weight, body composition and physical activity throughout the gestational period, as well as, for sufficient energy stores to assist in proper lactation after delivery. Basal metabolism, we learnt, increases during pregnancy as a result of accelerated tissue synthesis, increased active tissue mass, and increased cardiovascular and respiratory work. Based on these considerations the ICMR recommendation during pregnancy is given in Table 2.17. As you may have noticed the extra energy cost of pregnancy is 300 Kcal during the second and third trimester of pregnancy. This is over and above the women's habitual energy requirement before pregnancy. The additional energy allowance could be lowered in cases where women reduce their activity level during pregnancy.

Table 2.17: Additional energy cost of pregnancy

	Energy(Kcal)	
	ICMR	FAO/WHO/UNU 2004
1st Trimester	-	+85
2nd Trimester	+300	+285
3rd Trimester	+300	+475

Now let us look at the FAO/WHO/UNI_J 2004 recommendations. The FAO/WHO/ UNU 2004 recommendation for the extra energy cost of pregnancy is 85 Kcal/ day, 285 Kcal/day and 475 Kcal/day during the first, second and third trimesters, respectively as highlighted in Table 2.17. There are many societies with a high proportion of non- obese women who do not seek prenatal advice before the second or third month of pregnancy. Under these circumstances, this consultation recommends that in such societies pregnant women increase their food intake by 360 Kcal/day in the second trimester and by 475 Kcal/day in the third. Further, not all women have the option to reduce physical activity during pregnancy. In particular, women belonging to low- income group from developing countries must often continue a strenuous work pattem until shortly before delivery. Furthermore, women who are sedentary prior to pregnancy have little flexibility to reduce their level of physical activity. Consequently, this consultation does not recommend a reduction in the additional energy allowance for pregnancy.

Finally let us get to know about the requirement during lactation.

2.7.5 Energy Requirement During Lactation

The energy requirement of a lactating woman is defined as the level of energy intake from food that will balance the energy expenditure needed to maintain

a body weight and body composition, a level of physical activity and breastmilk production that are consistent with good health for the woman and her child, and that will allow economically necessary and socially desirable activities to be performed (assuming that she resumes her usual level of physical activity soon after giving birth). Table 2.18 presents the energy requirement for lactation. The ICMR has recommended an additional intake of 550 Kcal during the first six months of lactation and 400 Kcal during 7-12 months of lactation.

Table 2.18: RDA's for lactation

	Energy (Kcal)/day	
	ICMR	FAO/WHO/UNU (2004)
0-6 months	+550	+ 600
6-12 months	+440	+ 450

Exclusive breastfeeding is recommended during the six months after delivery, with introduction of complementary foods and continued breastfeeding thereafter. For women who feed their infants exclusively with breastmilk during the first six months of life, the mean energy cost as recommended by FAO/WHO/UNU 2004 over the six-month period is 600 Kcal/day (refer to Table 2.18). From the age of six months onwards, when infants are partially breastfed and milk production is on average 550 g/day, the energy cost imposed by lactation is 450 Kcal/day.

It further suggests that well-nourished women with adequate gestational weight gain should increase their food intake by 505 Kcal/day for the first six months of lactation, while undernourished women and those with insufficient gestational weight gain should add to their personal energy demands 675 Kcal/day during the first six months of lactation. Energy requirements for milk production in the second six months are dependent on rates of milk production, which are highly variable among women and populations.

With a review of the energy requirement during the different ages and physiological stages,we end our discussion on the requirements here. Finally, we shall look at the energy imbalance problems.

2.8 ENERGY IMBALANCE: AN OVERVIEW

Energy balance, we have learnt from our discussion so far, is achieved when input (i.e. dietary energy intake) is equal to output (i.e. total energy expenditure). When energy balance is maintained over a prolonged period, an individual is considered to be in a steady state.

The recommended intake of energy of a group is equal to the average energy requirement of individuals of the group because both lower and higher energy

intakes are associated with health hazards. Too much deviation on either side from appropriate range of body weight increases our risk of health problems. Just as overweight is the result of positive energy balance, underweight results when the energy balance is negative.

A growing literature supports the use of the body mass index (BMI) as a predictor of the impact of body weight on morbidity and mortality risks. BMI, defined as weight in kilograms divided by the square height in meters, is also termed the Quetelet's index. It is used in preference to other weight/height indices, including the weight/height ratio, the Ponderal Index and the Benn's Index as highlighted in Table 2.19.

Table 2.19: Indices for weight relative to height

Index	Formula
Weight/Height ratio	wt/ht
Body Mass Index (BMI)	$wt/(ht)^2$
Ponderal Index	$ht/\sqrt[3]{wt}$
Benn's Index	$wt/(ht)^P$

The power P in Benn's index is calculated to minimize the direct relationship with height. Weight in all indices is in kg and height in meters.

BMI, although only an indirect indicator of body composition, is now used to classify underweight and overweight individuals. Table 2.20 presents the WHO classification of underweight, overweight and obesity in adults according to BMI.

Table 2.20: WHO classification of underweight, overweight and obesity in adults according

Classification	BMI (Kg/m^2)	Risk of Comorbidity
Underweight	< 18.5	Low*
Normal range	18.5 - 24.9	Average
Overweight	25 - 29.9	Increased
Obesity	> 30.0	
Classs 1	30.0 - 34.9	Moderate
Class 11	35.0 - 39.9	Severe
Class 111 (morbid)	> 40.0	Very Severe

* Low for the non-communicable diseases associated with obesity, but increased mortality due to cancer and infectious diseases

Source: WHO (1998).

As both undenveight and obesity are associated with adverse health consequences, it has been suggested that each country should develop its own BMI and cut-off points indicative of various degrees of undernutrition and overnutrition based on

their own data on health problems in persons with varying BMI levels. It has been found that for a given BMI, Indians have more body fat than other ethnic groups, both within and outside Asia. This relative increase in adiposity in Indians has led to the suggestion that the BMI cut-off for non-communicable diseases such as obesity should be reduced for Indians to about 23 kghn2 or lower. In other words, we can refer to it as a public health action point at a BMI of 23 kg/m2. The point at which low BNII poses a health risk is poorly defined. The ability to identify persons with low BMIs who are at increased risk for morbidity and mortality is highly nonspecific. Weight status in children can be classified based on percentile curves for BMI for age. Table 2.21 presents the weight status based on percentile BMI for age. The latest BMI for age percentile for boys and girls, aged 2-20 years have been published by the United States Centre for Health Statistics (NCHS) in collaboration with the National Centre for Chronic Diseases Prevention and Health Promotion in the Year 2000 which may be applied to health of well-nourished Indian children also.

Table 2.21: WHO classification of weight status in children based on percentile curves for

Weight Status	BMI for Age
Underweight	$< 5^{th}$ percentile
At risk of overweight	$\geq 85^{th}$ to $< 95^{th}$ percentile

From our discussion above,it is clear that the common way to assess undernutrition or overnutrition (obesity) is in terms of body weight. Undernutrition is caused by a less than adequate intake of nutrient, most of which are related to the energy intake. In adults, this has led to the tenn 'energy deficiency'. Obesity,on the other hand, is energy imbalance where energy intake exceeds energy expenditure. Let us review these two conditions, linked to energy imbalance, briefly here.

Chronic Energy Deficiency (CED)

Energy deficiency we have seen refers to less than adequate intake of energy. It is further sub classified into acute and chronic energy deficiency. Acute energy deficiency is suspected when an involuntary weight loss of greater than 10% of body weight occurs over the preceding 3-6 months. We can say it is sudden and associated with a declining body weight. Chronic energv deficiency (CED), on the other hand, occurs over a long period of time, such that body weight over the preceding few months may be low, but stable. It is characterized by low body mass index in weight- stable individuals.

In 1994, FAO adopted the term 'chronic energy deficiency' for underweight. They categorized three degrees of underweight on the basis of BMI as presented in Table 2.22. WHO has adopted the same cut-off as presented in Table 2.22 to define three grades of low BMI, referred to as 'underweight' (refer to Table 2.22) rather than 'chronic energy deficiency'.

Table 2.22: FAO/WHO classification for chronic energy deficiency and/o underweight

Chronic Energy Deficiency Grade (FAO)	Underweight Grade (WHO)	BMI (kg/m^2)
Normal	Normal	> 18.5
Grade I	Mild Underweight	17.0 - 18.4
Grade II	Moderate Underweight	16.0 - 16.9
Grade III	Severe Underweight	< 16.0

Energy deficiency is associated with body weight loss along with changes in body composition (both body fat and the fat free mass are decreased), as well as, a reduced BMR and physical activity. Figure 2.3 illustrates how these factors interact with each other to attain lower energy expenditure when an acute negative energy balance exists.

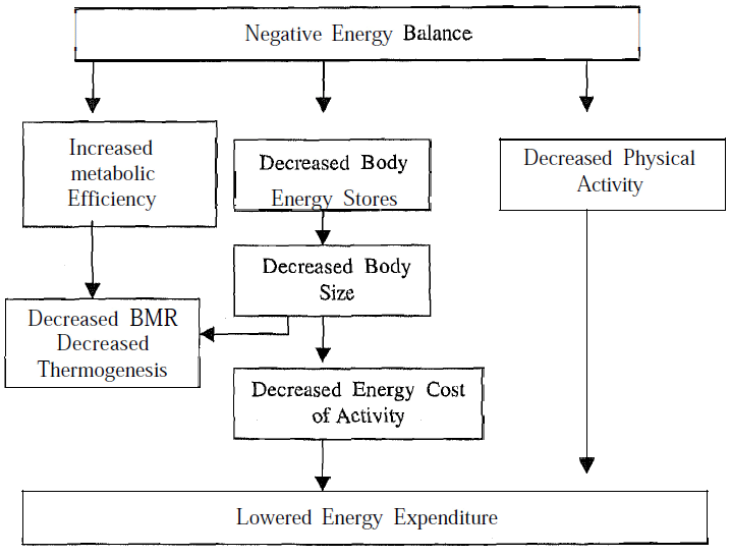


Figure 2.3: Factors leading to lowered ene1W expenditure

Now if the lowered energy expenditure (as illustrated in Figure 2.3) is adequate to compensate the lowered or decreased energy intake (which was the cause of negative energy balance in the first place) a new energy balance is achieved which allows a person to survive, albeit at a lower plane of nutrition and this is what is referred to as chronic energy deficiency. Thus, you would notice, it is a weight-stable condition, in the presence of lower than normal energy intake. It is characterized by low body weight and fat stores, but the individüal's health is normal and the body's physiological function is also not compromised and therefore the individuals ability to lead an economically productive life is maintained.

However, the consequences of inadequate energy intake during the childhood and adolescence of an individual is a reduced body size and a low BMI. In the

presence of concomitant repeated infections in childhood and adolescence, an individual with CED, will also show stunting. Both the body fat and the fat free mass are decreased as compared to a normally nourished individual. Reduction in muscle mass leads to reduced skeletal muscle performance, which may also be partly due to functional changes in skeletal muscles. Further adults with CED have lowered handgrip strength and they also fatigue faster when subjected to standard exercise protocols. Statistics suggest that nearly 25-50% of adults from developing countries, including India may be described as having CED. Low values of BMI in adults have been consistently associated with a decline in work output, productivity, and income-generating ability, as well as, a compronzised ability to respond to stressful conditions.

Eight percent (8%) of Indians do not get two square meals a day and there are pockets where severe undernutrition takes its toll even today. Every third child born is underweight. Around half of the preschool children suffer from undernutrition problem low birth weight is associated not only with higher infant mortality but also long-term health consequences including increased risk of non-communicable diseases such as' obesity, diabetes mellitus, coronary heart diseases etc.

Chronic energy deficiency and undernutrition is a public health problem in India. The contributory factors include:

- low dietary intake because of poverty and low purchasing power;
- high prevalence of infection because of poor access to safe-drinking water, sanitation and health care;
- poor utilization of available health and other facilities due to low literacy and lack of awareness.

Next, let us review another energy imbalance condition viz. obesity which is a state of excess energy intake over expenditure.

Obesity

The World Health Organization has declared obesity as the largest global chronic health problem in adults, which by 2025 will emerge as a more serious world problem than undernutrition.

Recent data from National Nutrition Monitoring Bureau (NNMB) repeat surveys indicate that there has been some reduction in undernutrition and alarmingly some increase in obesity over the last two decades in India. Data from National Family Health Survey-2 (NFHS) confirms that currently both undernutrition and overnutrition are problems in women (Table 2.23)

Table 2.23: Nutritional status of ever married women aged 15-49 years

	BMI < 18.5 (kg/m^2)	BMI > 25 (kg/m^2)
All India	35.8%	10.6%

Alterations in lifestyles and dietary intake have led to the increasing incidence of obesity and associated non-communicablediseases. Obesity results from an imbalance between energy intake and energy expenditure. The healtll risks associated with obesity include increased mortality, hyperlension, cardiovascular disease, diabetes mellitus, gallbladder disease, some cancers, and changes in • endocrine function and metabolism.

The risk factors for becoming obese are not entirely understood but are thought to include genetics, food intake, physical inactivity, and some rare metabolic disorders. Obesity rates in all age groups are increasing also mainly because of the reduction in physical activity without concomitant reduction in energy intake.' Energy expenditure by physical activity varies considerably between individuals, affecting the energy balance and the body composition by which energy balance and weight maintenance are achieved. Indeed, physical inactivity is a major risk factor for development of obesity in children and adults.

Therefore, a certain amount of habitual physical activity is desirable for biological and social well-being. The regular performance of physical activity by children, in conjunction with good nutrition, is associated with health, adequate„growth and well-being, and probably with lower risk of disease in adult life. There is consensus (FAO/WHO/UNU 2004) that, in order to promote general health, at least 30 minutes of moderate to vigorous activity should be performed, three or more days per week. In view of the known adverse health consequences of both excess and deficient energy intake, it is essential that appropriate recommendation for the RDA for Indians is evolved. This is important as the country is entering an era of goal disease burden of CED and infections on the one hand and that of obesity and non-communicable diseases on the other.

2.8 LET US SUM UP

In this mit we learnt about the human energy requirements. Energy requirement we learnt is the amount of food energy needed to balance energy expenditure in order to maintain body size, body composition and a level of necessary and desirable physical activity, and to allow optimal growth and development of children, deposition of tissues during pregnancy, and secretion of milk during lactation, consistent with long-term good health. For healthy, well-nourished adults, it is equivalent to total energy expenditure (TEE). The total energy expenditure over a 24-hour period is the sum of basal metabolic rate (BMR), thermic effect of feeding (TEF), physical activity and the energy cost of tissue synthesis. Further, we studied that the energy needs vary widely among individuals in a group.

A number of factors cause the BMR to vary among individuals. Major determinants are the body size, composition, age, sex, growth etc. Similarly, there are factors affecting the thermic effect of food and energy expended in physical activity which influence energy requirements. When energy balance is maintained over a prolonged period, an individual is considered to be in a steady

state. However, too much deviation on either side from the appropriate range of body weight, either due to intakes in excess of requirements or intakes lower than requirements, increases our risk of health problems. Just as overweight (obesity) is the result of positive energy balance, undernutrition (chronic energy deficiency) results when the energy balance is negative.

2.9 GLOSSARY

Glycogenolysis : catabolism of glycogen leading to glucose availability.

Sepsis : serious medical condition, resulting from the immune response to a severe infection.

2.9 CHECK YOUR PROGRESS

1) Define the followin

   a) Energy

   b) Kilocalorie

2) List the different components of energy requirements.

3) Define BMR? Give the factors which influence BM

4) Give the different lifestyle classifications with their PAL value

NOTES

UNIT

3

CARBOHYDRATES

STRUCTURE

3.1 LEARNING OBJECTIVE

After going through this unit, you will be able to:

describe the various physiological changes during pregnancy,

describe foetal growth and development and understand the importance of nutrition,

identify determinants of poor pregnancy outcome,

explain what is IUGR and LBW and their consequences,

discuss the vaious aspects about lactatioil and importance of human milk,

elaborate the nulritional requirements during pregnancy and lactation,

state dietary considerations to be followed to ensure successful regnancy and lactation, and

counsel mothers as per their individual requirements.

3.2 INTRODUCTION

In the previous unit we have studied about the energy requirements. You now know That energy must be supplied regularly to individuals through the diet for their survival and maintenance of life and to carry out all activities jointly termed as work. Our body derives energy from the catabolism of energy-yielding nutrients: carbohydrates, lipids and proteins Aiming these, carbohydrates are the single most abundant source of dietary energy comprising 50-70% of the total energy intake in different populations. In this we will learn about the different types of carbohydrates, their utilization by the body and how glucose homeostasis is maintained. In addition the health benefits (f dietary fiber and carbohydrates not absorbed in the small intestines, will also be covered in this unit.

Before going through this unit it is important for you to revise the sections on chemistry of carbohydrates, their structures and different metabolic pathways covered under Nutritional Biochemistry Course (MFN-002) in Unit I and 6, respectively.

3.3 CLASSIFICATION OF CARBOHYDRATES

Carbohydrates are defined as polyhydroxy aldehydes or ketenes or substances that produce such compounds when hydrolyzed. Carbohydrates are very diverse organic molecules and can be classified based on their:

a) Molecular size / degree of polymerization (DP

b)) b) Digestive fate

You may recall studying about the classification of carbohydrates in the Nutritional Biochemistry Course. The following brief discussion will help you to brush up / recapitulate the information presented in the Nutritional Biochemistry Course.

3.3.1 Classification on the Basis of Degree of Polymerization (DP

Carbohydrates are classified by their degree of polymerization as follows:

1) Sugar (DP: 1-2): Monosaccharide (consisting of a single unit of sugar. Also known as simple sugar) and Disaccharides (consisting of 2 monosaccharide)

2) Oligosaccharides (DP: 3-9): Each molecule containing 3-9 monosaccharide units.

3) Polysaccharides (DP: > 9): Each molecule containing more than 9, but usually several monosaccharide units.

A brief review follows: Examples of different classes of carbohydrates and their sources are also given in Table 3.1.

1) **Sugars:** This group includes monosaccharide and disaccharides. List down the names of sugars under both these groups and check it out with those given here, Monosaccharide's (DP: 1) are structurally the simplest form of carbohydrates and cannot be reduced in size to smaller units by hydrolysis. They are grouped according to the number of carbon atoms per molecule i.e. triodes, tortoises, pentose, hexoses. Nutritionally the most impotent carbohydrates are hexodes, Metabolically, the most important hexose is glucose. The disaccharides (DP.• 2) are sources of energy in the diet. Sucrose and lactose are more abundant than inaltose or malt sugar.

2) **Oligosaccharides (DP: 3-9):** Oligosaccharides consists of short chains of monosaccharide units joined by covalent bonds. The glycosidic bond may be a, or 13 in orientation. The number of units is designated by the prefixes - tris tetrn followed by 'saccharides'.

Table 3.1: Different types of carbohydrates

S.No.	Class	Examples	Component Monosaccharide	Sources
1.	Monosaccharides	Glucose Fructose Galactose		Fruits, honey etc. Fruits, honey etc. Milk and products
2.	Disaccharides	Maltose Lactose Sucrose	Glucose (2 molecules) Glucose + Galactose Glucose + Fructose	Glucose syrup Milk and its products Sugarcane, sugar used as additive
3.	Trisaccharides	Raffinose Maltotriose	Glucose, Fructose, Galactose Glucose (3 molecules)	Chick peas, legumes, pulses Glucose syrup
4.	Tetrasaccharides	Maltotetrose Stachyose	Glucose (4 molecules) Galactose (2 molecules), Glucose, Fructose	Glucose syrup Beans, Legumes
5.	Pentasaccharides	Verbascose		Beans, Legumes
6.	Sugar alcohols	Sorbitol Xylitol Mannitol		Exclusively present if used as food ingredients

3) **Polysaccharides (DP: > 9):** Polysaccharides are high molecular weight polymers of monosaccharide units formed by glycosidic bonding. They may be long unbranched inolecules or branched molecules. If the structure is composed of a single type of monosaccharide unit, it is referred to as a 'homopolysaccharide'. If two or more different types of monosaccharides make up its structure, it is called 'heteropolysaccharides.

Let us now have a look at another way of classifying carbohydrates.

3.3.2 Classification Based on Digestive Fate of Carbohydrates

The digestive fate of carbohydrates depends on their inherent chemical nature (monosaccharide composition and type of linkage between sugars) and on the supramolecular structures within foods of which they are a part.

Mc Cance and Lawrence in 1929 were first to classify carbohydrates as 'available' and 'unavailable'. According to them, carbohydrates that are digested to constituent monosaccharides and absorbed fell under the category of 'available' carbohydrates. Carbohydrates that are not digested by the endogenous enzymes of the human inteslinal tract and therefore not absorbed were classified as 'unavailable' carbohydrates.

However, these undigested carbohydrates enter the colon and are fermented by microflora. It is realized now that it is misleading to use the term 'unavailable' carbohydrates because some indigestible carbohydrates can provide body with energy through fermentation in the colon. Therefore, 'unavailable' carbohydrates are not really 'unavailable' and the term 'Non Glycemic Carbohydrates' is suggested for these by FAO (Food and Agriculture Organization) and WHO (World Health Organization). Non glycemic carbohydrates include the raffinose series of oligosaccharides, non-starch polysaccharides (NSP), some disaccharides such as lactulose and resistant starch (RS). You may recall reading about RS in the Principles of Food Science Course (MFN-008) in Unit 2. Here, we will get to know more about RS and the other non-glycemic carbohydrates.

Similarly, carbohydrates that are digested to monosaccharides and absorbed as such in the small bowel are termed as 'Glycemic' carbohydrates. They include disaccharides, starch, maltodextrin and glycogen.

Let us now study the functions of carbohydrates in the body in the following section.

3.4 FUNCTIONS

Carbohydrates in the body function primarily in the form of glucose, although a few have structural roles. Important functions of carbohydrates are listed below:

Source energy: Glucose is a major source of energy for all the body cells. One gram of carbohydrate provides 4 Kcal. RBCs are particularly dependent on glucose. It is also indispensable for the maintenance of functional integrity of the nerve tissue and under normal circumstances; it is the sole source of energy for the brain.

Similarly, glucose is important for heart muscles. Although fatty acids are the preferred regular fuel of heart muscle, glycogen in cardiac muscle is an important emergency source of contractile energy. In a damaged heart, poor glycogen stores or low carbohydrate intake may cause cardiac symptoms of angina.

Protein sparing effect: Carbohydrates help in regulating the protein metabolism. Presence of sufficient carbohydrates to meet energy demands prevents the channeling of too much protein for this purpose. This protein sparing action allows the major portions of protein to be used for its basic structural purpose of tissue building. Therefore, patients who are unable to eat are temporarily administered 5% glucose solution intravenously.

Antiketogenic effect: Presence of carbohydrates is necessary for normal fat Carbohydrates metabolism. In the absence of sufficient carbohydrates, larger amounts of fat are used for energy than the body is equipped to handle. This results in incomplete oxidation and accumulation of ketone bodies. This may in turn lead to acidosis, sodium imbalance and dehydration. In extreme conditions such as starvation (carbohydrates are inadequate) and uncontrolled diabetes (carbohydrates are unavailable for energy needs), ketoacidosis is a common coinplication.

Excretion of toxins: Glucuronic acid, a metabolite of glucose, combines with chemical and bacterial toxins and some normal metabolites in the liver and thereby helps in their excretion.

Act as precursors: Carbohydrates and their derivatives serve as precursors to compounds such as nucleic acid, connective tissue matrix and galactoside of nerve tissue.

Overall positive health: Non-glyceinic carbohydrates including non-starch polysaccharides are beneficial for the functions and physiology of gastrointestinal tract and thus have a positive effect on. the overall health.

Now that you have gone through the functions, let us move on to the mechanism of the digestion in the following section.

3.5 DIGESTION AND ABSORPTION

You are aware that 60-70% of energy is supplied by the dietary carbohydrates which are primarily present as polysaccharides (starch) followed by disaccharide and free monosaccharide. But the monosaccharides are present in very small amounts in our diet. To be absorbed from the gut, these carbohydrates must be broken down to their constituent monosaccharide units. Let us now briefly review how these carbohydrates are digested in the gut.

The hydrolytic enzymes involved in the digestion of carbohydrates are collectively called 'glycosidase' or 'carbohydrate's. The major carbohydratase enzyme secreted by the salivary glands and the acinar cells of the pancreas is the ends-glycosidase - amylase. This enzyme hydrolyzes a-I, 4-linkages in amylase and amyl pectin to yield maltose, maltotriose and dextrin's. The further hydrolysis of these and dietary sucrose and lactose are brought about by 'oligosaccharidases', which are expressed on the apical membrane of the epithelial cells on the small intestinal villi.

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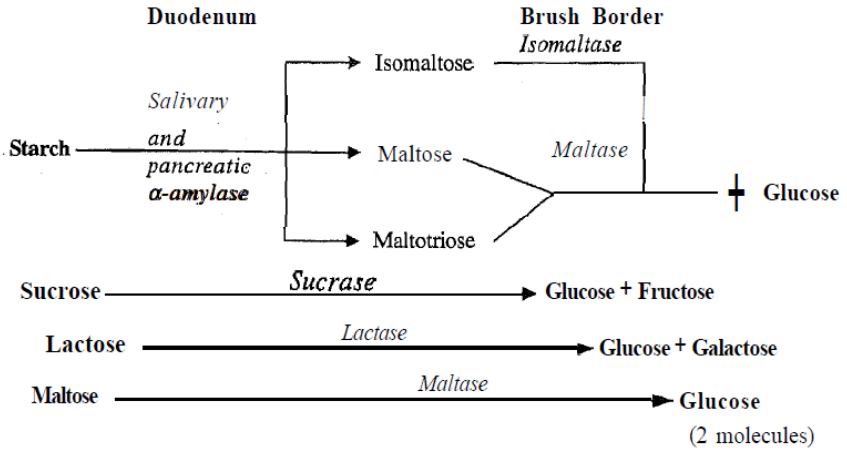

Figure 3.1: Digestion of carbohydrates

Glucose and galactose are absorbed into the mucosal cells by active transport which requires energy. The calTier of glucose and galactose is a specific protein complex known as 'sodium-glucose transport protein-I' (SGLT-I)S which is dependent on Na*/K+ ATPase pump. Glucose and galactose cannot attach to the carrier until it has been preloaded with sodium as illustrated in Figure 3.2. Hence, you would realize that oral rehydration syrup (ORS) always contains sodium chloride and glucose / sugar. Fructose is absorbed by a facilitated transport, involving a specific transporter— GLUT-5.

Another transport protein called GLUT-2, present on the basolateral membrane shuttles all three monosaccharide's from entrecotes towards the blood vessel. Study Figure 3.2 for a clearer understanding of the process of absorption

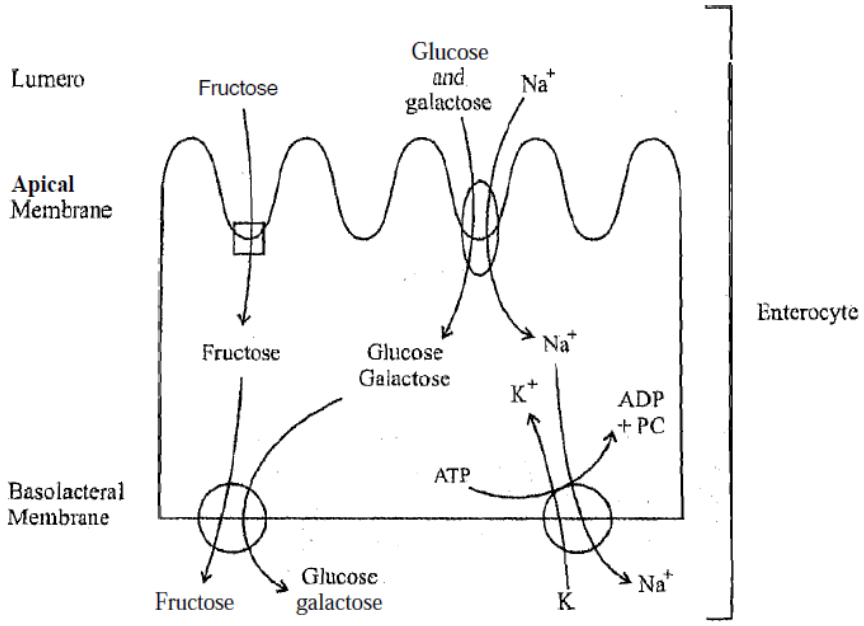

Figure 3.2: Absorption of carbohydrates across apical membrane

Before moving on to the utilization of carbohydrates, let have a look at the disorders of carbohydrate absorption.

Carbohydrate Malabsorption Carbohydrates malabsorption is usually caused by an inherited or acquired (in intestinal infection, celiac disease, PEM) defect in the brush border oligosaccharidases, the most common being 'lactose intolerance'. In such individuals, ingestion of lactose leads to passage of the sugar to the large bowel, where it is fermented to produce shrt chain fatty acids (SCFA) and gases. In humans, lactase activity declines as individuals grow.

NOTES

3.6 METABOLIC UTILIZATION OF CARBOHYDRATES

Following absorption, the monosaccharides enter the portal circulation and are carried to the liver. Both galactose and fructose are converted to glucose in the hepatocytes. A part of glucose is converted into glycogen while some is catabolized for energy in the liver. The remainder of glucose passes on into the systemic blood supply and is distributed among other tissues such as skeletal muscle, adipose tissue and kidney. Nearly all the cells in the body admit glucose passively by a carrier-mediated transport mechanism that does not require energy. The protein carriers involved in the process are called glucose transporters and are abbreviated GLUT. A brief description of human GLUT is given in Box 3.4.

BOX 3.1 Human Glucose Transporters (GLUT)

All GLUTs are the integral proteins, which penetrate and span the lipid bilayer of plasma membrane. Six isomers of GLUT have been described, the tissue distribution of which is given below:

Type	Major Sites of Expression
GLUT 1	Erythrocytes, blood, brain barrier, placenta
GLUT 2	Liver, β cells of pancreas, kidney, small intestine
GLUT 3	Brain
GLUT 4	Adipocytes, heart, skeletal muscle
GLUT 5	Small intestine
GLUT 7	Endoplasmic reticulum of hepatocytes

Among these, GLUT 4 is sensitive to insulin and its concentration increases in response to the hormone. Insulin resistance observed in NIDDM patients is believed to arise from abnormalities in the synthesis and activity of GLUT-4.

After going through the contents in Box 3.1, it must be clear to you that cells of brain, erython, liver and pancreas do not require insulin in order to permit entry of glucose. On the other hand, entry of glucose in the cells of adipose tissue and skeletal muscle is insulin dependent

The metabolic fate of glucose in different tissues depends to a great extent on the body's energy demands. The major regulatory mechanisms are hormonal, involving the action of hormones and allosteric enzyme activation and suppression.

NOTES

Further, the nature of diet especially with respect 10 calbohydrates modifies the activity of lipogenic pathway. A diet rich in carbohydrates stimulates lipogenic pathway, whereas starvation or a diet rich in lipids and poor in carbohydrates decreases the function of lipogenic enzyme. You have already studied metabolic pathways of carbohydrates in detail in Nutritional Biochemistry Course in Unit 6. For recapitulation, an integrated overview of these pathways is shown in Figure 3.3. For details we suggest you get back to the Nutritional Biochemistry Course

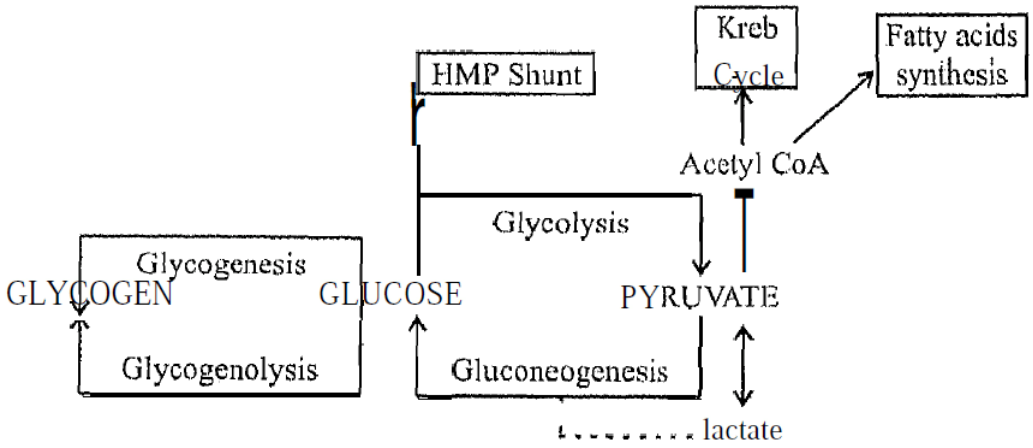

Figure 3.3: Integrated overview of metabolic pathways of carbohydrates

Next, let us get to know how glucose levels are regulated in the body.

3.7 REGULATION OF BLOOD GLUCOSE CONCENTRATION

A number of mechanisms function to maintain blood glucose at remarkably constant level of 70-100 mg/dl under fasting conditions. Regulation is the net effect of the organ's metabolic processes that remove glucose from the blood for either glycogen synthesis or for energy release and of processes that return glucose to the blood, such as glycogenolysis and gluconeogenesis.

Let us understand both of these mechanisms of blood glucose regulation.

After a meal, when blood glucose levels increase, the peptide hormones (such as cholecystokinin) secreted from enteroendocrine cells within the mucosa of the small bowel amplify the response of the ß-cells of pancreas resulting in the secretion of insulin. Insulin facilitates the transport of glucose by glucose transporter - GLUT 4 into the adipocytes and muscle cells and stimulates glycogenesis (synthesis of glycogen) and fatty acid biosynthesis, thus returning the blood glucose to homeostatic level.

This was the case when there are high glucose levels in blood. But what happens, when the level of glucose falls? How, then the energy demands of cells are met? Well, in case of post absorptive state, the fall in blood glucose level signals the reversal of the pancreatic hormonal secretion i.e. decreased insulin and increased glucagon release. Blood glucose levels are maintained by the breakdown of glycogen and in this way, the glucose demands Of brain, RBCs and testis are met

In long periods of fasting' or starvation, glucose is supplied from non-carbohydrate sources by gluconeogenesis. Glucose is synthesized from a range of substrates including pyruvate, lactate, glycerol and amino acids. Body proteins are catabolized to release amino acids while triacylglycerol yields glycerol.

These gluconeogenic processes are triggered by a fall in blood glucose concentration below 5.0 mmol (90 mg/dl) and are signaled to the tissues by the secretion of glucagon and glucocorticoid hormones. Figure 3.4 illustrates the regulatory process.

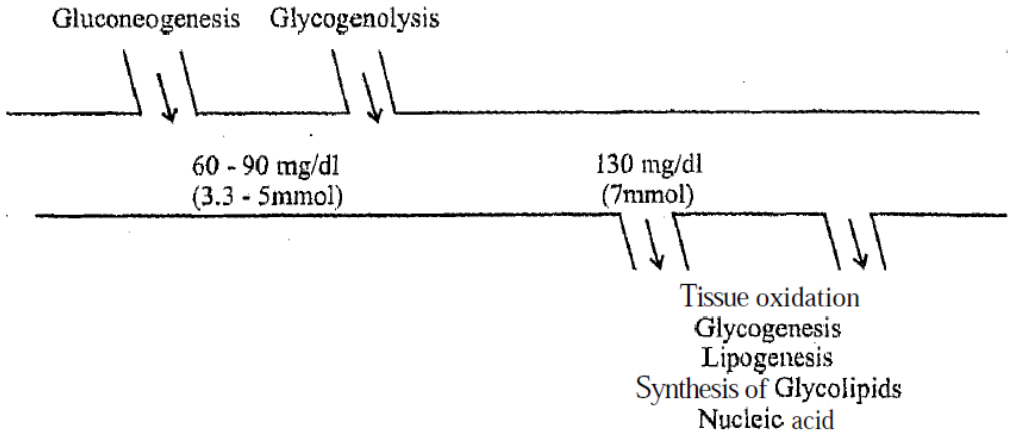

Figure 3.4: Regulation of blood glucose

With a brief review of the carbohydrate metabolism, let us now recapitulate what we have learnt so far by answering the check your progress exercise 1.

3.8 DIETARY FIBRE

You are all aware that fibre is an important component in the structure of plants. However, fibre as a dietaiy constituent was considered important in the early 1970's when Burkitt and Trowell proposed that many western diseases were due to a lack of fibre in the diet. These included metabolic diseases such as diabetes, cardiovascular diseases, as well as, the diseases which were a result of straining at stool such as diverticular disease, hiatus hernia and haemorrhoids. Protective effects of fibre against colon cancer were also suggested by Burkitt.

Since then, extensive research has implicated dietary fibre as important in various aspects of gastrointestinal function and in prevention and management of a variety of disease states. The varying effects of dietary fibre as observed by

researchers are obvious because it is made up of different components, each with its own distinctive characteristics. Methodologies have been developed to isolate these components, however, the definitions and methods of measuring fibre have changed over time. Let us see how definition of fibre has been modified over tim

Originally, Burkitt and Trowell defined fibre as 'the components of plant cell walls that are iitdigestible in the human small intestine'. Later the definition was expanded to include storage polysaccharides within plant cells also.

Recently, the American Association of Cereal Chemists (AACC) developed an updated definition of dietary fibre to ensure tliat the term enconipassed the complete charactefization of the components, as well as, their function. The AACC along with the Carbohydrate Technical Committee of the North Ame rican branch of International Life Sciences Institute developed the definition as:

"Dietary fibre is the edible part of plants or analogous carbohydrates that are resistant to digestion and absorption in the huinan small intestine with complete or partial fermentation in the large intestine. Dietary fibre includes polysaccharides, oligosaccharides, lignin and associated plant substances. Dietary fibre promotes beneficial physiological effects including laxation and/or blood cholesterol attenuation and / or blood glucose attenuation."

Now that we know the definition of fibre, let us learn about components of dietary fibre.

3.8.1 Components of Dietary Fibre

Dietary fibre (DF) includes many components which can be categorized on the basis of solubility or 'their location in the plant. Let us find out what are these.

Components classified on the basis of solubility are:

Insoluble DF	Soluble DF
Cellulose, Some hemi-celluloses, and Lignin.	Pectin, Gums, Mucilages, and Some hemi-celluloses.

Based on the locatiorz on tlie plant, DF components can be categorized as plnizt cell wall constituents and rzon-plant cell ~vall constituelzts.

Plant cell wall constituents include:	Non-Plant cell wall constituents include:
Lignin Cellulose, Hemicelluloses, and Pectins	Gums, Mucilages, Algal polysaccharides, Suberin, and Cutin

Table 3.2 presents the structure, properties, functions and food sources of different components. Kindly study it carefully.

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Table 3.2: Important components of dietary fibre

Component	Structure	Properties	Foods High in Content
Cellulose	Long, linear polymer of 1, 4 β-linked glucose. Hydrogen bonding between sugar residues in adjacent parallel running cellulose chain imparts the microfibril a three-dimensional structure.	Water-insoluble but can he modified chemically (sodium carboxy methyl cellulose) to be more soluble. Poorly fermented by colonic bacteria.	Bran, legumes, peas, vegetables of cabbage family, outer covering of seeds, apples.
Hemicellulose	Consists of heterogenous group of polysaccharide substances containing number of sugars in its backbone and side chains. Sugars which form backbone include xylose, mannose, galactose. Sugars present in side chain are arabinose, glucuronic acid and galactose. Hemicelluloses are categorized on the basis of predominant sugar in their backbone e.g. xylan, mannan, galactan.	Hemicelluloses that contain acids in their side chains are slightly charged and water soluble. Others are insoluble. Fermentability by intestinal flora is influenced by the sugars and positions e.g. hexose and uronic acids are more accessible to bacterial enzymes.	Bran and whole grains.
Pectin	They are polymers of D-galacturonic acid with a-1,4 glucosidic bonds. Rhamnose is also part of this backbone. Side chain consists of galactose, glucose, rhamnose, arabinose. Galacturonic acid monomers of backbone can also be in methyl ester forms.	They are water-soluble and gel forming. They have ion-binding potential. They are completely metabolized by colonic bacteria.	Apples, guavas, strawberries, citrus fruits.
Lignin	Main non-carbohydrate component of fibre. It is a three-dimensional polymer composed of phenol units - trans-coniferyl, trans-sinapyl and trans-p-coumaryl.	It is highly insoluble in water and responsible for the structural adhesion of plant cell wall components. It has hydrophobic binding capacity. It is not fermented by colonic microflora.	Mature root vegetables such as carrots. Wheat and fruits with edible seeds such as strawberries.
β Glucan	It is a polymer of glucose with mixed glucosidic bonds of both the β (1 – 3) and β(1 – 4) types.	It is soluble and hydrate, well forming viscous solutions and are often referred to as food gums or mucilage.	Grains, especially barley and oats.
Gums	Gums are secreted at the site of plant injury. They are comprised of a variety of sugar and sugar derivatives, the important ones being galactose and glucuronic acids. Gums used as food additives: i) Guar gum: It is a linear non-ionic galacto mannan. ii) Gum arabic: Has β (1 – 3) galactose backbone with side chains of arabinose, rhamnose, glucuronic acid, methyl glucuronic acid. iii) Guin karaya: It is a cylindrical complex polysaccharide, partially acetylated and highly branched with galacturonorhamnose chains to which galactose and rhamnose are attached.	They are water-soluble. They are highly fermented by colonic bacteria. It is highly soluble and possess gelling characteristic.	Oat meal, barley and legumes.

These components are present in varying proportions in different plant foods and their content is dependent upon the part of the plant (leaf, root, stem, seed) and maturity. What are the properties of fibre? This is elaborated in the next section

3.8.2. Properties of Fibre

The structural make up of fibre influences its properties which in turn affects the physiologic and metabolic roles. This is well-depicted in the Figure 3.5 given herewith.

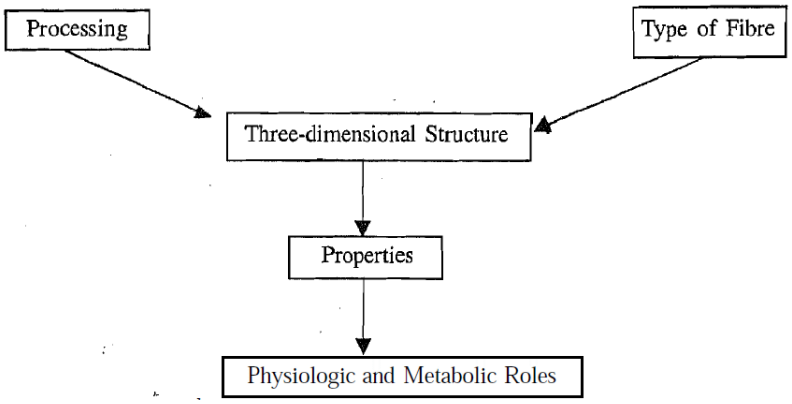

Figure 3.5: Relationship between structure and fibre propertie

The polymeric backbones and / or side chain units determines the fibre's 2-dimensional structure, which influences the 3-dimensional structure i.e. how the polymer interacts with itself and other polymers e.g. because of their two-dimensional linearity, cellulose molecules interact with theinselves via hydrogen bonding to form crystalline regions. Besides the type of fibre, the type and degree of processing will influence its structure and hence its profiles

Significant properties / characteristics of dietary fibre that affects its role ar

1) Solubility in water
2) Hydrationlwater holding capacity and viscosity
3) Adsorptive attraction (ability to bind organic and inorganic molecules)
4) Degradability or fermentability by intestinal microflora

Let us briefly review these properties.

1) **Solubility in Water**: Fibres that dissolve in hot water are soluble and those that do not, are insoluble. Several structural features affect solubility. We shall not go into the details of these features since it is not within the purview of this course, we will however, study the functions of soluble and insoluble DF.

   Generally soluble fibre:

   delays gastric emptying;

   increases the transit time (slower movement) through the intestine; and decreases nutrient absorption (glucose).

   Insoluble fibre:

decreases (speed up) intestinal transit time, and

increases faecal bulk.

We will now move on to the next characteristic of DF i.e, water holding capacity and viscosity.

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Water Holding/H ydration Capacity (WHC) and Viscosity: WHC refers to the 'ability of fibre to bind water', just as dry sponge does when soaked in water. WHC of the fibre is influenced by a variety of factors. These are listed as

solubility

- pH of the gastrointestinal tract,
- size of the fibre particles

Many water-soluble fibres such as pectin, gums and some hemicelluloses have a high WHC. Further, pectin, gums and mucilage form viscous, solutions with the gastrointestinal tract. Cellulose and lignin have a low WHC.

These fibres

- delay emptying of food from stomach;
- reduce mixing of gastrointestinal conte~ltsw ith digestive enzymes;
- reduce enzyme function;
- decrease nutrient diffusion rate and delayed nutrient absorption; and
- alter small intestine transit time

3) **Adsorption or Binding ability**: Some fibre coinponents have the ability to bind (adsorb) substances in the gastrointestinal tract. Wheat bran, guar gum, mannan and isolated lignin have been shown to bind bile acids in small intestinal contents. In humans, pectin, guar gum, oat bran and wheat bran have been shown to increase faecal bile acid excretion. Among the fibre components, pectin and lignin seem to have the greatest ability to adsorb bile acids.

Mechanisms suggested for bile acid adsoi-ption are:

hydrophobic interactions between lignin and bile acids, hydrogen binding between bile acids and pectins, and

fibre (phenolic and uronic residues) inay sequester or even chemically bind bile acids particularly when PI-I in Iiunen is low.

Physiological effects of ingestion of fibres with adsorption properties are

Diminished absorption of lipids: Within the small intestine, bile acids and phospholipids are required for micelle formation and subsequent digestion and absorption. Hence, interaction between bile acid and fibre reduces lipid absorption.

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Increased faecal excretion of bile acids absorbed to fibre cannot be reabsorbed and recirculated.

- hypocholesterole~nic properties, and
- altered mineral balance.

4) **Fermentability or. Degradability**: As you are aware that colon contains over 400 known species of bacteria that exist in a symbiotic relationship with the host. All fibres are broken down to some extent by these microorganisms. Fermentation depends on the accessibility of the molecules to the microorganisms, which in turn depends on physical properties particularly solubility. Soluble fractions especially pectin, gums, mucilages and algal polysaccharides are very accessible and ferment rapidly. Insoluble fibre fraction ferment much more slowly.

The first step in fermentation is the breakdown of polysaccharides, oligosaccharides and disaccharides to their monosaccharide subunits by hydrolytic enzymes of bacteria. Monosaccharide are further converted to various end products as seen in Figure 3.6.

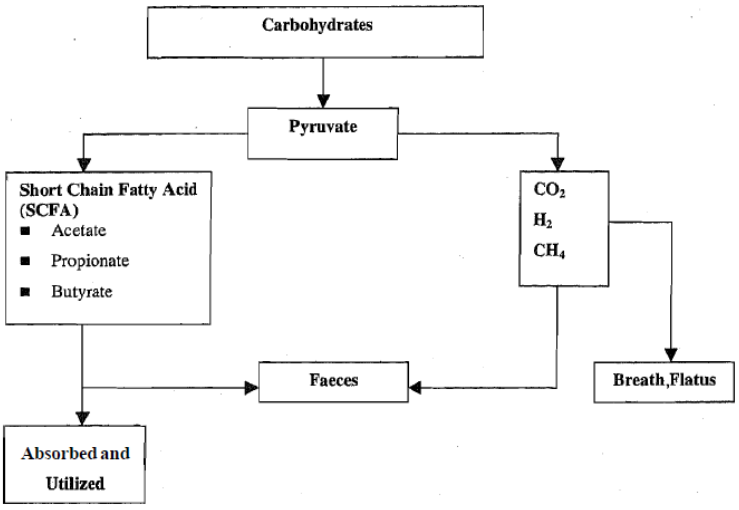

Figure 3.6: Overview of carbohydrate fermentation on colon.

According to the calculations by Cummings and Macfarlane, if approximately 20 g of fibre is fermented in the colon each day, 200 mM SCFA will be produced, of which 62% will be acetate, 25% propionate and 16% butyrate. Of these, butyrate is almost completely consumed by the colonic mucosa, while acetate and propionate enter the portal circulation. The mechanism by which SCFAs cross the colonic mucosa is thought to be a saturable process-passive diffusion of unionized acid into mucosal cells.

In addition to these acids, other products of fibre fermentation are hydrogen, carbon dioxide and methane gases (refer to Figure 3.6) that are excreted as flatus or expired by the lungs.

We will see in the next section that fermentability of dietary fibre is an important property linked to physiological effects.

3.8.3 Effects of Fibre

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After reviewing the properties of fibre, we will now study various physiological effects of fibre, as it passes through the gut. The effect of dietary fibre in the intestinal tract depends on the type of fibre ingested (physicochemical / physical properties), the physical state of subjects and their previous diet, as well as, other components of diet.

Dietary fibre has major effects on:

a) Satiety: Several investigators have speculated that ingestion of a high fibr food induces a feeling of satiety, reduces meal size and food intake. Fibres forming viscous gels slow the rate of gastric emptying and create a feeling of postprandial satiety.

b) Nutrient Absorption: Inclusion of fibre has been shown to retard the absorption of some nutrients. The inclusion of viscous polysaccharides reduces the postprandial glucose level concentration. Guar gum and pectin have been shown to be beneficial in controlling hyperglycemia. Increasing the viscosity of gastrointestinal contents delay absorption in a number of ways. These include:

inadequate mixing of luminal contents due to increased viscosity may slow the movement of digestive enzymes to their substrate thus delaying digestion; and

viscous properties inhibit the access of nutrients to the epithelium. Nutrients have to diffuse across the thin, relatively unstirred layer of flui lying adjacent to epithelium. This is achieved by intestinal contractions, which create convection currents, thus bringing the material from the centre of the lumen close to the epithelium. Increasing the viscosity of the luminal content impairs convective effects and thus delays absorption.

The absorption of nutrients is also reduced by mechanisms other than increasing the viscosity of gastrointestinal content. These mechanisms are:

Soluble fi res (pectin, guar gum, oat bran), as well as, insoluble fi relignin, may affect lipid absorption by their ability to adsorb fatty acids and cholesterol, thereby inhibiting their incorporation in miscelle. Further adsorption of bile acids to these fibres reduces the availability of bile acids for micelle fonnation.

In case of unrefined whole plant material, the nutrients are sequestered within.the cellular matrix and hence unavailable for absorption. Grinding of food material and thorough chewing can influence absorption.

The altered mineral availability associated with diets high in fibre appear to be due to binding of metal ions. Fibres which possess uronic acid

(pectins, hernicellulose gum) can form cationic bridges with minerals. Lignin, with both carboxyl and hydroxyl groups, can adsorb minerals. Certain constituents of plants e.g. phytates, silicates and oxalates also chelate divalent cations. However, the overall effect that a fibre will have on mineral balance will depend on the composition of diet and degree of fermentability of fibre.

SCFAs (short chain fatty acids) have a stimulatory effect on sodium absorption from colonic lumen. The unionized SCFA crosses the epithelial cell where it disassociates. The hydrogen ion is then moved back into the lumen in exchangefor sodium. Thus, SCFAs provide a powerful stimulant to sodium and water absorption.

c) Integrity of gut/colon: Dietary fibre especially fermentable fibres, play an important role in maintaining the integrity of gut. SCFAs generated during fermentation stimulate the proliferation of mucosal cells in the gut and thus maintains its integrity.

Butyrate serves as a preferred energy source for colonic cells and regulates colonic cell proliferation.

Also, SCFAs acidify the colon thus reducing the solubility of bile acids. Further, the activity of 7 a-dehydroxylase diminishes which decreases the conversion of primary bile acids to secondary bile acids. These changes may protect against colon cancer.

d) Stool weight and laxation: The amount of stool excreted varies markedly from individual to individual and in an individual over a period of time. Faeces are complex and consist of water, unfermented fibre, excreted compounds and bacterial mass. Of the dietary constituents, dietary fibr has been shown to influence the stool weight to a great extent

The ability of different types of fibres to increase faecal bulk depends cn a complex relationship between the chemical and physical properties of the fibre and the bacterial population in the colon. In general, faecal bulk increases as fibre fermentability decreases

The mechanism by which a fibre increases stool weight is through the water- holding capacity of unfermentedfibre. Animal and human studies have indicated that cereal fibres have the greatest faecal bulking power. Wheat bran added to the diet increases stool weight in a predictable linear manner and decreases intestinal transittime. Besides quantity, the particle Size is also important. Coarsely ground wheat bran has little or no effect and may even be constipating. Fibre may influence faecal output by another mechanism. Colonic microbial growth may be stimulated by ingestion of fermentable fibre sources. Bacteria are an important component of faecal mass. However, increase in weight does not always occur from eating these fibres. Some laxative effects may be due to volatile SCFAs produced during fermentation. Osmotic effects of these fermentation products may also be important but this mechanism is not yet well defined

e) Other effects: In addition to all the physiological effects mentioned above, dietary fibre may exert other effects. Acetate and propionate enter the portal circulation, thus sxtending the effects of dietary fibre beyond the intestinal tract. Initial in-vitro experiments have indicated that cholesterol synthesis by isolated hepatocytes is inhibited by propionic acid. However, a wide variety of data from human and animal studies do not consistently support this finding. Thus, whether inhibition of cholesterol synthesis by propionate occur in-vivo at physiological concentration is not clear. After knowing the effects of dietary fibre, we will now very briefly review some of the potential health benefits of fibr

3.8.4 Potential Health Benefits of Dietary Fibre

A number of expelimental studies in animal models, as well as, epidemiological studies have established protective role of dietary fibre against chronic degenerative diseases. Its relation with colon cancer and cardiovascular diseases will be discussed in this section.

Dietary fibre and colon cancer

The relationship between colorectal cancer and dietary fibre remains complex. Although a cause-and-effect relationship between fibre and colon cancer has not been established, the majority of epidemiological studies (descriptive, case-conk01 and cohort) support an inverse relationship between consumption of vegetables and fruits and colorectal cancer risk. Fruits, vegetables and grains, in addition to fibre, also contain a variety of anticarcinogenic compounds, which may contribute to this protective effect. Epidemiological evidence that whole grains protect against colorectal cancer is also strong. However, evidence from prospective, large epidemiological studies for protective effect of dietary fibre on colorectal cancer is not strong.

Several plausable mechanisms have been formulated by which fibre may provide protection against colon cancer. These include:

Fibre that increases stool bulk results in the dilution of carcinogens. Fibre also decreases transit time thereby reducing the interactions of carcinogens with colonic mucosal cells.

Fibre binds potential carcinogens.

High bile acid concentrations are associated with increased risk of colon cancer.

Fibres adsorb bile acids, thereby reducing the risk.

Fibre by providing fermentable substrate to colonic rnicroflora, alters species and number of microorganisms which may inhibit proliferation of tumor cells or conversion of procarcinogen to carcinogens.

Fermentation to SCFAs, reduces the pH, which in turn reduces synthesis of secondary bile acids. These bile acids have been shown to promote tumors.

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Butyrate has been shown to have an effect on chromatin structure and thus could slow the proliferation and differentiation of cancer cells. Butyrate induces apoptosis (disintegration of cells).

Lignin may act as a free radical scavenger, thus reducing the risk of cancer.

Further, fiber has been shown to lower serum oestrogen concentrations, and therefore may have a protective effect against hormone-related cancers. Recent studies have shown a decreased risk of endometrial cancer, ovarian cancer, and prostate cancer with high fiber intakes. More research is needed before conclusions can be drawn on these relationships.

From our discussion above it is evident that dietary fibre by different mechanisms mentioned above can play a role in reducing the risk of cancer. Let us now get to know the relationship between fibre and cardiovascular disease.

Fibre and Cardiovascular Disease (CVD)

The role-df dietary fibre in modulation of blood lipids was demonstrated by Keys and his co-workers in a series of experiments conducted during 1960's. Later Trowell supported the protective effect of dietary fibre against hyperlipidemia and ischemic heart disease.

An inverse relationship between CVD and dietary fibre has been shown in many prospective and epidemiological studies and cross-sectional population survey. However, uniform results have not been yielded across studies. Studies in which diets were modified to reduce fat and increase carbohydrate and fibre level have shown favourable impact on the incidence and regression of CVD. Evidence supports a protective effect of dietary fiber for CHD, particularly viscous fibers that occur naturally in foods, which reduce total cholesterol and LDL cholesterol concentrations. Reduced rates of CHD were observed in individuals consuming high fiber diets. These studies used fiber-containing foods; fiber supplements may not have the same effects.

The type of fiber is important, oat bran (viscous fiber) significantly reduces total cholesterol, but wheat bran (primarily non-viscous fiber) may not. Viscous fibers are thought to lower serum cholesterol concentrations by interfering with absorption and recirculation of bile acids and cholesterol in the intestine and thus decreasing the concentration of circulating cholesterol. These fibers Inay also work by delaying absorption of fat and carbohydrate, which could result in increased insulin sensitivity and lower tiiacylglycerol concentrations, Dietary fiber intake has also been shown to be negatively associated with hypertension in men but not women. Fiber intake was shown to have an Inverse relationship with systolic and diastolic pressures.

Thus, it is important to note that with respect to CVD, only soluble fibres which are also viscous have been shown to reduce serum cholesterol. This effect is not simple but could be due to multiple factors operating simultaneously. Possibly

dietary fibre displaces fat from the diet. Also polyunsaturated fatty acids consumed in conjuction with fibre play a role. Some fibres reduce the reabsorption of bile acids in the ileum, thus affecting the enterohepatic circulation. Enterohepatic pool is renewed by increased synthesis of bile acids from cholesterol, which in-turn reduces body cholesterol. Fibres such as oat bran and pectin may decrease absorption of dietary cholesterol by altering the composition of bile acid pool. Since exogenous cholesterol represents only a small proportion of the body's cholesterol, this mechanism may contribute partially to the fibre-induced hypocholestermia.

Data is available from some animal studies, which indicate that endogenous cholesterol synthesis is affected by feeding dietary,' fibre. HMG CoA reductase, the rate limiting enzyme in cholesterol biosynthetic pathway is inhibited by deoxy cholic acid (DCA) as compared to cholic acid or chenodeoxycholic acid. Administration of certain fibres increases the proportion of DCA in bile acid pool. The importance of this mechanism needs to be studied in humans.

All these factors may contribute to the hypocholesterolemic effect of fibre, but the relative importance of each is not well known. Further, many natural plant constituents have been shown to affect lipid metabolism. These components are frequently present in dietary fibre sources and. may confound effects of dietary fibre. A diet that prevents CVD or slows its progression is the one which is low in fat and high in complex carbohydrates. Such diets, which are minimally processed, are high in dietary fibre and may contain other hypocholestermic components like phytoesterogens.

So, we have seen the benefits of fibres, as well as, its role in preventing the disease like cancer and CVD. But is there a minimum amount of daily fibre intake or we can consume much as Me like? Let's find out in the next section, what is the desirable level of fibre intake as recommended by the Nutritional Institutes/ Associations.

3.8.5 Recommended Intake of Fibre

A minimum of fibre intake of 20 g/day is recommended by the American Dietetic Association (ADA), the National Cancer Institute, US and the Federation of American Societies for Experimental Biology (FASEB).

Alternately, 10-13 g dietary fibre intake per 1000 Kcal also has been suggested by ADA. FASEB, the National Cancer Institute and ADA suggest an upper limit of 35 g/day.

Dietary fibre is now a niandatory component of US food labels.

Thus, dietary fibre is now .recognized as important component of diet and plays an important role in gastrointestinal physiology and has a number of potential health benefits.

Answer the questions given in check your progress exercise 2 and recapitulate what you have learnt so far.

3.9 RESISTANT STARCH

Until 1980's starch was thought to be completely hydrolyzed and absorbed from the small intestine of man, independent of its source, type and preparation. However, about two decades ago, it became apparent that appreciable amounts of starch are not digested and enter the colon. The term 'Resistant Starch' (RS) was coined for this fraction. Recently, RS has been an active area of research because of its potential health benefits especially its effect on the large bowel functions. Therefore, in this section we will talk about what RS is, how RS content of food is' influenced and its beneficial effect

What is RS?

Well, RS is defined as the starch, which escapes enzymatic hydrolysis in the small intestine and passes to the colon where it is fermented by colonic microflora which results in the formation of short chain fatty acids (SCFAs).

From the physiological perspective:

RS is defined as the sum of starch and products of starch degradation not absorbed in the small intestine of healthy individuals,

Thus, starches can be subdivided into 'digestible' and 'indigestible' starch. The former may be hydrolyzed at a particular rate but nevertheless has an ideal digestibility of 100%. On the other hand, indigestible starches (i.e. RS) have an ideal digestibility of less than 100%.

RS can be further sub-classified into 4 classes. The four types of RS and the foods in which they are present are given in Table 3.3.

Table 3.3: Classification of resistant starch

Type	What it Constitutes	Examples of Occurrence
RS1	Comprises of physically inaccessible starches	Partially milled grains and seeds
RS2	Consists of starch in certain granular form, which is inherently resistant to enzymatic digestion	Raw potatoes, green bananas, some pulses
RS3	Includes retrograded starch formed by cooking and then cooling starchy food	Cooked and cooled potato, rice and other high starch products
RS4	Chemically modified starches used in food industry for their technological attributes. Modifications include esterification and etherisation.	Modified starches

In the subsequent sub-sections we shall look at the factors influencing RS content of foods and the potential benefits of RS. We begin by understanding the factors influencing the RS content of foods.

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3.9.1 Factors Influencing RS Content of Foods

Different fractions of RS mentioned in Table 3.3 may be naturally present in some foods or may be generated as a result of industrial or home level processing. The amount of RS produced is influenced by several factors. As we will see in this section that inherent properties of food, ingredients added during processing, as well as, different processing techniques influence the RS content of the food. Some of these factors are discussed here in brief.

i) **Amylose/Amylopectin ratio**: general, foods containing high amylose/ amylopectin ratio lead to higher yield of RS. Arnylose retrogrades very rapidly and results in a material highly resistant to arnylolysis. In contrast, amylopectin undergoes retrogradation more slowly and is almost completely degraded by amylase.

ii) **Water content**: The yield of RS formed in heat-moisture treatment is closely related to water content, which may be an inherent component of food or added during cooking. Generally, optimum water content leads to proper and complete gelatinization followed by retrogradation, thus contributing to the RS.

iii) **Presence of sugar and lipids**: Studies so far show that presence or addition of lipids and sugar reduces RS content.

iv) **Calcium and potassium ions**: Investigations have indicated that the yield of RS in starch gels decreases in the presence of calcium and potassium ions. These ions are adsorbed on starch and prevent the formation of hydrogen bonds between amylose and amylopectin .chains.

v) Polyphenols and phytic acid Polyphenols (catechin, tannic acid) and phytic acid may affect starch digestibility through their interaction with amylose activity and contribute to RS formation.

vi) **Antinutritional factors**: Presence of certain anti-nutrients, such as a-amylase inhibitors, greatly determines the extent of starch hydrolysis and hence the RS content.

vii) **Processing techniques**: Freezing, storage, heating-coolingcycle, baking, flaking, popping increase the RS content while reheating of stored food, germination, fermentation results in reduction. Thus, you have seen that a number of factors influe ce the RS content. It is important to note that at any given time, more than one factor may operate simultaneously thereby influencing the RS in a complex manner

In addition to what is termed as 'chemical' RS i.e. the value obtained by standard analytical procedures, certain factors which may vary from one individual to

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another such as extent of chewing, mastication and intestinal Iransit time may also influence the digestibility.

Therefore, RS determined analytically (in-vitro) need not represent the total RS, occurring 'in-vivo'. The latter quantity is termed as 'physiological RS'. Therefore there is a need to develop analytical procedures that take into account the physiological influences on starch digestibility.

Next, let us learn about the potential health benefits of RS

3.9.2 Potential Health Benefits

Like dietary fibre, RS can also play a potential role in helping to maintain or improve health of an individual. As you have already seen that dietary fibres exert their effects through their physical presence, as well as, through their metabolism by microflora. But in case of RS majority of effects are related to fermentation by colonic bacteria. In fact, unlike some fibres (bran) very little starch appears in the faeces under normal circumstances. Thus, like soluble fibre, RS is fermented in the colon producing SCFAs (acelate, butyrate, propionate) gases and bacterial biomass. However, fenuentation of RS produces higher amounts of butyric acid compared to soluble dietary fibre.

The physiological effects of SCFA's can be summarized as follows. They:

lower the pH in the gastrointestinal tract, which in tum reduces the colonization of pathogenic bacteria (acid-sensitive). Lowering of pH also increases ionization of toxic compound, thereby reducing their absorption,

stimulate colonic blood flow and motor activity,

enhance water and electrolyte absorption,

stimulate colonocyte proliferation,

butyrate is a preferred substrate for colonocyte and contributes to energy needs of the colonic epithelial cell. Acetate and to a lesser extent propionate are absorbed into the system and contribute to energy needs of the host.

butyrate enhances DNA stabilization and repair, induces apoptosis in potential cancer cells and thus promote a normal cell phenotype,

All these effects have a positive influence on intestind function and health and subsequently whole body.

The sum of evidence suggests that RS has beneficial effects on large bowel physiology. Numerous studies in animals have shown that feeding of RS improved indices of bowel health as evident by low pH, high SCFA concentration. Many of these studies were invasive and not practical for humans. Therefore, human studies have relied on indirect measures such as greater hydrogen breath or changes in faecal variables. In humans direct benefit has been observed in cholera patients. Addition of RS to oral rehydration solution (ORS) reduced faecal fluid loss and shortened the duration of diarrhoea. These benefits probably stem from the increased absorption of sodium and water.

It has been proposed that RS may have protective effect against colon cancer. The anticarcinogenic effect of RS may be attributed to the following:

protective effects of butyrate,

reduced concentrations of total and secondary bile acids. Lowering of pH by SCFAs reduces activity of 7 a dehydroxylase,

reduced bacterial ß-glucosidase activity. ß-glucosidases are related to the risk of colon cancer because they release potential chemical carcinogens. A high RS diet has been shown to reduce bacterial ß-glucosidase activity, and

reduced concentration of ammonia. Ammonia has a range of toxic effects. It may damage colonic epithelium, enhance cell proliferation, favour growth of malignant cells in preference to normal cells. The higher amount of carbohydrate available for bacterial fermentation may reduce protein fermentation and in turn ammonia production.

Many of the above observations are made in animals and their relevance to humans needs to be explored.

It has been shown that generally foods high in RS yield low glycemic index values in humans. Also postprandial plasma glucose values have been shown to decrease proportionately with increasing RS content. Thus, a higher RS content could be important in the management of diabetes. Experimental studies in animals and a few human studies indicate that RS may play a regulatory role in post prandial triglyceridemia and in a limited number of cases, in plasma cholesterol concentration. However, more work is warranted in this aspect. Thus, in view of potential health benefits, inclusion of RS in the diet would be beneficial. Ingestion of high starch foods should lead to a substantial appearance of the RS in the large intestine.

The amount of RS can also be increased during processing by modifying the processing parameters without affecting the sensory qualities of food. Alternately, various methods are now available to produce starches high in RS, with desirable properties as food ingredient. Commercial RS has a better appearance and is devoid of certain drawbacks of commercial fibres such as high water holding capacity, viscosity, gritty mouthfeel and characteristic fibre taste.

From our discussion above surely you may have got a deep insight into the functions and the role of RS in our diet. Another non-digestible carbohydrate about which we need to know are the fructo oligosaccharides. What are fructo oligosaccharides? What are its sources, role and properties? Let us read and find it out

3.10 FRUCTO OLIGOSACCHARIDES (FOS)

FOS are polymers of fimctose, usually attached to an initial glucose molecule. The total number of fructose units range from 2 to 8 and are linked by (2 $\pm$ 1),

linkages. They are naturally present in certain foods like onion, banana, leak, wheat, garlic, chicory root and artichoke. FOS can also be obtained commercially by an enzymatic action on sucrose. Like other non-digestible oligosaccharides, they resist hydrolysis by human digestive enzymes. They enter the cecum without significant changes, where they are fermented by the resident microflora into short chain fatty acids, lactic acid, carbon dioxide and hydrogen. They enhance the growth of intestinal flora especially growth of bifidobacteria. Thus, like dietary fibre and resistant starch they exert many health benefits

FOS are low-energy bulk ingredients that have a taste profile similar to that of sucrose. Also their physical and chemical properties match precisely those of sucrose. Thus, they can replace sucrose and have been successfully used in food industry, especially bakew industry.

We will get to know more about FOS later on 'functional foods'. While talking about carbohydrates, you may have realized that some carbohydrates are rapidly digested and absorbed, some are digested slowly while some are not digested at all. Different carbohydrates have different glycemic index. What is glycemic index? What is its significance?

3.11 GLYCEMIC INDEX (GI)

In the previous sections, we have studied that some carbohydrates are rapidly digested and absorbed, some are digested slowly while some are not digested at all. Thus, it is obvious that different carbohydrates will raise blood glucose levels to a different extent. The ability of carbohydrates to raise blood glucose is , referred to as "Glycemic Index" (GI).

GI is a quantitative assessment of foods based on post prandial blood glucose response (i.e. blood glucose level after a meal) expressed as a 'percentage of the response to an equivalent carbohydrate portion of a reference food'. The reference food is white bread with a GI set at 100. Glycemic indices of some foods are given in Table 3.4. Here you can see 2 columns indicating GI. In the first one, the reference food is white bread (Wb), while the second column has glucose (g) as its reference food with a GI of 100.

What is the relevance of knowing about GI of foods? Let us see how this index is helpful in prescribing therapeutic diets. You would realize that the dietary GI provides an indication of the rate at which, carbohydrate foods are digested. High and low GI diets may be a better measure for assessing the physiological effects of dietary carbohydrates than the traditional 'simple' and 'complex' carbohydrate definition. It allows ranking of foods from those which give rise to the highest blood glucose and insulin responses (high glycernic food) to those associated with the lowest blood glucose and insulin responses (low GI foods).

Food	G/ wb	G/ g
Sucrose	92	67
Glucose	138	100
Fructose	32	23
Honey	104	75
Milk	39	28
Beans	40 - 60	30 - 43
Lentils	30 - 40	22 - 30
Pasta	50 - 70	36 - 51
Potatoes	120	87
Banana (ripe)	85	62
Banana (under-ripe)	43	31
Oranges	62	45
Grape fruit	36	26
Tomatoes	13	9

G/ wb - Standard food White bread

G/ g - Standard food: Glucose $G/g = \frac{G/wb}{1.38}$

Table 3.4: Glycemic indices of some foods

This index integrates multiple influences on glucose availability and is proposed as a means for prescribing diabetic and energy controlled diets. We will learn the practical application of this concept in the Clinical and Therapeutic Nutrition Course in Unit 10 as mentioned above. Let us get to learn about the factors which influence GI of foods next.

3.11. 1 Factors Affecting GI of Foods

A variety of factors affect GI of foods. The factors which affect the rate of glucose absorption from starchy foods and therefore the GI value are:

Nature ofstarch: High levels of amylase decreases GI while low levels increase the GI.

Nature of monosaccharide components: High levels of fructose and galactose decrease the GI whereas high levels of glucose increase the GI.

Viscous Fibre: Presence of guar gum and P-glucan reduce the GI.

Cooking/processing: Parboiling, cold extrusion decrease the GI while flaking, popping increase it

Particle size: Consumption of large particles of starchy foods reduces the GI. On the contrary, grinding of starchy foods results in an increase in the GI.

Ripeness and food storage: Cooling of starchy food before consumption , decreases the GI. Similarly, unripe or under ripped fruits have a lower GI. I

a-amylase inhibitors: Presence of a-amylase inhibitors like lecithin, phytates lowers the GI.,

Nutrients-starch interactions: High levels of protein and fat decreases the GI. Fat and protein appear to modify the glycemic response to a carbohydrate food by slowing gastric emptying and increasing insulin secretion, respectively. However, neither protein nor fat in amounts found in most foods significantly b affect the GI. Protein levels of 30 g and fat levels of 50 g per 50 g of available carbohydrate may decrease the GI.

Now we shall understand the role of GI in chronic disease such as diabetes, coronary heart disease and cancer.

3.11.2 GI in Chronic Diseases

In addition to serve as an aid in planning diets for diabetics, GI of diets has been linked to a number of chronic diseases. Several health benefits appear to exist by reducing the rate of carbohydrate absorption by means of a low GI diet.

The health benefits include reduced insulin demand, improved blood glucose control and reduced blood lipid levels. All these factors play an important role in the prevention and management of chronic diseases including diabetes, coronary heart disease and certain cancers. Epidemiological evidence suggests a direct association between GI and risk of diabetes, coronary heart disease (CI-ID), obesity and certain cancers.

Let us first deal with diabetes, the most widespread disease. In some studies, a positive association between GI, Glycemic load (GL i.e. product of the average GI and total carbohydrate intake) and risk of type II diabetes has been observed. This could be because high GI foods lead to a rapid rise in blood glucose and insulin levels. Hyper insulinemia in turn may down regulate insulin receptors and therefore reduce insulin efficiency resulting in insulin resistance. On the contrary, low GI foods result in reduced peak insulin concentrations and reduced insulin demand thus decreasing the risk of type II diabetes.

Next, we move on to CHD.

As similar to studies conducted on diabetes certain epideiniological evidence suggests that low GI diet may reduce the risk of CHD independently. The possible positive effects of a low GI diet in the prevention of CHD may be due to improvements in blood lipid profile, insulin levels, thrombolitic factors and endothelial function. Further, it has been suggested that generally low GI foods are associated with greater satiety as compared to high GI foods or meals. High GI foods result in fast carbohydrate absorption, large blood glucose and hormonal (insulin/glucagon) fluctuations and reduced satiety. All these factors may favour over eating and weight gain. Thus, low GI food appears to play a role in prevention

and management of obesity, which is a risk factor for many diseases.

Available evidence thus suggest that low-fat, high-carbohydrate diets advocated by the heath organizations can be further improved by switching from a high GI to a low GI diet. Finally, we shall end our discussion on carbohydrates with a brief insight into the kind of modifications recommended for carbohydrate intake for specific disorders.

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3.12 MODIFICATION OF CARBOHYDRATE INTAKE FOR SPECIFIC DISORDER

In our daily diet almost 60-70% of energy is contributed by carbohydrates. Majority of them are comprised of starch (from cereals, millets, pulses and root vegetables), while a small amount is also contributed by sucrose (sugar), glucose and fructose (fruits), as well as, lactose (milk and milk products). However, there is a need to modify carbohydrate intakes in certain disorders such as:

1) Lactose intolerance: This has been covered under the section on digestion and absorption earlier. We learnt that in case of lactose intolerance, the ingestion of lactose leads to passage of the sugar to the large bowel, where it is fermented to produce SCFA and gases, which causes discomfort. Lactose is present in daily products such as milk, cheese, yoghutt, ice cream etc. Hence, these foods need to be avoided.

2) Diabetes mellitus: You are aware that diabetes may be diagnosed as an exaggerated response in blood glucose concentration following ingestion of a fixed amount of glucose (glucose tolerance test). The most common forms of diabetes are insulin-dependent diabetes mellitus (IDDM or type I diabetes) and non-insulin-dependent diabetes mellitus (NIDDM or type 2 diabetes). IDDM results from the autoimmune destruction of the a-cells the endocrine pancreas, the consequence of which is insulin insufficiency. In this, the patient requires exogenous supply of insulin. The amount of carbohydrate and frequency of feeding is modified and depends on the insulin dose, type of insulin and the weight of the person.

In contrast, expression of NIDDM is due to lifestyles (excessive energy intakes and low physical activity) resulting in obesity, Early stages are characterized by insulin insensitivity/ resistance. Management of these patients involves maintenance of ideal body weight. In both types of diabetes, the diet should be high in fibre, and in complex carbohydrates and low in simple sugars. Foods with low glycemic index should be encouraged. For detail regarding principles of planning diet for diabetes we suggest you look up the Unit/ Practical in the Clinical and Therapeutic Theory and Practical Courses (MFN- 005, MFNL-005), respectively. Now tlY to answer the questions given in the check your progress exercise 3 to ascertain your knowledge regarding the issues discussed so far.

3.13 LET US SUM UP

In this unit, we studied about carbohydrates, its functions and types. We learnt that carbohydrates provide energy (4 cal/g). They are formed by plants in bewildering array of possible single unit and polymer structures.

Humans have the ability to digest only a few of the many possible bonds linking carbohydrate units with each other and with other types of organic molecules. About 80% of edible carbohydrates are absorbed as single glucose and metabolized. For optimum function of nervous system and cells, blood glucose concentrations are tightly controlled by hormones (insulin in the absorptive phase; glucagons, adrenaline and cortisol in the post absolptive phase) utilizing several possible metabolic pathways for glucose anabolism and catabolism.

Depending on the structure, non-digestible carbohydrates pass into the colon. They are fermented in varying degrees to short-chain fatty acids, carbon dioxide, hydrogen and methane in the large bowel, Absorbed short chain fatty acids are metabolized in colonic epithelial, hepatic and muscle cells. Thus, these perform a number of beneficial functions Intakes of optimum amounts of different types of carbohydrates are associated with good health through effects on energy balance, digestive function, blood glucose control and other risk factors for several chronic diseases.

3.14 GLOSSARY

Apoptosis : disintegration of cells into membrane-bound patticles that are then eliminated by phagocytosis or by shedding.

Degree of polymerization : the length in monomeric or base units of the average linear polymer chain at any time in a polymerization reaction.

Diverticular disease : a condition in which small pouches called diverticulae, develop at the weak spots in the wall of the colon, that eventually bulge out to form pouches.

Glucose transporters : the integral proteins which penetrate and span the lipid bilayer of plasma membrane.

Glycemic index : ability of carbohydrates to raise blood glucose.

Glycemic load : a product of average glycemic index total carbohydrate intake.

Glycosidases : hydrolytic enzymes involved in the digestion of carbohydratres. Also termed as carbohydrases.

Haemorrhoids : also called as piles; these are the small troublesome tumors or swellings with a painful mass of dilate veins in anal tissue.

Hiatus hernia : the protrusion of part of the stomach through the diaphragm.

Homopolysaccharide : a polysaccharide composed of single monosaccharide unit.

Resistant starch : starch which escapes enzymatic hydrolysis in the small intestine and passes to the colon where it is fermented by colonic bacteria and forms SCFA.

Water holding capacity : the ability of fibre to bind water

3.15 CHECK YOUR PROGRESS

1) List some important functions of carbohydrates.

2) Explain the mechanism of absorption of monosaccharide from the gastrointestinal tract.

3) Explain the following:

   a) Starvation or uncontrolled diabetes can lead to ketosis.

   b) ORS always contains sodium chloride and glucose/sugar.

4) What is a Dietary Fibre? What are its components?

5) Explain the physiological effects of ingestion of fibres with respect to

   a) WHC

   b) Absorption property

6) Discuss the effect of dietary fibre on the absorption of nutrients

7) List the mechanisms by which fibres provide protection against colon cancer.

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UNIT

4

PROTEINS

STRUCTURE

4.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

discuss the classification and functions of proteins,

identify the food sources of proteins,

explain the processes of digestion and absorption of proteins,

recognize the methods of estimating the protein quality, as well as, requirements at various stages of life, and

describe the symptoms of protein deficiency

4.2 INTRODUCTION

The term protein was first suggested by Berzelius to describe the complex organic nitrogenous substances found in animal and plant tissues. Proteins form three-fourths of the animal body on a moisture-free basis. They are essential for life processes. All the basic functions of life depend on proteins. Indeed, no form of

life exists without proteins. They are found in every cell, make up the contractile elements and enzymes that catalyze the release of energy for the maintenance of life and there is no physiological function in which they do not participate. Now in this unit let us get familiarized with the chemical nature, digestion, absorption, utilization and other nutritional aspects of proteins.

4.3 PROTEINS - AN OVERVIEW

We just read that proteins are essential for maintaining and sustaining life. What are proteins or what constitutes proteins that make it so important for us? Proteins contain carbon, hydrogen, nitrogen, sulphur and some also contain phosphorous. Proteins are chains of amino acids held together by peptide bonds, when a peptide chain is extended by more and more amino acids, until a chain length of one hundred to several thousand amino acid residues is reached, it is classified as a 'protein'. The nitrogen content of proteins varies from about 14 to 20 percent. The average value of 16 percent is used commonly for converting nitrogen content of food stuffs or tissues into proteins by multiplying with the factor 6.25 (i.e. Crude protein = Nitrogen x 6.25).

4.3.1 Classification

Proteins vary widely in their properties. You may recall reading about the properties of proteins in the Nutritional Biochemistry Course, in Unit 2. We suggest you look up this unit once again now as the information about proteins and their properties given there will supplement your understanding of the functions and other aspects of proteins discussed here in this unit.

Let us consider the two very familiar proteins. One of them is the egg white protein, which is very sensitive. It denatures heating, dissolves easily in water and is quite reactive, while the other one is keratin of nails and hoofs, is wholly insoluble, tough and chemically inert and resistant. Hence, it is not easy to classify proteins.

We simply distinguish proteins which are insoluble and fibrous and function as structural -material (scleroproteins) and globular proteins, those represented by egg white or serum proteins, which are soluble in water or salt solution and consist of spherical molecules. Besides classifying proteins on the basis of soluble and insoluble, proteins have been further classified based on the following attributes:

Classification based on chemical nature

Classification based on chemical properties

Classification based on amino acid conten

A) Classification based on chemical nature

Frequently proteins are classified based on the chemical nature of amino acids

(such as solubility and prosthetic group), as simple, conjugated and derived proteins. Let us get to know each of these.

1) *Simple proteins:*

Simple proteins are those which contain only amino acids or their derivatives and no prosthetic group. They yield only amino acids or their derivatives on hydrolysis. Let us see which are these and where are they found.

a. **Albumins**: Proteins such as egg albumin and serum albumin are soluble in water and coagulable by heat.

b. **Globulins**: These proteins are insoluble in pure water, but soluble in neutral salt solutions. For example, serum globulin, tuberin (potato), arachin and conarachin (peanuts).

c. **Glutelins**: These are insoluble in all neutral solvents but soluble in very dilute acids and alkalis. e.g. glutenin of wheat.

d. **Prolamins**: Proteins soluble in 70-80% alcohol. e.g. gliadin and zein.

e. **Fibrous proteins**: These proteins are characteristic of the skeletal structures animals and also of the external protective tissues, such as the skin, hair,etc. e.g., collagen, elastin and keratin.

f. **Histones**: Soluble in water and insoluble in very dilute ammonia. On Proteins hydrolysis, they yield several amino acids, among which the basic ones predominate. The important proteins of this group are the thymus, Histones and the globin of haemoglobin.

Let's now move on to the next category of proteins i.e. conjugated proteins and its types.

2) *Conjugated proteins:*

Conjugated proteins contain some non-protein substances. Most proteins occur in cells in combination with prosthetic groups and hence are important for the nutritionist. These include:

a) Glycoproteins: Most of the naturally occurring conjugated proteins are glycoproteins. Sugar molecules are covalently bound to them, especially those secreted from the cell. They range in size from a molecular weight of 15,000 to more than one million. The carbohydrate component varies from I to 85%. Glycoproteins with more than 80% of their molecules as carbohydrates are called 'proteoglycans.'

b) Lipoproteins: These are the multi component complexes of lipids and proteins that form distinct molecular aggregates. They contain polar and neutral lipids, cholesterol or cholesterol esters in addition to protein.

The proteins and lipids are held together by non covalent bonds. Lipids are primarily hydrophobic and cannot be easily transported through an aqueous environment as blood. The lipoprotein combination renders the lipid molecule hydrophilic and is transported in the blood to tissues which can use or store the lipids.

c) Nucleoproteins: Nucleoproteins are combinations of nucleic acids and simple proteins, which usually consists of a large number of basic amino acids. Nucleoproteins have very coinplex structures and numerous functional activities. All living cells contain nucleoproteins. Some cells, such as viruses, are composed of nucleoprotein.

d) Other conjugated proteins: The phospho proteins and the metallo proteins are loose (as with phosphate carrying protein) or tight (as with the phosphate in casein or the iron in ferritin) associations of proteins with phosphate groups or such ions as zinc, copper and iron. What are derived proteins? Let us find out next

3) *Derived proteins:*

Derived proteins are the derivatives (f the protein molecule, apparently founded through hydrolytic changes in the molecule. These are either primary or secondary protein derivatives. Let us get to know them.

I) Primary Protein Derivatives: These are the derivatives of the protein molecule formed by hydrolysis involving slight alterations. Examples include:

a) Proteins: These are the insoluble products which result from the incipient action of very dilute acids or enzymes. e.g. casein (curdled milk), fibrin (coagulated fibrinogen

b) Meta proteins: Proteins resulting from the action of acids and alkalis whereby the molecule is sufficiently altered to form proteins soluble in weak acids and alkalis, but insoluble in neutral solvents.

c) Coagulated Proteins: Insoluble proteins which result from the action of heat on protein solutions or the action of alcohol on the protein. e.g. cooked egg albumin or egg albumin precipitated by alcohol.

II) Secondary Protein Derivatives: These are the products of further hydrolytic cleavage of the protein molecule, Examples include:

a) Proteoses:Soluble in water, not coagulable by heat, precipitated by saturating their solutions with ammonium.

b) Peptones: Soluble in water, not coagulable by heat and not precipitated by saturating their solutions with ainmonium sulphate. These represent a further stage of cleavage than the proteoses.

c) Peptides: These are the compounds containing two or more amino acids. An anhydride of two amino acids is called a 'dipeptide', one having three amino acids, a 'tripeptide' and containing several amino acids, a 'polypeptide'. Peptides result from further hydrolytic cleavage of the peptones.

B) Classification based on chemical properties

Depending on their chemical properties and optical activity, the amino acids in proteins are classified under the following heads:

a. Mono amino mono carboxylic acids: Examples include glycine, alanine, valine, leucine, isoleucine, serine and threonine.

b. Mono amino dicarboxylic acids: Examples include aspartic acid and glutamic acid.

c. Diamino mono carboxylic acids: Arginine and lysine.

d. Sulphur containing amino acids: Cysteine, cystine and methionine

e. Aromatic and heterocyclic amino acids: Phenylalanine, tyrosine, histidine, tryptophan , proline and hydroxyproline.

The next classification is based on the amino acid content. Let us get to learn about this classification.

C) Classification based on amino acid conten

Nutritionally, amino acids are classified on the basis of the body's ability to synthesize them — as essential (indispensable and not synthesized in the body) and non-essential (dispensable and that can be synthesized in the body) amino acids. Indispensable amino acids must be a part of the diet while dispensable amino acids need not be present in food. These definitions, however, become blurred at the metabolic level. Lysine and threonine are perhaps the only metabolically indispensable amino acids because they are not transaminated to any nutritionally significant extent.

This is a crucial point because lysine and threonine are the first and second limiting amino acids in cereal proteins. Lysine is the first limiting amino acid in human milk. Glutamic acid and probably serine are the only truly dispensable amino acids since these are the only amino acids which can be synthesized by the reductive amination of the appropriate keto acid. There is a third group of amino acids which are ‘conditionally essential', and are characterized by two features.

Firstly, their synthesis uses other amino acids as carbon precursors and is confined to specific organs. This is an important metabolic distinction from the dispensable amino acids. For' some conditionally essential amino acids, e.g., tyrosine, the precursor is a dispensable amino acid; while for others such as cysteine both an essential amino acid, methionine as sulphur donor and a non essential amino acid, serine are required. At the metabolic level, the organism's

ability to synthesize a conditionally essential amino acid is constrained by the availability of a suitable amino acid precursor.

Secondly, the maximum rate at which their synthesis proceeds may be limited and potentially restricted by developmental or path physiological factors. Thus, very low birth weight infants are unable to synthesize cysteine and proline and lack the ability to synthesize glycine. These factors are important because human milk proteins have low glycine content.

Table 4.1: Classification of amino acid

Essential (indispensable)	Conditionally-essential	Non-essential (dispensable)
Methionine	Tyrosine	Glutamic acid
Tryptophan	Cystine	Alanine
Valine	Aspartic acid	Proline, Hydroxyproline
Isoleucine	Serine	Glycine
Leucine		
Phenylalanine		
Lysine		
Threonine		
Arginine		
Histidinc (only for infants)		

We now know that proteins are composed of amino acids and that proteins differ in their amino acid make-up. Proteins lacking in one or more of the essential amino acids, cannot be utilized to meet the protein requirements of the body hence they are not good quality proteins. The nutritive value of a protein will be high if the amino acid make-up is very similar to that of the body proteins and will be low if it lacks partially or completely any one of the 10 essential amino acids (refer to Table 4.1) or if its amino acid composition is very much different from that of the body proteins. Based on their nutritive value or amino acids make-up, proteins are therefore classified as:

I) Complete proteins — e.g., egg proteins. These proteins promote growth and provide all the essential amino acids.

II) Partially complete proteins — e.g., wheat proteins. These promote moderate growth and partially lack one or more essential amino acids.

III) Incomplete proteins — e.g., gelatin or zein. They do not promote growth and completely lack one or more essential amino acids.

After understanding how proteins are classified, let's move on to sources of protein in our next sub-section.

4.3.2 Food Sources

The important sources of proteins in the diets of low-income groups are cereals and legumes. Meat, fish, eggs and milk are important sources of proteins of high

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biological value. Oilseeds, oilseed meals and soy are rich potential sources of proteins. The protein content of some important foods is given in Table 4.2.

Table 4.2: Protein content of some important foods

Foods	Protein (g/100g)	Foods	Protein (g1100g)
Cereals	6 - 14	Milk	53.5 - 4.0
Legumes	18 - 24	Milk powder (full cream)	26 - 27
Soybean	43	Milk powder (skimmed)	35 - 38
Nuts and oilseeds	18 - 40	Fish	18 - 20
Oilseed meals	45 - 55	Meat and liver	18 - 22
Egg, hen	12 - 13		

We shall continue with our discussions on the metabolism and function of proteins. However, you must first attempt the check your progress exercise given below before proceeding further to recapitulate the learnt concepts.

4.3.3 Digestion, Absorption and Transport

Under this sub-section, we shall learn how proteins that we consume are digested, absorbed and transported to various body tissues We suggest you look up this unit now, This will facilitate your understanding on this topic.

A brief review on the process of digestion, the enzymes involved, their location and target amino acids is present next for your recapitulation.

4.3.3.1 Digestion

The daily protein intake (of about 50-100 g) and the protein of enzymes, sloughed (bled or drop off) epithelial cells and mucins, which are found in the gut is almost completely digested and absorbed. This is a very efficient process and ensures a continuous supply of amino acids to the whole body's amino acid pool. The purpose of protein digestion is to liberate the amino acids of the consumed proteins.

Table 4.3 : Enzymes and their target linkages

Enzyme	Location	Target Linkages
Pepsin	Stomach	Peptide bonds involving the aromatic amino acids
Trypsin	Small intestine	Peptide bonds involving arginine and lysine
Chymotrypsin	Small intestine	Peptide bonds involving tyrosine,tryptophan, phenylalanine, methionine and leucine

Elastase peptidase A	Small intestine	Peptide bonds involving alanine, serine and glycinc
Carboxy peptidase A	Small intestine	Peptide bonds involving valine, pepticlase A leucine, isoleucine and alanine
Carboxy peptidase B	Small intestine	Peptide bonds involving lysine and pcptidase B arginine.
Endopeptidase Aminopeptidase Dipeptidase	Cells of brush	Di and tripeptides that enter the aminopeptidnse brush border of the absorptive dipeptidase cells.

The protein hydrolases, called as peptidases, fall into two categories. Those that attack internal peptide bonds and liberate large peptide fragments for subsequent altack by other enzymes are called the 'end peptidases' and those that attack the terminal peptide bonds and liberate single amino acids from the protein structure are called 'exopeptidases'. The exopeptidnses are further subdivided according to whether they attack at the carboxy end of the amino acid chain (carboxy peptidases) or the amino end of the chain (amino peptidases).

The initial attack on the intact protein is catalyzed by the intestinal epithelial cells. The hydrolysis of proteins in the gastro- intestinal tract is completed by proteases secreted in the gastric juice and pancreatic juice and also by proteases in the intestinal mucosa. The digestion of protein starts only in the stomach. In contrast to carbohydrate and lipid digestion, which is initiated in the mouth with the salivary amylase and the lingual lipase, protein digestion does not begins until the protein reaches the stomach and the food is acidified with the gastric hydrochloric acid (HCI). Let us get to know about gastric digestion in greater details.

Gastric digestion

If gastric HCI production is low and not adequate to maintain the pH of the stomach contents between 2 and 3, protein digestion in the stomach may be negligible. This will happen in achlorhydria (a condition characterized by the failure of the intragastric pH to fall to less than 4.0), achylia gastrica (absence of gastric juice, partial or complete) or pernicious anaania. The I-ICI serves several functions in gastric digestion. It acidifies the ingested food, killing potential pathogenic organisms. However, not all pathogens are killed. Some are acid-resistant or are so plentiful in the food that the amount of gastric acidification is insufficient to kill all of the pathogens. HCI also serves to denature the food proteins, thus making them more vulnerable to attack by the proteolytic enzymes present in the gastric juice namely, pepsin and endopeptidase (it hydrolyzes peptide bonds in the interior of the protein molecule). Pepsin has a strong clotting action on milk. This factor

is important in the digestion of milk proteins in infants. The optimum pH of pepsin action is about 2.0.

Actually pepsin is.not a single enzyme. It consists of pepsin A which attacks peptide bonds involving phenylalanine or tyrosine and several other enzymes which have specific attack points. The pepsins are released into the gastric cavity as pepsinogen. When the food entering the stomach stimulates HCI release and the pH of the gastric contents fall below 2, the pepsinogen looses a 44-amino acid sequence. The activation of the pepsins from pepsinogen occurs by one of the two processes—autoactivation and autocatalysis. Let's understand what these are. The first one is called autoactivation and occurs when the pH drops below 5.

At low pH, the bond between the 44^{th} and 45^{th} amino acid residue falls apart and the 4th-amino acid residue (from the arnino terminus) is liberated. The liberated residue acts as an inhibitor of pepsin by binding to the catalytic site until pH value of 2 is achieved. The inhibition is relieved when this fragment is degraded. Degradation occurs at pH 2 or by the action of pepsin. Thus, pepsin hydrolyzes mainly peptide bonds containing phenylalanine, tyrosine or tryptophan and leucine and other acidic amino acids and since food remains in the stomach for a limited time, dietary proteins are hydrolyzed mainly into a mixture of polypeptides.

$$\text{Dietary proteins} \xrightarrow{\text{Pepsin}} \text{Polypeptides}$$

'Autocatalysis' occurs when already active pepsin attacks the precursor pepsinogen. This is a self-repeating process and serves to ensure ongoing catalysis of the resident protein. The cleavage of the 44-amino acid residue, in addition to providing activated pepsin, also serves as a signal peptide for cholecystokinin release in the duodenum. This sets the stage for the subsequent pancreatic phase of protein digestion.

Proteolysis in the intestines: The main digestion of polypeptides produced in the stomach takes place in the intestines. Cholecystokinin stimulates both the exocrine pancreas and the intestinal mucosal epithelial cells to release its digestive enzymes. The proteases involved in the digestion are trypsin, chymotrypsin and carboxypeptidase secreted in pancreatic juice and arnino peptidases present in the intestinal mucosa. The intestinal cells release an enzyme, enteropeptidase or enterokinase, which serves to activate the psotease trypsin, released as trypsinogen by the exocrine pancreas.

This trypsin not only acts on food proteins, it also acts on other preproteases released by the exocrine pancreas, thus activating them. Thus trypsin acts as an endoprotease on chymotrypsinogen by releasing chymotrypsin, on proelastase by releasing elastase and on procarboxypeptidase by

releasing carboxypeptidase. Trypsin, chymotrypsin and elastase are all endoproteases, each having specifici y for particular peptide bonds. Trypsin and chymotrypsin act at pH 7.4 to 8.0. Trypsin hydrolyses mainly peptide linkages containing tyrosine or phenylalanine.

$$\text{Proteins and polypeptides} \xrightarrow{\textit{Trypsin and Chymotrypsin}} \text{Peptides} + \text{Amino acids}$$

Each of the three proteases i.e. trypsin, chymotrypsin and elastase have serine as a part of their catalytic site so that any compound that ties up the serine will inhibit the activity of these proteases. One such inhibitor, di-isopropylphosphofluoridate reacts with serine and stops protein digestion. Through the action of pepsin, trypsin, chymotrypsin and elastase, nuinerous oligopeptides are produced which are then attacked by the amino and carboxypeptidases of the pancreatic juice and those on the brush border of the absorptive cells. Carboxypeptidase A hydrolyzes the end group in peptides containing aromatic or aliphatic amino acid, thus releasing free amino acids as shown herewith. Carboxypeptidase B hydrolyzes peptides containing arginine and lysine residues. The intestinal mucosa contains a group of amino peptides which complete the hydrolysis of peptides to amino acids. The intestinal mucosa also contains tripeptidase, dipeptidase, etc., which hydrolyze tri and dipeptides as highlighted in the reaction given herewith:

$$\text{Peptides} \xrightarrow{\text{Carhoxy peptidnsr}} \text{Amino acids}$$

$$\text{Dipeptides} \xrightarrow{\text{Dipeptirlase}} \text{Amino acids}$$

$$\text{Tripeptides} \xrightarrow{\text{Tripeptidase}} \text{Amino acids}$$

Thus, the ultimate products of digestion of proteins, namely, amino acids are liberated from these chains one by one and are absorbed and appear in the portal blood.

4.3.3.2 Absorption

Although single amino acids are liberated in the intestinal contents, there is insufficient power in the enzymes of the pancreatic juice to render all of the amino acids singly for absorption. The brush border of the absorptive cell, therefore not only absorbs the single amino acid but also the di- and tri- peptides. In the process of absorbing these small peptides, it hydrolyzes them to their constituent amino acids. There are specific transport systems for each group of functionally similar amino acids and peptides. The site of absorption is the 'small intestine'. The process of absorption requires energy. It is observed that L-isomers (natural isomers) of amino acids are more rapidly absorbed than D-amino acids and are hence biologically more

important. What are L and D isomers of amino acids? These isomers are transported by an active carrier system against a concentration gradient. Similarly, neutral amino acids are mote rapidly absorbed than the basic amino acids and in general, amino acids compete with one another for absorption. In several instances, the carrier is a shared one, that is, the carrier transports more than one amino acid. Vitamin BG is essential for amino acid absorption .

4.3.3.3 Transport of Amino Acids

More than one transport or carrier system functions in the absorption of amino acids. The active carrier system for neutral amino acids shares a common membrane carrier. Neutral amino acids and those with the short or polar side chains (serine, threonine and alanine) are transported by the shared carrier system. The basic amino acids, that is, lysine, arginine and histidine share a carrier system with cystine.

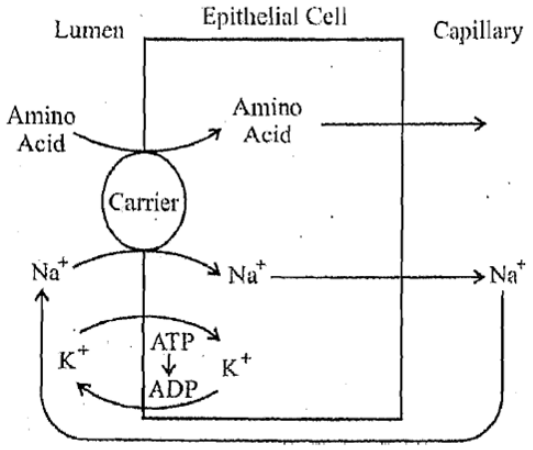

Figure 4.1: Carrier-mediated sodium-dependent amino add transport

The amino acid transport is dependent on the Na+ ion. The dependence of amino acid transport on Na+ ion suggests a direct interaction between the carrier and Na+ ion. This is similar to that observed in the absorption of glucose, as you may recall studying in the last unit. The amino acid associates with the carrier and Na+ ion in the microvilli and the complex travels to the inner side of the membrane where it dissociates, releasing the amino acid and Na ion into the cytoplasm. Thus the amino acid leaves the absorptive cell with sodium. The carrier, Na ion is re circulated back to the lumen for reuse. As sodium enters the cell, potassium is pumped out via a Na+ K+ ATPase system. As sodium leaves the cell, potassium flows back in and the electrolyte balance is maintained. The Na+ ion is then actively transported out of the cell. So we have looked at the digestion, absorption and Transport

of proteins and amino acids.

4.3.4 Functions

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Each of the various proteins in the body serves a specific function in the maintenance of life. Any loss in body protein, in reality, means a loss in cellular function. In contrast to lipids and carbohydrates, proteins have no true body reserve. Humans when deprived of or insufficiently supplied with protein, compensate for this dietary deficiency by catabolizing some, but not all, of their tissue functionality. Cells, tissues, organs and whole systems cannot exist without proteins serving their various functions.

So let us get to know the varied function of proteins in our body. We begin our discussion on functions, first with the body-building function.

1) **Body-building functions of proteins:** The primary functions of proteins, as you might be aware, is tissue growth and maintenance. Protein contains amino acids the building blocks - that our bodies use to build and maintain muscles, bone, skin, blood and other organs. Thus, proteins play an important role in growth and body-building. For the constant growth of human beings from birth to adulthood, a regular supply of dietary protein is required. Now this does not mean that the body does not require proteins once the growth ceases. During adulthood, worn out cells, body tissues need continuous replacement. Proteins are required for maintenance of our body. Proteins, therefore, are crucial and required throughout our life span for growth, body-building and maintenance.

2) **Protein as an energy source:** Proteins contribute to the body's energy need. If diet does not furnish enough calories from carbohydrates and fats, proteins are catabolized to give energy. One gram protein yields 4 Kcal. But, what is important for us is to understand is that this is not the mqior fimction (f proteins. This only happens when, as mentioned earlier, the diet does not supply enough energy-giving nutrients.

3) **Proteins as enzymes:** From conception to death, living cells use oxygen and metabolize fuel. Cells synthesize new products, degrade others, and generally are in a state of metabolic flux. For these processes to occur, catalysts are needed to enhance each of the many thousands of reactions occurring in the cell. These catalysts called 'enzymes' are proteins. Enzymes make up the largest and the most specialized class of proteins. Each enzyme is unique and catalyzes a specific kind of reaction. In the cell, enzymes are found in cellular compartments (cytoplasm, nucleus, mitochondria, etc.), as well as, the membranes within and around the cell wall. The location of an enzyme is one of its characteristics and dictates, in part, its role in

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metabolism. Many enzymes ate complex proteins; they consist of a protein component and a prosthetic group. The protein part is called apoenzyme and the prosthetic group, 'coenzyme'.

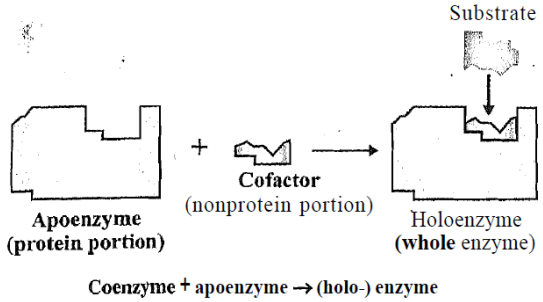

Figure 4.2: Holo enzyme

Enzymes consist of specific sequences of amino acids. The catalytic function of an enzyme is intimately related to its amino acid sequence. Enzymes must possess a shape that will complement the reactive molecular shape of the substrate in the same way as a key fits into a lock. This is commonly referred to as 'lock and key mechanism'. This shape is a function of the enzyme protein's primary', secondary, tertiary and quaternary structure. In the same way, substrates should also have specific shapes in order to be catalyzed by their respective enzymes.

$$\text{Enzyme} + \text{Substrate} \rightleftharpoons \text{Enzyme} — \text{Substrate}$$

$$E + S \rightleftharpoons E\,S$$

This is the reason why only D-sugars or L-amino acids can be metabolized by mammalian cells. These stereo-isomers conform to the shape required by the enzyme which serves as its catalyst. While enzymes show absolute specificity, the specificity generally applies to the entire molecule. If however, the substrate is large and complex, the structural requirements are less stringent in that only that part of the substrate involved in the enzyme-substrate complex should have the appropriate molecular arrangement. The portion of the substrate not involved in the reaction need not be the appropriate conformation.

Some enzymes are specific for only one substrate; others may catalyze several related reactions. While some are specific for a particular substrate, others are specific for certain bonds. This is called 'group specificity'. For example, glycosidases act on glycosides, pepsin and trypsin act on peptide bonds and esterases act on ester linkages. Within this group, certain enzymes exhibit greater specificity. Chymotrypsin preferentially acts on peptide bonds in which the carboxyl group is a part of the aromatic ainino acids (phenylalanine, tyrosine or tryptophan). Enzymes such as carboxypeptidase catalyze the hydrolysis of the carboxy-terminal or amino-terminal amino acid of a polypeptide chain.

This bond specificity, rather than molecular specificity, is useful to the animal in that it reduces the number of enzymes needed within the organism. Incidentally, the above enzymes are very useful to the protein chemist in his / her determination of the amino acid sequence of a given protein. Cells synthesize enzymes in much the same fashion as they synthesize other proteins; yet enzymes are relatively short lived. Cells must continually synthesize their enzymes if they are to survive.

4) **Proteins as carriers:** A large variety of compounds are carried in the blood between tissues and organs of the body. Some of the compounds require specific protein for their transport. Not only is this specific protein necessary for the transport of compounds insoluble in blood, but it is also necessary to protect these compounds from further reactions that take place during the transport process. Some of the membrane proteins are carriers and some are both carriers and enzymes. Both intracellular and extracellular carriers have been identified.

The plasma proteins which can have a carrier function are the albumin and the α- and ß-globulins. The best studied of the plasma carriers are those associated with the transport of lipid (called lipoproteins), since these lipoproteins (carriers plus lipids), when levels are elevated, appear to be related to the development of a variety of diseases. These lipoproteins comprise of about 3% of the plasma proteins.

They are the loose associations of such lipids as phospholipids, triacylglycerols and cholesterols and represent an example of how proteins function as carriers. The lipids they carry are either from the diet or are synthesized de novo in tissues, such as the liver.

The globulin proteins carry these lipids to such sites as muscle or adipose tissue, where they are either used or stored. The release of the lipid from the protein carrier is a complicated process. In adipose tissue, the lipoprotein is attached to a membrane receptor site-an enzyme, lipoprotein lipase cleaves the lipid from the protein.

The lipid is then picked up by another protein called a lipid binding protein and is carried to the interior of the cell for storage. The ß-globulin protein carrier, once free of its lipid, returns to the liver or intestinal mucosa and is recycled.

The plasma lipids, phospholipids, acylglycerols, cholesterol, cholesterol esters and free fatty acids are usually transported as loosely associated lipid-protein complexes. At least three different proteins have been identified. Albumin usually transports the free fatty acids, whereas the a and ß-globulins transport the phospholipids, acylglycerols and cholesterols. The different lipoprotein complexes can be separated and identified on the basis of their antigenicity, their electrophoretic mobility and their density. The low density or ß-lipoproteins contain

the ß-peptide, cholesterol and some phospholipids. The majority of phospholipids are carried as a-lipoproteins. With age, the lipid content of the plasma tends to rise and the rise is reflected almost entirely as an increase in ß-lipoproteins

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As the density of the lipoproteins decreases, the molecular weight and complexity of the lipid it carries decreases. The a-lipoproteins carry mainly (up to 60%) acylglycerols. These glyceroles are usually those synthesized in the body rather than coming from the diet. The dietary acylglycerols are usually carried as chylomicrons. These particles are the largest and least dense of the lipid-protein complexes.

In addition to serving as carriers of lipids, some of the globulins in the plasma can combine with iron and copper, as well as, with other divalent- cations.

These combinations are called 'metalloproteins'. The globulins serve to transport these cations from the gut into the tissues where they are used. The monovalent cations, sodium and potassium, do not need carriers but most other minerals do. Many hormones and vitamins require transport or carrier proteins to take them from their point of origin to their active site. In addition, there are intracellular transport proteins such as the lipid binding proteins that are responsible for the transport of mateiials between the various cellular compartments. Lastly, there are transport proteins which carry single molecules. The classic example is haemoglobin, the red cell protein, responsible for the transport of oxygen from the lungs to every oxygen- using cell in the body.

From carrier function, we move on to the regulatory function of proteins.

5) **Proteins as regulators of water balance:** As substrates and solutes are transferred or exchanged across membranes, water has a tendency to follow to maintain equal osmotic pressure on each side of the membrane. If osmotic pressure is not maintained, the individual cells either shrink from lack of internal Proteins water or burst from too much.

The balance of water between intracellular and extracellular compartments is closely regulated. Water balance across the capillary membrane is carefully controlled. A close balance is maintained between the osmotic pressure of the plasma, the interstitial fluids and the cells and the hydrostatic pressure exerted by the pumping action of the heart. The total osmotic pressure of the plasma and of the intra- and extracellular fluids is the result of its content of inorganic electrolytes, its organic solutes and its proteins.

The concentrations of the electrolytes and organic solutes in plasma, interstitial fluid and cells are substantially the same so that the contribution to the osmotic pressure by these substances is practically equal. However, since there are more proteins in plasma than in the cells, plasma exerts an osmotic pressure on the tissue fluids The result of this inequity of solutes is the drawing of fluids from the tissue spaces and from the cells into the blood. Opposing this is the hydrostatic

pressure, exerted by the pumping action of the heart, which moves fluids from the blood into the tissue spaces and into the cells. The hydrostatic pressure is greater on the arterial side of the capillary loop than on the venous side.

There is some land of interplay between these four kinds of pressure- blood osmotic pressure, tissue osmotic pressure, blood hydrostatic pressure and tissue hydrostatic pressure. This interplay results in the filtration of solutes and metabolites and the transfer of oxygen from the arterial blood into the tissues and cells it supplies and on the venous side, a resolution from the tissue space of CO_2, metabolites and solutes back into the blood supply, Albumin plays a more significant role in maintaining the osmotic pressure than theother blood proteins because of its size and abundance. It is a small molecule and has a greater number of particles per unit volume than the other larger serum proteins. With fewer proteins in the serum, water leaks out into the interstitial space and accumulates. You may be familiar with this condition commonly referred to as 'oedema'.

The oedema of protein deficiency may also be the result of the body's inability to regulate the protein hormone, particularly, Anti-Diuretic Hormone (ADH). This hormone plays a role in controlling water balance. The effect of protein is on the distribution of water amongst the various body compartments than on the total body water. So now you have understood what important role, proteins can play in regulating the water balance. Proteins also function as biological buffers. What do we mean by this and how proteins function as biological buffers.

6) **Proteins as biological buffers:** Proteins have the ability to accept or donate hydrogen ions and by doing so they serve as biological buffers .In blood, there are three important buffering systems — plasma proteins, haemoglobin and carbonic acid bicarbonate.

The equilibrium reactions for each of these buffering systems are as follows:

H Protein $\leftrightarrow$ H^+ + Protein-

$H_2CO_3 \leftrightarrow H^+ HCO_3$

HHb $\leftrightarrow$ H^+ Hb

The first of these buffering systems, the plasma proteins, functions as a weak acid/ salt buffer when the free carboxyl groups on the protein dissociate, or as a weak base/salt buffer when the free amino groups dissociate. Although the buffering ability of the plasma protein is extremely important in maintaining blood pH, it is not as important as the other two systems.

The second buffering system, carbonic acid-bicarbonate, is extremely effective because there are reactions which follow this equilibrium which will regulate either acids or bases. The H_2CO_3 level in plasma never goes too high because it is in equilibrium with CO_2 ($H_2CO_3 \rightarrow CO_2 + H_2O$), which is expired by the lungs. In blood, this equilibrium proceeds very quickly because of the presence of carbonic anhydrase, an enzyme found in red blood cells which catalyze it. If the carbonic acid-bicarbonate reaction goes in the opposite direction, the concentration of the

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HCO_3- so formed will be regulated by the kidneys.

The third important buffering system in blood results from haemoglobin. Haemoglobin has six times the buffering power of the plasma proteins. It functions well as a buffer because it is present in large amounts, it contains 38 histidine residues and because haemoglobin exists in blood in two forms, reduced haemoglobin and oxy haemoglobin. It is thus a weaker acid and a better buffer.

7) **Proteins as structural elements and structural units:** The liver cell membrane analysis shows that this membrane contains 50-6000 protein, 35%lipids and 5% carbohydrates. The carbohydrate present is joined plimarily to the protein forming glycoproteins, compounds which constitute the receptor sites of several hormones. The protein portion of the membrane is so oriented that its hydrophilic aspects are also in close proximity to the intracellular and extracellular fluids.

The protein molecules are interspersed within the lipids and lend both structural stability and fluidity to the membrane. Membrane function depends on how the proteins are placed in the membrane and on the fluidity, which results from the combination of proteins in a lipid mixture.

If the lipid is more saturated, a more rigid crystalline structure will form. Many lipids being fluid and less rigid, allow the proteins to change their shape in response to ionic changes and hence these proteins function as enzymes, carriers, binding or receptor sites or entry ports for a large variety of materials binding, entering or leaving the cell. Thus proteins serve as the structural and functional units of the cell membrane. Proteins are also important intracellular structural units. Muscle is composed of 2000 protein, 75% water and 5% inorganic mate ial, glycogen and other organic compounds. The major proteins in muscle are myosin — a large globular protein, and actin — a smaller globular protein.

These two proteins, plus the filamentous tropomyosin and troponin a e the molecular components of the muscles. The muscle proteins are characterized by their elasticity, which contributes to the contractile power of the tissue.

The most important structural function of protein is related 10 skin and connective tissue. The skin is composed of epithelial tissue which covers not only the exterior of the body but also lines the gastrointestinal tract, respiratory tract and the urinary tract. One of the major protein found in the skin is 'melanin'. Melanin is a tyrosine derivative and provides the pigmentation or characteristic colour to the skin. Persons unable to form this pigment are albinos and the disease is called 'albinism.' Keratin is the protein which forms hair, nails, hooves, feathers or horns. Each of these structures is slightly different but all contain keratin. This protein is insoluble in water and is resistant to most digestive enzymes. It has a high percentage of cystine.

Connective tissue is that tissue which holds various cells and tissues together. It includes bones and teeth also, since they staff with a matrix protein into which

various amounts of minerals are deposited. Collagen and elastin are the two distinct types of proteins in the connective tissue. It contains proline, hydroxyproJine and glycine. These proteins are not easily degradable and are inert metabolically. Even in protein deficient states, the body will synthesize collagen and elastin and these proteins will not be catabolized for needed amino acids. However, this protein can be degraded to a limited degree by boiling in acid. It is then converted to gelatin. The collagen of bone, skin, cartilage and ligaments differ in chemical composition from that of Proteins the white fibrous tissue which holds individual cells together within muscle, liver and other organs. Elastin and chondroalbumoid are two other proteins in the connective tissue. They are present in small amounts and serve as a part of the structural protein.

Proteins as structural elements have been studied above. Interestingly proteins also surround the joints and function as lubricants. Let's look at this lubricant function of proteins next.

8) **Proteins as lubricants:** The mucous of the respiratory tract, oral cavity, vaginal tract and the rectal cavity reduces the irritation which might be caused by materials moving through these passages. This inucous is a mucoprotein, a conjugated protein which contains hexosamine. Proteins as lubricants also sunound the joints and facilitate their movement. The absence of these lubricants or substantial decrease in their fluidity through deposition of minerals makes skeletal movement difficult and painful.

Last but not the least; proteins also have an important role to play in the immune system. Let us find out how.

9) **Proteins in the immune system:** Proteins such as Y-globulin serve to protect the body against foreign cells. The immunoglobulin's produced by lymphocytes are the large polypeptides having more than one basic monomeric unit. These proteins differ in their amino acid structure, which in turn, affect their secondary, tertiary and quaternary structures. Just as the amino acid sequence of an enzyme determines substrate specificity, the amino acid sequence of the immunoprotein assures antigen-antibody specificity. The initiation of synthesis of particular immunoglobulin's by the lymphocytes requires the binding of an antigen (a foreign protein) to the cell surface at particular locations called 'antigen receptors'. The immunoglobulin synthesized binds with the foreign protein immobilizing it. Thus, the complex antigen-antibody is formed.

4.4 METHODS OF DETERMINATION OF PROTEINS AND AMINO ACID CONTENT IN FOODS

The methods for protein quality evaluation are grouped under the following headings:

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Analytical methods for the determination of nitrogen and amino acids in foods

Chemical and microbiological assays of protein quality

Evaluation of protein quality in experimental animals

Clinical methods for evaluation of protein quality

In this section we shall review both the qualitative and quantitative evaluation of protein and amino acid content in foods. We shall begin with the quantitative/ analytical method for the determination of nitrogen and amino acid in foods.

Quantitative/Analytical Method for Estimation of Nitrogen and Protein

You may recall reading earlier that proteins contain nitrogen along with carbon, hydrogen and some other substances. Nitrogen (N) in food not only comes from amino acids in protein but also exists in additional forms that may or may not be used as a part of the total nitrogen economy of humans and animals. Thus, determination of nitrogen is commonly used to determine the protein content of a sample. Total nitrogen, which is determined by the Kjeldahl procedure, is converted to crude protein by a factor of 6.25, as mentioned earlier.

Thus, the conventional measure of "protein" or "crude protein" in foods is N x 6.25, and it is recommended that this one factor be used in nutritional studies in which whole diets contain more than one source of nitrogen.

The Kjeldahl's method is commonly used in estimation ofprotein content of foods and has been extensively used for protein estimation of various foodstuffs. Although over a period of time many other methods have emerged for determination of organic nitrogen, this method still remains an old favourite because it is reliable and has very well standardized procedures.

Qualitative Estimation of Protein/Amino Acid Content in Foods

The protein and amino acid content of foods helps to interpret nutritional differences among foods in terms of their amino acid make-up. This has been obtained only through experiments on animals or human beings. The methods available to determine protein quality are based on several parameters. They are categorized as methods based on:

A). Growth and body, weight changes: The methods under this category include—

Protein efficiency ratio (PER)

Net protein ratio (NPR)

Gross protein value

Rat repletion method

Nitrogen growth index

Slope ratio method

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B) Carcass nitrogen analysis: This method includes—

Nitrogen retention method

Net protein utilization (NPU)

Rat repletion methods

C) Nitrogen balance includes—

Nitrogen balance

Digestibility coefficient, Biological value and net utilization of dietary proteins

Nitrogen balance index

Egg replacement method

D) Regeneration of blood and liver constituents includes—

Liver protein regeneration

Blood protein regeneration

Regeneration of liver enzymes

E) Availability of amino acids includes—

Chemical methods

Enzymic methods

Microbiological methods

Animal assays

F) Miscellaneous parameters include—

Plasma amino acid levels

Microbiological methods

G) Chemical scoring include—

Chemical score

Essential amino acid index

Simplified chemical scor

Only a few of these methods measure the overall nutritive value of a protein - protein efficiency ratio (PER), net protein utilization (NPU) and biological value (BV). PER, NPR and NPU are widely used as the methods for the evaluation of dietary proteins and amino acids. You would realize that no single method gives a complete evaluation of protein quality and hence a combination of method is preferred. Let us get to know these methods.

Protein Efficiency Ratio (PER)

PER method was developed by Osborne, Mendel and Ferry in 1919 and is based on the growth of young rats. The diets usually contain 10% of dietary protein to be tested and are complete in all other dietary essentials. Groups of albino rats (21

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days old) are fed for a period of 4 weeks on different diets. Records of the gain in body weight and protein intake of the rats are maintained. The protein efficiency ratio (PER) is calculated using the following formula:

$$PER = \frac{\text{Gain in body weight (g)}}{\text{Protein intake (g)}} = \text{gain in weight per g of protein consumed}$$

PER, therefore, is a measurement of the efficient utilization of the proteins in the body. You would be interested to know that the egg protein has the highest protein efficiency ratio. Hence, egg protein is the standard to which all other forms of proteins are measured.

Digestibility Coefficient

You have earlier learnt that dietary proteins are hydrolyzed to amino acids during digestion. The digestion begins in the stomach by the action of pepsin and later completed in the intestines by trypsin, erepsin and other enzymes. Proteins differ in their digestibility. Egg and milk proteins are easily digested and converted into amino acids while pulse proteins are slowly digested to amino acids. Amino acids are absorbed into the blood stream and the unhydrolyzed portion of the protein is wasted in the faeces. Thus, digestibility coefficient of protein refers to the percentage of the ingestd protein absorbed into the blood stream after the process of digestion is complete.

When an animal is fed on nitrogen (N)-free diet, certain amount of nitrogen is excreted in the faeces. This is derived mainly from the digestive juices. This is called 'endogenous faecal N.' When a protein food is given, the N found in faeces consists both of endogenous N and food N lost in digestion. To find out N lost in digestion, endogenous faecal N should also be determined. For the determination of the digestibility coefficient, therefore, the data on food nitrogen intake (I), total faecal nitrogen excreted (Fn) and endogenous faecal nitrogen (Fe) are required. The digestibility coefficient can thus be calculated using the formula

$$\text{Digestibility coefficient} = 100 \times \frac{\text{N intake} - (\text{N in faeces} - \text{endogenous faecal N})}{\text{N intake}}$$

$$= \frac{100 \times I_n - (F_n - F_e)}{I_n}$$

where, $F_n - F_e$ is the food nitrogen lost in digestion.

The digestibility coefficie ts of proteins are influenced by several factors, such as, the presence of indigestible carbohydrates like cellulose and hemi-cellulose and the presence of proteolytic enzyme inhibitors.

Biological Value

A method for determining the biological value of proteins was developed by Mitchell in 1925. It measures the quantity of dietary proteins utilized by the animal for meeting its protein needs for maintenance and growth. Groups of albino rats (28 days old) are fed successively on the following diets for a period of 10 days: (l) protein-free diet, and (2) diet containing 10 percent protein to be tested. Urine and faeces are collected by keeping them in metabolism cages. Records of food intake are maintained. The diet, urine and faeces are analyzed for nitrogen. Biological value is then calculated using the following formula:

$$\text{Biological value} = \frac{(\text{Nitrogen digested} — \text{Nitrogen lost in metabolism}) \times 100}{\text{Nitrogen digested}}$$

Let us determine the expression for numerator and denominator.

Nitrogen digested = N intake (1,,)— N in faeces (F,,) on the protein diet — N_m faeces (F,) on protein free diet, i.e.

Nitrogen digested = I_n — (F_n — F,)

Nitrogen lost in metabolism = N in urine (I-Jn) on protein diet— N in urine (U,) on an protein free diet = U_n— U_e

Hence, Biological value can be expressed as:

$$BV = \frac{I_n - (F_n - F_e) - (U_n - U_e)}{I_n - (F_n - F_e)} \times 100$$

Thus, BV is a measurement of protein quality expressing the rate of efficiency with which the protein is used for growth. On a scale with 100 representing top efficiency

Table 4.4: Biological values of proteins in several foods

Food Items	BV
Whole egg	93.7
Milk	84.5
Fish	76.0
Beef	74.3
Soybeans	72.8
Rice, polished	64.0
Wheat, whole	64.0
Corn	60.0
Beans, dry	58.0

Net Protein Utilization (NPU)

Mitchell (1922) introduced the term 'Net Utilization of Dietary Protein' which is a product of digestibility coefficient and biological value divided by 100, as shown herewith.

$$NPU = \frac{\text{Digestibility coefficient x Biological Value}}{100}$$

A direct method of estimating Net Protein Utilization (NPU) was developed by Miller and Bender (1955). Groups of albino rats 28 days old were used. One group was fed on a non-protein diet while the other groups were fed on the test diets containing different proteins at 10 percent level for a period of 10 days. The food intakes of the animals were measured. The animals were killed at the end of 10 days and the body nitrogen was determined by Kjeldahl method on a sample of dried and powdered carcass. The NPU is calculated according to the formula:

$$NPU = \frac{\text{Body N of the test group — Body N of the non-protein group + N consumed by non-protein group}}{\text{N consumed by test group}}$$

The main advantage of determining NPU of a food or diet is that it helps in the calculation of the net available protein of the diet. Studies have shown that there is a good correlation between the values for PER, NPU and chemical score.

Net Protein Ratio (NPR)

This method was introduced by Bender and Doell (1957) and is a modification of the PER method. In this method, an allowance is made for the protein requirements for maintenance. The method consists of feeding a group of weanling rats on a diet containing 1 0 percent of the test protein and another comparable control group on a non-protein diet for a period of 10 days. The NPR is calculated by adding the loss in weight of the control group to the gain in weight of the test group and dividing the total weight (g) by the quantity of protein consumed by the test group according to the following formula:

$$NPR = \frac{\text{Gain in weight (g) of the test group + loss in weight (g) of the non-protein group}}{\text{Protein intake (g)}}$$

NPR values have been reported to correlate closely with NPU values.

Chemical Score

Since egg proteins contain all essential amino acids in adequate amounts and possess the highest nutritive value among dietary proteins, Block and Mitchell

(1946) assigned a chemical score of 100 to egg proteins. Since the nutritive value of the proteins depend on the essential amino acid most limiting in the dietary proteins, they evolved a chemical score (based on the most limiting essential amino acid) which can serve as an index of the nutritive value of the proteins. The chemical score is the 'ratio between the content of the most limiting amino acid in the test protein to the content of the same amino acid in the reference protein (egg protein) expressed as a percentage'. The chemical score formula is given herewith. Chemical score of milk proteins is 65 and those of gelatin and zein are 0.

$$\text{Chemical Score (CS)} = \frac{\text{mg of amino acid in lg of test protein}}{\text{mg of amino acid in I g of reference protein}} \times 100$$

Protein-Energy Ratio (NDP Cal Proteins

Platt and his colleagues (1961) are largely responsible for the introduction of the ratio of protein energy to total energy (PE ratio) as a useful measure of dietary quality in human nutrition. To take into account both the quality and concentration of the protein, they introduced the concept of the net dietary protein calories as a percentage of total calories (NDP Cal%). The NDP Cal%, is the net dietary protein value expressed as percent of total calories. The NPU or the chemical score could be utilized in calculating the NDP Cal% as both of them are indicative of protein value. The formula used is as under:

$$\text{NDP Cal\%} = \text{x NPU} \frac{\text{Protein calories in the diet}}{\text{Total Calories}} \times 100$$

OR

$$\text{NDP Cal\%} = \frac{\text{Protein calories in the diet}}{\text{Total ca101ies}} \text{x Chemical Score x } 100$$

For adults, diet with an NDP Cal% of 5% would be adequate to maintain health. In infants, children, adolescent and pregnant women, growth is supported only by a diet providing an NDP Cal% of 8% or above. Now that we have studied and understood the various methods of determining proteins, it is important that we practically assess the protein/amino acid quality of our diet or perhaps of other population groups. To help you in this task, we have included various activities in the Practical Manual (MFNL-004) accompanying this course. So go ahead carry out these activities.

4.5 IMPROVEMENT OF QUALITY OF PROTEININ THE DIET

Since the net protein utilization (NPU) values of milk or egg proteins are higher

than those of proteins of average diets consumed in different countries, a correction has to be made for this variation in the NPU of dietary proteins, This is shown herewith:

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$$\text{Dietary protein requirements (g)} = \frac{\text{Safe level of intake of egg or milk proteins x NPU of egg or milk proteins}}{\text{NPU of dietary proteins}}$$

For example, if the NPU of the dietary proteins is 45 and egg protein is 90, the correction factor will be 2. In other words, the amount of this dietary protein needed to satisfy the requirements of a given population group will be twice as high as that of egg or milk protein.

The next thing that might come to your mind is regarding the protein quality of the Indian diets. Average Indian diets as consumed in different parts of the country consist chiefly of vegetable source of protein. The amount of animal protein depends on the diet habits, with only milk providing a source of animal protein in vegetarian diets to varying amounts of meat and flesh in the non vegetarian diets.

The question of whether the protein quality of our predominantly vegetarian diets is adequate and what are the ways in which the quality of protein in our diets can be improved has been addressed through a number of studies. Habitually, Indian diets are cereal-based diets, limiting in lysine, an essential amino acid critical for growth and development in children. The term limiting is used describe that indispensable amino acid which is present in the lowest quantity in the food, in comparison with the same amino acid in a reference protein such as egg or milk, the quantity of the amino acid expressed in terms of per g nitrogen. Further, the diet is predominantly vegetable-based, and foods of animal origin do not usually find a place because of their high cost.

A large percentage of people are vegetarian and their diets include pulses, vegetables, cereals and grain products. These plant foods tend to have too little of one or more indispensable amino acids (i.e. lysine, threonine, tryptophan or methionine, particularly in legumes). In other words, individual plant foods such as cereal alone or pulses alone tend to be relatively deficient in one or more essential amino acids and thus exclusive consumption of single plant foods such as chiefly rice or wheat would result in deficiency of an essential amino acid and if this consumption pattern is continued over a long period of time, it can result in protein deficiency. However, a combination of plant foods, such as cereal-pulse-vegetable based diets are fully capable of meeting protein needs, when consumed in amounts that satisfy energy needs.

Fortunately, for us, the amino acid deficient in cereals, namely lysine is present in ample quantities in pulses and green leafy vegetables. Similarly, the essential amino acid methionine which is relatively low in pulse, is present in larger quantities in cereals. Thus, the different sources of vegetable proteins

complement each other in terms of the amino acids they provide. Therefore, if we ensure that diet at every meal is a combination of cereals, pulses, and vegetables with nuts and milk contributing wherever one can afford, it will take care of the protein requirements. In this context, when we consider the Indian cuisine we notice, North and West Indian meals consist of chapatis or rotis and rice as staples, eaten with a wide variety of side dishes like dals, curries, yoghurt, chutney and achars.

South Indian dishes are mostly rice-based, sambhar, rasam and vegetables being important side dishes. The pulses/legumes, included in the diet, with their high content of lysine but low content of methionine, complement the grains (cereals), which are more than adequate in methionine and cystiene but limiting in lysine. Such cereal-pulse combination diets when consumed help the body receive all the indispensable amino acids.

Hence, there is no need to worry about protein if we are eating a varied vegetarian diet! It is easy to get protein from lentils, dal, beans, curd, rice, soy milk, and cereals when eaten in combination so that their amino acid patterns become complementary. The inclusion of pulses in cereal-millet-based diets is critical not only in increasing the protein content, but also in improving the nutritional quality of the protein.

So, then, that brings us to the second question i.e. can we improve the nutritive value of protein? Yes, as discussed above, the nutritive value of a protein can be improved in two ways :

(1) by mutual supplementation, that is, by blending two or more proteins so that the excess of essential amino acids present in one protein makes up the deficiencies of the same amino acids in another protein and

(2) by supplementation of the dietary proteins with limiting essential amino acids. Let us understand these methods by way of few examples.

1) *Mutual supplementation*

a. Improvement of cereal proteins: Cereals, in general, are limiting in lysine and threonine while legumes, milk, meat and fish are good sources of the amino acids. Hence, the proteins of legumes, milk, meat and fish supplement effectively cereal proteins.

b. Soyabean and sesame proteins: Soyabean proteins are good sources of lysine but are deficient in methionine while sesame proteins are good sources of methionine but are deficient in lysine. Hence, the proteins of sesame supplement effectively those of soyabean.

c. Improvement of cereal diets with legume and milk proteins: The proteins of poor diets based on different cereals are limiting in lysine and threonine and their quality can be improved effectively by incorporation of legumes, soyabean or milk proteins in the diet.

2) *Supplementation with individual amino acids*

a) Improvement of cereal diets by supplementation with lysine and threonine: Cereal diets supplemented with lysine alone or a mixture of lysine and threonine markedly increases the PER of cereal proteins or proteins of poor cereal diets.

b) Improvement of soybean and cow's milk protein with methionine: The proteins of soybean and cow's milk are deficient in methionine. Supplementation with methionine increases the PER of the diet from 2.0 to 2.9 for soy bean and 3.0 to 4.0 for milk proteins.

c) Improvement of sesame and sunflower seed proteins with lysine: Supplementation with the limiting amino acid lysine increases the PER of sesame proteins from 1.7 to 2.9 and sunflower seed proteins from 1.2 to 1.8.

4.6 METHODS OF ESTIMATING AND ASSESSING PROTEIN REQUIREMENTS AT DIFFERENT STAGES OF LIFE CYCLE

In this section, we are going to deal with the methods that are used to estimate protein requirements, as well as, the factors which affect it. Let's read and find out first what we mean by protein requirement and its significanc

Human protein and amino acid requirements have been studied for well over 100 years using a variety of techniques. Nutrition scientists have collected data on the quantity of protein foods consumed in health, growth and weight gain of various populations. The assumption was made that whatever healthy people ale was probably what kept them, healthy ‘and should, therefore, be used as a standard of comparison for other diets. These standarcls with respect to protein were invariably high for populations having an abundance of meat, milk, poultry and fish in their diets. Voit and Atwater around the turn of the 20th century, found intakes of 118 and 125 g protein/ day, respectively for an adult woman and man.

As nutrition developed as a science, more accurate methods for assessing nutrient needs were developed. Among these methods were those for assessing the intakes and excretion of nitrogen compounds. The Kjeldahl method, about which we learnt above, and other methods for determining the nitrogenous end products of metabolism were devised. These methods made possible the development of the concepts which today's scientists use to determine the nutrient requirements of humans, as well as, other species.

In protein nutrition, it was realized that the body consists of two pools of protein: one which has a short half life and which must be constantly renewed and one which is slowly broken down and rebuilt. If one assumes that over a short period of time, the pool having the long half life contributes almost nothing to the

nitrogenous metabolic end products and then a measure of the amount of nitrogen excreted will reflect only the turnover of the short lived proteins. These proteins have to be replaced by proteins newly synthesized from the amino acids provided by the diet. Hence, the term protein requirement means that 'amount of protein which must be consumed to provide the amino acids for the synthesis of those body proteins irreversibly categorized in the course the body's metabolism'. The intake of nitrogen from protein must be sufficient to balance that excreted; this basic concept is called nitrogen balance. This concept is useful in understanding the minimal need for protein in the diet.

Protein requirement is greatly influenced by many factors such as age, environmental temperature, energy intake, gender, micronutrient intake, infection, activity, previous diet, trauma, pregnancy and lactation. Let us take up each of these factors in detail.

1) **Age:** Protein in excess of maintenance needs is required, when a new tissue is being formed. Certain age periods, when growth is rapid, require more dietary protein than other periods. Age differences in protein turnover, as well as, protein synthesis explain some of the effects of age on protein needs. Premature infants (those born before their 10 lunar month gestation time) growing at a very rapid rate require between 2.5 to 5 g protein/kg/day if they are to survive.

Studies of full term infants have indicated that a protein intake of 2.0 to 2.5 g/kg/day resulted in a satisfactory weight gain and that further increases in protein intake did not measurably improve growth. Older infants and children, whose growth rate is not as rapid as the premature or new born infant, require considerably less protein (l .25 g/kg/day). As growth rate increases during adolescence, the protein needs increase. Again, this can be related to the demands for dietary amino acids .to support the growth process. As the human completes his growth, the need for protein decreases until it arrives at a level which is called the 'maintenance level'. It is at this level that the concept of body protein replacement by dietary protein applies.

During the growth period, it is very difficult to separate the requirements for maintenance from those of growth. The impulse for growth is so strong that it will occur in many instances at the expense of the maintenance of body tissues. For example, malnourished children will continue to grow taller even though their muscles, as well as, other tissues show evidence of wastage due to dietary protein deficiency. Growth carries with it not only a total nitrogen requirement but also a particular amino acid requirement. Maintenance, on the other hand, appears to have only a total protein requirement. The adult can make a number of short-term adjustments in his protein metabolism that can compensate for possible inequities of imbalances in amino acid intake as long as the total protein requirement is met. The young growing animal is not that flexible.

The essential amino acid requirements are age dependent. Although histidine

can be synthesized in sufficient quantity by the adult to meet maintenance needs, yet it is not synthesized in great enough amounts to support growth or tissue repair. Thus, histidine is an essential amino acid for the infant, growing child and injured adult. This is due to the nature of the growth and repair processes.

2) **Environmental temperature:** As environmental temperatures rise or fall above or below the range of thermic neutrality, animals begin to increase their caloric expenditure to maintain their body temperature. In environments that are too warm, vasodilation (widening of blood vessels) occurs along with sweating and increased respiration. All of these mechanisms are designed to cool the body and all require an increase in the basal energy requirement expressed as per unit of body surface area. In cool environments, vasoconstriction and shivering occurs in an efforts to warm the body and prevent undue heat loss. Again, an increase in basal energy requirement is observed. Smuts (1934) found that nitrogen requirements were related to basal energy requirements. Through the study of a large number of species, he concluded that 2 mg nitrogen were required for every basal kilocalorie required when the energy requirement was expressed on a surface area basis. Thus, any increase in basal energy needs due to a change in environmental temperature will be because of the relationship between protein and energy.

In addition, profuse sweating as occurs in very warm environments carries with it a nitrogen loss which must be accounted for in the determination of minimal protein needs.

3) **Previous diet:** The effects of previous diet in the determination of protein requirements may be rather profound. If, for example, the subjects selected for studies on protein needs have been poorly nourished prior to the initiation of the study, their retention of the protein during the study will be greater than would be observed in subjects who have been well nourished Plior to the initiation of the study. In other words, malnourished subjects have a higher protein requirement than well-nourished subjects. This of course raises the issue of whether there are body protein reserves. Voit, Wilson, Cuthbertson, Fisher (1890) and others observed that animals fed on' a protein-free diet exhibit a lag before their nitrogen excretion level is minimized. During this phase, the animal is metabolizing his protein reserve. Other investigators maintain that every protein in the body has a motion and if some of these proteins are lost, there is a loss in body function. Support for this concept is seen in the reduced ability of protein depleted animals to fight infection or respond to the metabolic effects of trauma. Whether one believes that there is such an entity as a protein reserve may depend upon whether one perceives a difference between personal opinions on how nutrient requirements should be defined, Some nutritionists believe in stating the absolute minimum requirement to sustain life and then

adding on increments for each body function above mere survival. This is known as the Particulate approach'. Other nutritionists believe that one cannot separate and quantify the individual requirements of each function beyond survival.

They advocate a protein intake sufficient for optimal function of the animal. This is known as the 'integrative approach. ' The particulate and integrative approaches each have their merits when argued intellectually. However, since humans do not merely exist, many human nutritionists tend to take the integrative approach to human nutrition requirements in their determination of protein needs.

4) **Physical activity:** Research on protein needs for muscular work had its beginning in 1863 when Von Leiberg postulated that muscle protein was destroyed with each contraction of the muscle. On this basis, he recommended that heavy muscular work required a heavy protein diet. This theory has been amply disproved, yet even today many believe that a protein rich diet will contribute to athletic prowess. Today, we know that muscle contraction does not result in destruction of the muscle. It however, requires energy in the form of ATP, glucose and fatty acids and does result in the breakdown of creatine phosphate to creatine which is then converted to creatinine, a nitrogenous waste product excreted in the urine.

As the energy requirement is increased to support the increase in muscular activity, so too is the protein requirement in much the same manner as described above for the effects of temperature. In a number of studies, the athletic performance of subject's could not be directly related to the quantity of protein consumed above that determined to be the requirements, their muscular deficiencies were reduced unless a vigorous training programme was included as a pan of the experiment's protocol, Since most of the studies were of short duration and since muscle protein has a relatively long half-life, the lack of any demonstrable effect of protein intake on muscle performance is not surprising

Other factors such as sex, pregnancy, lactation and trauma affecting the protein requirements have been studied. As can be anticipated, males due to their greater physical activity and larger body size have a larger protein requirement than females. Pregnancy, lactation and trauma increase the protein requirements. So, now you realize that a large number of factors play a role in determination of protein requirements. Let us next find out what are the recommended allowances for proteins for different age-groups.

4.7 NUTRITIONAL REQUIREMENTS AND RECOMMENDED ALLOWANCES FOR PROTEINS AND AMINO ACIDS

The FAO/WHO Committee (1973) expressed the protein requirements in terms

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of egg or milk proteins. The committee defined safe level of protein intake as 'the amount necessary to meet the physiological needs and maintain the health of nearly all the individuals in a specified age/sex group.

The committee followed three procedures in arriving at the protein requirements:

1) Amino acid requirements,

2) The factorial method, in which the obligatory nitrogen losses and N required for growth, pregnancy and lactation are estimated, and

3) Measurements of minimum protein intake required for satisfactory growth and N balance in infants and children and N equilibrium in adults.

Let us briefly discuss each of these and try to understand these better, starting off with amino acid requirements:

1) Amino acid requirements

Data regarding the essential amino acid requirements of infants, children and adults are given in terms of egg protein and cow's milk protein (g/kg/day) required to meet the amino acid needs. These requirements are given in the Table 4.5.

Table 4.5: Essential amino acid requirements

S.No.	Age-Group	Egg Protein (g)	Cow's milk (g) Protein
1.	Infants	**1.6**	2.0
2.	Children (10-12 yeas)	0.9	0.9
3.	Adults	0.18	0.28
	a) Women	0.18	0.28
	b) Men	0.26	0.43

The Committee suggested a Reference Amino Acid Pattern in 1973. Since adequate experimental evidence for the suitability of the pattern was not available, the Committee adopted egg and milk proteins as reference proteins and expressed protein requirements in terms of egg or milk proteins. The Committee assumed that the proteins of milk or eggs me utilized to the same extent in children and gave a protein score of 100 to egg and milk proteins.

2) Factorial method

The nitrogen requirements have been calculated by a factorial method suggested by different expert groups, described as follows:

R=U+F+S+G

where

R = N requirements,

U = loss of endogenous N in urine,

F = loss of endogenous N in faeces, Proteins

S = loss of N through skin, i.e., sweat and integumental losses, and

G = N required for growth.

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a) Obligatory N losses: The Committee estimated the total obligatory nitrogen losses through faeces, urine, skin and other miscellaneous routes in adult men as 2.0 mg N/basal Kcal. The obligatory N losses in adult men on a protein-free diet is given in Table 4.6,

Table 4.6: Obligatory nitrogen losses (mg)

Route	N per kg of Body Weight	N per Kcal of Basal Energy
Urine	37	3.4
Faeces	12	0.4
Skin	31	0.13
Miscellaneous	2	0.08
Total	54	2.0

The Committee used the same figure of 2.0 mgN per basal Kcal for the total obligatory losses in women, infants and children.

b) N requirements for growth: The nitrogen requirements for growth of infants and children

Table 4.7: Nitrogen requirements for growth

Age	Nitrogen for Growth (mgN/kg/day)
Infants	
0 - 3 months	154
3 - 6 months	104
6 - 9 months	77.4
9 - 12 months	35.5
Children	
1 year	19.9
2 year	13.8
3 year	11.8
4 - 6 year	12.2
7 - 9 year	12.3
10 - 12 years	9.9

c) N requirements in Pregnancy and Lactation: The nitrogen accretion in the pregnant woman (assuming that the foetus weighs 3.3 kg at term),

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estimated by the Committee,

Table 4.8: Nitrogen accretion during various stages of pregnancy

Stage of Gestation	N Accretion /day (mg)
First quarter	80
Second quarter	400
Third quarter	740
Fourth quarter	860

After having a thorough knowledge of the factorial method of estimating N requirements, surely you would be now in a position to calculate protein requirements.

The nutritional requirements of protein for Indians in different age groups and physiological stages as suggested by the ICMR is given in Table 4.9.

Table 4.9: Nutritional requirements of protein

Group	Particulars	Body Weight(kg)	Protein g/d
Man	Sedentary work Moderate work Heavy work	60	60
Woman	Sedentary work Moderate work Heavy work	50	50
	Pregnant woman	50	+15
	Lactation 0 - 6 months 6 - 2 months	50	+25 +18
Infants	0 - 6 months 6 - 12 months	5.4 8.6	2.05/kg 1.65/kg
Children	1 - 3 years 4 - 6 years 7 - 9 years	12.2 19.0 26.9	22 30 41
Boys Girls	10 - 12 yews 10 - 12 years	35.4 31.5	54 57
Boys Girls	13 - 15 years 13 - 15 years	47.8 46.7	70 65
Boys Girls	16 - 18 years 16 - 18 years	57.1 49.9	78 63

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4.8 PROTEIN DEFICIENCY

One of the most common nutritional disorders in the world today is the deficiency of protein. Both adults and children are affected, as the populations in the less developed nations of the world exceed their food supply. Due to the ubiquitous nature of protein and its role in bodily function, protein deficiency is characterized by a number of symptoms. In many situations, not only is protein lacking in the diet but also calories. For this reason, it is difficult to segregate symptoms due solely to protein deficiency from those of energy deficit. In children, one may observe the different symptoms and visualize them all as parts of a continuum called protein-energy or protein- calorie malnutrition (PEM or PCM) rather than distinctly different nutritional disorders. 'Kwashiorkor' was the term used to describe a disease first observed in the Gold Coast of Africa by Dr. Cicely Williams in 1935 and at first was regarded as a dietary state where only protein was deficient, not energy. Marasmus, on the other hand, was regarded as a dietary state where both protein and energy are deficient.

Now it has become apparent that the symptoms of any one of the twin diseases may intermingle with the other so that a clear-cut diagnosis is impossible. We suggest you look up the unit now as you go about reading regarding PEM here in this unit. Here a very brief overview of the disorder has been presented.

A. Kwashiorkor

The term Kwashiorkor means the 'disease the first child gets when the second baby is born', that is, 'the sickness of the deposed child'. Thus, the disease could be cured 126 by milk.

Kwashiorkor usually affects the young child after he is weaned. The child is usually Proteins between 1 and 3 years old and is weaned because the mother has given birth to another child or is pregnant and cannot support both children. If the child has no teeth, he is given the gruel. This may be a fruit, vegetable or cereal product mixed with water and hence not. a good protein source. Can you think of a few reasons which could limit or decrease the protein intake? Let us see what these are. Cultural food practices or taboos may further limit the kinds and amount of protein given to the child. Apart from this, concurrent infections, parasites, seasonal food shortages and poor distribution of food amongst the family members may also contribute to the development of kwashiorkor. The deficiency develops not only because of inadequate intake but also because at this age the growth demands for protein and energy are high.

The symptoms of kwashiorkor are as 'follows:

1). **Growth failure:** This is manifested by decreased body length and low body weight in spite of retention of water in the body (oedema) and presence of subcutaneous fat in some children. This growth retardation is primarily due to the general quantitative lack of proteins.

2). **Mental clzanges:** Several workers have stressed on the constant finding of mental changes described as apathy and peevishness. In advanced cases, children tend to live in an inert listless condition and show no interest in the surroundings.

3). **Oedema:** Oedeina occurs at first in the feet and lower legs and then may involve the hands, the thighs and face. The oedema is mainly due to lowered serum albumin and probably also due to high sodium and low potassium levels in serum. There is also some evidence that the nonnal diuretic-antidiuretic honnonal control of urine secretion gets disturbed.

4). **Muscle wasting:** Muscle wasting is a constant featute of kwashiorkor and a reduction in the circumference of the upper arm is usually evident. It is less affected by oedema than in the forearm or leg.

5). **Moon-face:** The full, well-rounded face, known as moon-face, is often present in kwashiorkor.

6). **Liver clzanges:** Liver is slightly enlarged and fatty infiltration of liver is usually present.

7). **Gastrointestinal tract:** Loss of appetite and vomiting are common. Diarrhoea is present in most cases.

8). **Skin and hair changes:** The characteristic skin changes of kwashiorkor are known as the 'crazy pavement' dermatosis. This is most marked on the buttocks, back of thighs and axille. These lesions consist of dark hyperpigmental brownish black areas of skin.

9). **Anaemia:** Anaemia is invariably present. It is due to the deficiency of iron and folic acid. Anaemia may be aggravated by parasitic infection which prevents the absorption of nutrients.

10). **Vitamin Deficiency** Signs and symptoms of vitamin A deficiency such as xerophthalmia and keratomalacia are widely prevalent. Angular stomatitis and glossitis due to deficiency of riboflavin may be present. Biochemical changes: Several biochemical changes have been reported in children suffering from kwashiorkor.

11). **Serum Albumin:** The serum albumin content is usually low ranging from 0.7 to 2.2 g/ 100 ml. Serum albumin level is a good index of the severity of the disease and the rise in serum albumin level during treatment is a reliable index of the rate of recovery.

12). **Enzymes in Serum and Digestive Juices:** Low levels of choline ester; alkaline phosphatase, amylase and lipase have been reported in kwashiorkor experimental animals fed on protein deficient diet, reduction in lipase, amyl and protease activities of pancreas have been reported.

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B. Marasmus

Although children of all ages and adults can suffer from deficiencies of both energy and protein, the marasmic child is usually less than one year old. In developing countries, a common cause for inarasmus is the cessation of breast-feeding. Milk production by the mother may have stopped because of her poor-health, death deliberate decision of the mother to bottle-feed her baby. This decision might have a socio-economic connotation.

Can you think of it? Well, it is just that the moth may view bottle-feeding as a status symbol or she may be forced to work to ea a living and may be unable to have her baby with her, or she may not be able lactate. While under optimal conditions of economics and sanitation, it seems that the bottle-fed child may be well fed in emerging nations but this is not always true.

The mother may not be able to buy the milk formula in sufficient quantities to adequate nourish the child, she may over dilute the milk or she may use unsafe water are unsanitary conditions to prepare the formula for the child. This plus the insufficient nutrient content often precipitously leads to the development of marasmus, a form (starvation characterized by growth failure with prominent ribs, a characteristic monkey like face and 'match stick limbs' with little muscle or adipose tissue development

Tissue wastage but no oedema is present. Whereas the kwashiorkor child has a poor appetite, the marasmus child is eager to eat. The child is mentally alert but no irritable. Anaemia and diarrhoea are present for the same reasons as in kwashiorkor. The skin and hair appear to be of normal colour. Protein hormones which regulate and coordinate the use of dietary nutrients are now found in adequate amounts.

Cell hormone receptor sites are affected which further dampens the effectiveness of the hormones produced. Marasmic and Kwashiorkor children have decreased blood sugar levels, decreased serum insulin and growth hormone levels and in marasmus, decreased thyroid hormone levels. The clinical features of marasmus are as follows:

- **Nutritional Marasmus:** Nutritional marasmus is principally due to the consumption, of diets markedly deficient in both proteins and calories. It is seen most commonly in the weaned infants of about I year of age in contrast to kwashiorkor, which occurs more often among children of the age group 2-4 years. Nutritional marasmus usually is precipitated by diarrheal diseases.
- **Clinical Features:** The two constant features of nutritional inarasmus are growth retardation and severe wasting of muscle and subcutaneous fat.

    a) **Growth retardation:** This is usually very severe. Loss of weight is much more marked than decrease in height. The child is usually below 60 percent of the standard weight.

    b) **Wasting of muscle and subcutaneous fat:** The subject is severely emaciated. The muscles are wasted. The arms are thin and the skin is

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loose. Subcutaneous fat is practically absent.

c) **Other changes:** The skin is dry and atrophic. The subject shows signs of dehydration. Eye lesions due to vitamin A deficiency and anaemia may be present.

d) **Biochemical changes:** There is a slight lowering of serum albumin. Vitamin A content of serum is low. The important difference in the clinical and biochemical features between marasmus and kwashiorkor.

Table 4.10: Clinical and biochemical features of marasamus and kwashiorkor

Features	Marasmus	Kwashiorkor
Age of maximum incidence	6-18 months	12-48 months
Loss of body weight	+ + +	+ to + +
Emaciation (Loss of muscle and subcutaneous fat)	+ + + +	+ to + +
Oedema	Absent	+ to + +
Fatty infiltration of liver	0 to +	+ + +
Skin changes	+	+ + +
Serum albumin	Slightly less	Markedly less
Serum enzymes	Slightly lowered	Markedly lowered
Serum lipids:		
Triglycerides	Normal	Normal
Cholesterol	Normal	Lowered
Non-esterified fatty acids	Elevated	Elevated
Blood sugar	Normal	Slightly lowered
Response to adrenaline	Exaggerated	Lowered
Blood urea	Normal	Lowered
Increase in body weight after high protein and high calorie therapy during the first 4 weeks	Slow	Satisfactory

What is the treatment of Kwashiorkor and Marasmus?

The treatment of both kwashiorkor and marasmic children requires care and caution. As their enzymes for digestion and their protein absorption and transport systems are less active, feeding these children with large quantities of good quality protein would be harmful. Well, this might sound strange to you. But it is so. Their diets must gradually be enriched with these proteins to allow their body sufficient time to develop the metabolic pathways to handle a better diet. Giving these children solutions of either predigested proteins or solutions of amino acids may be of benefit initially, but these solutions too must be used with care. If the amino acids in excess of immediate use are deatninated and if the pathway for

synthesizing urea is not fully functional, ammonia can accumulate in the child and become lethal. Marasmic Kwashiorkor

Marasmic Kwashiorkor

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In countries where the incidence of protein-calorie malnutrition (PCM) is high, a large number of cases show signs and symptoms of marasmus and kwashiorkor. These intermediate forms are called 'Marasmic-kwashiorkor'. In addition, the inter-relationship between the two major syndromes is such that the changing circumstances may result in a transition from one clinical picture to another. A child with early kwashiorkor can develop nutritional marasmus by severe infective diarrhea and ill-advised prolonged under-feeding. Conversely, an infant with nutritional marasmus may develop kwashiorkor if fed on protein deficient carbohydrate rich foods along with adequate common salt.

4.9 LET US SUM UP

This unit covered the important macronutrient proteins. Proteins, you learnt, are vital to all body cells, tissues, organs and functions of organ systems. The process of digestion, absorption and metabolism of protein are complex and involve several nutritional and non-nutritional factors. Proteins are widely distributed in nature, the richest vegetarian source being soy beans. Egg protein has the highest biologic value. Several methods can be employed to determine the protein content of foods, the most popular being those based on growth and body weight changes. Protein quality in the diet may be improved by mutual supplementation of protein rich foods and cereals. Nutritional requirements of proteins vary with age and physiological activity/stage. Deficiency of proteins leads to the twin disorders of marasmus and kwashiorkor and may be cured by dietary intervention.

4.10 GLOSSARY

Albinism : disease caused in persons unable to form melanin pigment.

Amino acids : the building blocks of proteins composed of carbon, hydrogen, oxygen and nitrogen.

Conjugated proteins : proteins which contain some non-protein substances.

Derived proteins : derivatives of the protein molecules formed through hydrolytic changes in the molecule.

Oedema : accumulation of' water in the interstitial space.

Essential amino acids : amino acids that are indispensable and are not synthesized in the body.

Kwashiorkor : disease the first child gets when second baby is born.

Limiting amino : acids the amino acids present in the least proportion in a food.

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4.11 CHECK YOUR PROGRESS

1) Write a note on the enzymes that are involved in protein digestion.

2) Bring out the role of HCI in gastric digestion.

3) List the functions of protein.

4) Which protein plays an important role in maintaining the osmotic pressure?

5) Give examples of proteins as carriers.

UNIT

5

LIPIDS

STRUCTURE

5.1 LEARNING OBJECTIVE

After studying this unit, you should be able to:

recommend necessary modifications in types and amount of dietary fat keeping in mind visible and invisible fat, fåtty acid composition and effect of dietary fat on lipid profile,

critically analyze the implications of excessive fat intake and changing lifestyle, and

generate guidelines for use of fats and oils in diet and selection of dishes to avoid excessive intakes.

5.2 INTRODUCTION

If somebody discovers that you have some knowledge of nutrition, you will be promptly shooted with two questions, first, "Oh! You really can tell much to eat?' and second, "Tell me which oil to eat 'X' or 'Y'? In view of learning about other macronutrients in previous units on carbohydrates and proteins, let us now embark to learn more about lipids.

This unit will detail on types and functions of fats and oils, their tequirements and significance in health and disease. Changing dietary patterns can sometimes lead to higher risk of some diseases. On the other hand, pmdent decisions on

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qualitative and quantitative aspects of fat can in fact prevent the onset of certain diseases associated with contemporary lifestyles.

At the end of going through this unit, you must do self assessment and recapitulate various dimensions of knowledge pertaining to dietary fats and oils. You will acquire adequate skills and confidence to prescribe fats and oils to any community. Tips will be given to reduce fat intake from human dietaries and will come handy in counseling patients of obesity, heart diseases, diabetes and cancer. You will be able to modify fat intake of patients with fat malabsorption and liver diseases. We hope you find this unit relevant and handy.

5.3 FATS: SOME BASIC FACTS

Body Fat Measurements

Obesity is best classified in adults based on Body Mass Index (BMI) classification. BMI, you already know, is a measure of body fat based on. height and weight. However, in clinical practice, body fat (BF%) measurements are also gaining importance. Body fat was always measured in sports subjects to monitor level of practice and piysical fitness. Body fat is gene ally considered a predictor of storing unused fuels when energy intake exceeds energy expenditure. In initial stages, the net body weight may be within the normal range but body fat exceeds. However, level of body fat also depends on the level of physical inactivity, sex, age and genetic predisposition.

In adults, the body fat 2 24% and in women, 2 27% fat is considered to be overweight over fat. However, these cutoffs are used for pure academic study rather than actually classifying obesity. Classification of obesity based on BMI and BF% do not necessarily overlap and BMI has many more rclinical correlates to risk of diseases than BF%. Generally, BF% per se correlates best to physical activity levels. Do you know how body fat can be measured?

The conventional golden method of measuring BF% is by under water weighing. Difference of weight in air and in water gives density, from which the body fat is computed. As these methods limits field application, two methods have been used extensively:

1) Skin fold method, and
2) Impedance method.

'Let us learn about these.

1) Skin fold method: The skin fold method utilizes predication of body fat from sum of three or four skin folds (at biceps, triceps, sub scapular, suprailiac regions). Specific prediction equations for each age category and both sexes are available as presented in Table 5.1.

Table 5.1: Age and sex adjusted equation by.Durnin and Womersley (1974) for calculating body fat %

Age of Women (in years)	Equation
30 - 39	D = 1.1423 − 0,0632 × (Log Σ)
40 - 49	D = 1.333 − 0.0612 × (Log Σ)
50 +	D = 1.339 − 0645 × (Log Σ)

where, D = body **density** (g/ml)

(Log Σ) = log of summation **of four skin fold** i.e.: biceps, **triceps,** sub scapular, suprailiac

$$\text{Fat mass (kg)} = \text{body weight (kg)} \times \frac{4.95 - 4.5}{D}$$

$$\text{Body fat (\%)} = \frac{\text{Fat mass (kg)}}{\text{Body weight (kg)}} \times 100$$

$$\text{Fat free mass (kg)} = \text{Body weight (kg)} - \text{Fat mass (kg)}$$

Similar equations are also available for men.

2) Impedance method: This method can give entire body composition like total body water (TBW), fat free mass (FFM) or lean body mass (LBM), fat mass (FM) and body fat (BF%) and body mass weight (kg/lb). The analyzer requires data or height and correction for weight of clothing. It computes wt/ht2 to give BMI also, The principle of this method is to pass a small electric current through the body and the subject stands on electrodes as on a weighing scale. The impedance is printed with body composition analysis data.

Many more methods have been used in research but these three methods (under water weighing, skinfold method and impedance method) have been widely used. The other methods like dual energy X-ray absorptiometry (DXA), Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are accurate and can find fat distribution. The method has a disadvantage of being expensive, involves radiation exposure and is not suitable for field work.

Having learnt about some basic facts about fats and about methods of assessing body fat, let us now study the types and significa ce of fatsllipids in human diet. We must know the amount necessary for optimal functioning of the body. We must also know if we eat in excess than the suggested requirements, what arc the implications on long term health of the human being. These are a few issues covered in the following sections.

5.4 TYPES OF FATS AND ITS METABOLISM

The type of fat consumed by a person is solely dependent on:

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- which oil(s) the family purchases,
- eating out pattern, and
- choice of foods eaten outside or purchased and brought home to be consumed by the family.

Consider the following'situation. In a household, say the family (four members) consuines one kg packet of ghee and 2-3 litres of different vegetable oils, like one litre bottle of mustard oil and 5 litre can of groundnut/sunflower oil at any given time. An adolescent boy of this family consumes one breadroll everyday from canteen and upto three pastries/week. He loves to eat besan coated fried peanuts during TV watching. Further, his father brings aloo-kachori while returning home from office to eat at teatime atleast twice a week. Hence the boy lands up consuming 5-6 different sources of fats and oils. Can yoll tell how?

Well, any diet comprises of visible fat and invisible fat. Visible fats are the fats and oils used as such at the table or used for cooking. For example, vegetable oils, ghee, salad dressing, mayonnaise, butter, creain etc. Invisible fats are present naturally as an integral component of different foods. Hence, flesh foods, whole milk, peanuts, soyabean, nuts and oilseeds, spices etc. have a high invisible fat content. Cereals contain only 2-3% of invisible fat but they constitute bulk of Indian diets and thus contribute significantly to overall fat intake.

Visible fats can be derived from both plant and animal origin. The fats traditionally used in India are reasonably region or state-specific. Ghee is popular among all affluents and during festivals, whereas, vanaspati is consumed by lower middle class. Generally, groundnut oil is popular in Western and Southern parts of India; coconut oil in Kerala, rapeseed and mustard oil in North and East i.e. West Bengal, Punjab and Jammu and Kashmir; safflower oil is consumed in Northern Kamataka and Southern Maharaslztra. Newer sources of oils are becoming increasingly popular like rice bran oil, palinolein and soya oil. Apart from this, cotton seed oil, sesame oil, castor oil and nigerseed oil is also produced in India. Solvent Extractors Association of India reported in March 2003 that the per capita availability of fats and oils is L 5- 17 g/day, of which 10-12 g is vegetable oils.

So we have just seen that a wide variety of fats/oils are consumed. Do you know how these fats/lipids are classified? Let us read and fiid it out in the following sub- section.

5.3.1 Classification of Fats and Fatty Acids

You must be wondering in this unit on lipids why we are talking about fats and oils and not using the term lipids. Definitely, you may also recall reading earlier in the Nutritional Biochemistry Course, in Unit 2, that when we talk about fats/oils, chemically we are referring to lipids. Lipids which are solid at room temperature are referred to as fats and those which are liquid are oils. Lipids are more apt when referred to all of them. However, in nutrition textbooks, fats and oils are referred in diets and lipids are referred in body fluids, like, serum lipid profile

Chemically, lipids are the organic molecules poor in oxygen content, soluble in organic solvents but insoluble in water. They are classified as

Simple lipids

Compound lipids

Derived lipids

Let us get to know each of these.

Simple lipids are fatty acid esters of glycerol, called triacyglycerols or triglycerides (for e.g. fats and oils) or higher alcohols (for e.g. waxes). Triglycerides are the major form of lipids present in human dietaries. They are the major sources of fatty acids to the body. Look up Unit 2 in the Nutritional Biochemistry Course for the structure of triglycerides.

Compound lipids are the simple lipids which combine with proteins (lipoproteins), carbohydrates (glycolipids), phosphates (phospholipids) etc.

Derived lipids refer to fatty acids, glycerol, cholesterol and other derived compounds including fat-solublevitamins, hormones and bile. Man can synthesize cholesterol in the body but some amount also comes from the diet. Cholesterol is present only in foods of animal origin.

Nature of fatty acids present in the triglyceride determines the physico-chemical properties and biological significance of the lipid. Triglycerides made up of saturated fatty acids are solids at room temperature and are called fats. If unsaturated fatty acids are present, they are liquid at room temperature and are called oils. What do we mean by saturated and unsaturated fatty acids? Certainly, you must be aware of this! Let us understand fatty acids in a little more detail.

The fatty acids can be discussed under following heads:

Saturated and Unsaturated,

Short chain, medium chain and long chain,

Essential fatty acids, and

Trans-fatty acids.

These categories are more suitable from the nutritional standpoint of view and are not essentially exclusive. The fatty acid per se may overlap in these categories but their. applications in normal and therapeutic diets warrants this classification. For example, a dietitian prescribes medium chain triglycerides in liver disorders. On the other hand, saturated fatty acid intake should be limited in normal diets for prevention of heart diseases.

So, then, let us now get to know them.

Saturated fatty acids (SFA) are those fatty acids which lack double bond, example palmitic acid (16:0), stearic acid (18:0). For your convenience, we have given the structure of some lipids in Box 5.2. Look up the structure of palmitic and stearic acid. Sources of SFA are animal fats, coconut oil, palm oil and vanaspati. Refer to Table 5.2 which gives the fatty acids found in fats and oils.

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Box: 5.2 Structure of Lipids

Saturated Fatty Acids (SFA)

$CH_3(CH_2)_{14}COOH$ Palmitic acid (6:0)

$CH_3(CH_2)_{16}COOH$ Stearic acid (18:0)

Monounsaturated Fatty Acids (MUFA)

$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$ Oleic acid (ω9; 18:1)

Polyunsaturated Fatty Acids (PUFA)

$CH_3(CH_2)_4CH{=}CH\text{-}CH_2\text{-}CH{=}CH(CH_2)_7COOH$ Linoleic acid (ω6 18:2)

$CH_3(CH_2)CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}(CH_2)_7COOH$ Linoleic acid (ω3 18:3)

Triglyceride (R_1, R_2, R_3 are Fatty acids)

CH_2COOR_1

CH_2COOR_2

CH_2COOR_3

Lecithin (contains glycerol R_1 and R_2 fatty acids, phosphoric acids and choline)

CH_2COOR_1

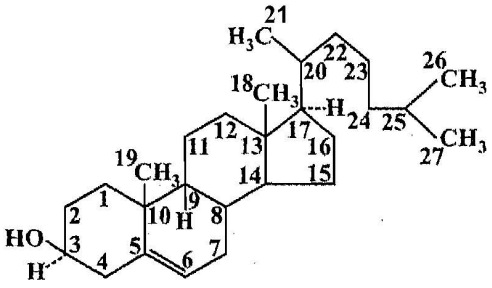
$CHCOOR_2$

O

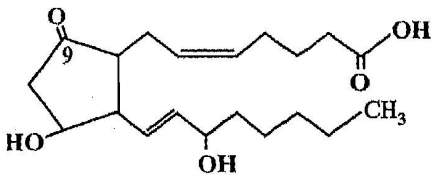
$CH_2\text{-}O\text{-}P\text{-}O\text{-}CH_2\text{-}CH_2\text{-}N^+(CH_3)_3$

O_n

CH_2COOR_3



Cholesterol ($C_{27}H_{45}OH$)



Prostaglandin E_2

Monounsaturated acids (MUFA) contain a single double bond (as shown in Box 5.2). The examples include palmito oleic acid (16 : 1) and oleic acid (18 : 1). Its sources are olive oil, canola oil, groundnut oil, rice bran oil, red palm oil and sesame oil (Refer to Table 5.2).

Polyunsaturated fatty acids (PUFA) contain more than one double bond in their structure. These double bonds can be counted from —COOH end or —CH3 end (refer to Box 5.2). 18:29'12 stands for linoleic acid which is C-18 stearic acid

derivative having two double bonds between carbon 9 and 10, as well as, carbon 12 and 13. Hence, when we count from CH3 end, the double bond appears at carbon number 6. We therefore also call linoleic acid as omega (co-6) (or n-6) fatty acid. Linoleic acid (C18:2, n-6) and Linolenic acid (18:3, n-3) are essential fatty acids, which are not synthesized in the body. They are obtained from oils rich in PUFA content. PUFA is present mostly in vegetable oils but fish oil is particularly rich in PUFA,

Table 5.2: Fats and oils and their fatty acids

Saturated Fatty Acids	Monounsaturated Fatty Acids	Polyunsaturated Fatty Acids	
		Linoleic (n-6)	Linolenic (n-3)*
Ghee/Butter Coconut (89%) Palm kernel (86%) Palm oil (51%) Vanaspati *(24%)*	Olive (77%) Canola (58%) Groundnut (50%) Rice bran oil (45%) Sesame (42%) Palmolein Red Palm oil (40%)	*Low* (<10%): Red Palm oil Palmolein Olive oil *Medium*(< 35%): Groundnut oil Rice Bran oil Sesame oil *High* Safflower oil Sunflower oil Cottonseed oil Soyabean oil Sesame oil Corn oil	Mustard oil (10%) Canola (8%) Soyabean oil (5%) Rice bran oil (1%)

*Other food sources: wheat, bajm, blackgram, cowpea, rajmah, soyabean, green leafr vegetables, fenugreek and mustard seeds and fish. Fish also contains C20 and C22, n-3 PUFA.

( ) Parenthesis indicates g/100g that category of fatty acids.

Short chain fatty acids are less than six carbon chain length i.e. smaller than caproic acid (C6:0). Butter contains small chain fatty acids. They are also obtainéd during fermentation.

Medium chain fatty acids are 6-10 carbon chain length. They are present in butter and coconut oil. They are recommended in liver disorders due to ease in their absorption.

Long chain%' acids contain more than 12 carbon chain. Lauric acid (C12:0) and myristic acid (C14:0) are known to be atherogenic. Palmitic acid (C16:0) and stearic acid (C18:0) are major fatty acids present in diet. Their derivatives are equally important. Essential fatty acids are all long chain fatty acids. What are essential

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fatty acids and their roles in our body? Let us read and find out next

Essential Fatty Acids (EFA)

There are two essential fatty acids — linoleic and linolenic acid as mentioned above. Their structures are depicted in Box 5.2. They are both 18 carbon compounds with more than one double bond — linoleic (n-6) C $18:2^{9,12}$ while linolenic acid is (n-3) C $18:3^{9,12,15}$. The human cell cannot place double bonds between ninth carbon and methyl end hence, omega-3 (n-3) and omega-6 (n-6) fatty acids need to be derived from the daily diets. Linoleic acid (n-6) can be lengthened to C-20 and dehydrogenated to give arachidonic acid Linolenic acid (n-3) can be lengthened and dehydrogenated to C20 and C22 compounds like eicosapentaenoic acid, EPA (C20:5) and docosahexaenoic acid, DHA (C22:6). These are known to be cardio-protective and are also present in fish oil.

Omega-3 and Omega-6 fatty acids are pan of vital body stmctures, perform important role in immune system, formation of cell membrane and produce hormone-like compounds called eicosanoids. These hormone-likecompounds include prostacyclins, prostaglandins, thromboxanes and leukotrienes. These coinpounds are potent regulators of vital body functions like blood pressure, child birth, blood clotting, immune response, Lipids inflammatory responses and stomach secretions.

Note: Aspirin is known to inhibit blood clotting because it blocks synthesis of eicosanoids. Physicians prescribe small doses of aspirin on regular basis for patients at high risk of heart at tack.

Next, we move on to understand what do we mean by trans-fatty aci&, how theseare produced and what are its sources.

Trans fatty acids

Plant derived fats and oils contain cis-fatty acids. You may recall reading about the cis and trans isomers in the Nutritional Biochemistry Course. Cis and trans-isomers, we learnt, have the same chemical formula but different chemical structure and properties.

Trans-fatty acids are produced when vegetable oils are hydrogenated to make margarines, partially hydrogenated vegetable shortening and vanaspati. Hence, major sources of trans-fatty acids to human diets are commercially baked products, deep fried snacks in vanaspati and mithai. Small amount of trans-fatty acids are present in milk fat formed by bacterial conversion of cis into trans-fatty acids in cow's stomach. Metabolically,trans-fatty acids and saturated fatty acids raise blood cholesterol levels.

Before moving on to the understanding of digestion of fats in our body, let us, review what we have learnt so far.

5.4.2 Digestion of Fats

The enzyme in human gut which is responsible for fat digestion is 'lipase', Lipase is secreted by both stomach and pancreas. In stomach, the dietary lipids gel liquidized in presence of heat and gastric contractions. Gastric lipase can only hydrolyze 30% of triglycerides comprising short and medium chain length. Hence, the lipolytic activity of stomach is not important. Only fat which contains some short and medium chain fatty acids tends to be hydrolyzed. These short chain fatty acids can then get absorbed through stomach wall into portal vein. Mostly diets have fats which provide long chain fatty acids. Long chain Salty acids entirely depend on emulsification by bile in gut.

The pancreatic juice and the bile are secreted together through common bile duct in the duodenum. Bile emulsifies fat into hydrophilic miscelles making lipase more efficacious to act. Pancreatic lipase is specific to hydrolyze primary ester linkages at carbon position 1 and 3 of glycerol in a triglyceride. After this action, mixture of products is obtained for absorption in jejunum. The products are — glycerol, fatty acids, monoacylglycerol and cliacylglycerol. Phospholipases act on phospholipids giving glycerol, fatty acid, lysolecithin etc., while cholesteryl esterase acts on esterified cholesterol to give free cholesterol and fatty acids. Let us now know how after digestion these products are handled for absorption.

5.4.3 Absorption of Fats

After digestion, only 25% of triglycerides are broken completely to glycerol and fatty acids. Major digestion product is 2-monoacylglycerol. This is because lipase can hydrolyze ester linkages at the positions 1 and 3 of glycerol preferentially. The 2- monoacylglycerol,fatty acids and 1-monoacylglycerol leave the oily phase and diffuse into micelles consisting of bile salts, lecithin and cholesterol into the aqueous phase of intestinal lumen towards brush border of the mucosal cell.

The utilization of free fatty acids is by activation of fatty acids and glycerol inside the mucosal cell to resynthesize triacyglycerol. These triacylglycerols and phospholipids, cholesteryl esters, cholesterol and small amount of protein form chylomicrons. What are 'chylomicrons'?

Yes, so you now know that chylomicrons are basically lipoprotein molecules which are water miscible. They are poured into lymphatic vessels through lacteals to reach the liver.

Hence long chain fatty acids of more than 10 carbon chain, phospholipids and cholesterol are absorbed in lymphatic vessels. Short-chain and medium-chain fatty acids are absorbed without bile emulsification into portal vein as unesterified acids. Plant sterols, fat-soluble vitamins A, D, E and K are all absorbed like long chain fatty acids. In liver disorders, long chain fatty acids may be replaced by medium chain triglycerides for better tolerance and increasing energy intake. In deficiency or absence of adequate bile, long chain triglyceride absorption may or may not be affected, hence fat is given to patients of liver disorders as per their

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tolerance. .

Bile itself undergoes reabsorption to be recycled 6-10 times a day. This is called 'enter hepatic circulation of bile'. In patients of familial hypercholesterolemia, more bile gets reabsorbed. Excretion of bile is an important route of eliminating endogenous cholesterol.

As bile is derived from cholesterol inside the liver cells, the loss of bile from body would mean utilizing cholesterol for bile synthesis. Clinically, hypercholesterolemia may be treated by interruptingenterohepatic circulation of bile.

Drugs can be given to prevent reabsorption of bile so that more and more endogenous cholesterol converts into bile and gets eliminated from the system. In the previous sections, we learnt how fats and lipids are digested and absorbed in various forms — short chain, medium chain and long chain fatty acids. Let us now try to understand how these are transported and stored in our body.

5.4.4 Transport and Storage of Fats in the Body

The chylomicrons circulate in blood for about 2 hours or more after the meal. They are acted upon by lipoprotein lipase giving free fatty acids (FFA) and glycerol. Muscles, adipose and other cells pick up FFA and utilize them to derive energy. Muscles derive energy but adipose cells re-esterify FFA with glycerol to store as triacyglycerol.

If a body consumes more energy than expended, liver uses the carbon skeletons of protein, carbohydrate and alcohol to synthesize lipids including cholesterol. Hence, liver is lipogenic whereas adipose cells store lipids rather than synthesizing these. Liver decides transport of lipids in aqueous phase of blood. It coats the triacylglycerols and cholesterol with proteins and phospholipid shell (similar to chylomicrons), synthesizing very low density lipoproteins (VLDL). VLDL losses fatty acids after the action of lipoprotein lipase in blood and then its density increases. These are called 'intermediate density lipoproteins' (IDL) and 'low density lipoproteins' (LDL). LDL contains all the cholesterol present in VLDL having therefore a higher cholesterol/ triacylglycerol ratio rather than VLDL and IDL. LDL is therefore referred to as 'bad' cholesterol and is strongly associated as a risk factor of heart diseases.

LDL delivers its contents into the cell through LDL receptors. Liver contains 50-75% of LDL receptors in the body. Liver hence plays an important role in regulating serum cholesterol levels. Serum LDL of < 130 mg/dl is desirable. Some LDL oxidizes, which is usually scavenged by WBC. This scavenging releases cholesterol in vessel walls and over the years develops plaques inflicting atherosclerosis, This is promoted by smoking, diabetes, high blood pressure, high blood LDL levels and viral or bacterial infections. Consuming fruits and vegetables rich in antioxidants like vitamin C, vitamin E, carotenoids and certain phytochemicals inhibit LDL oxidation.

Liver and intestine produce another lipoprotein called high density lipoprotein (HDL). In blood, circulating HDL picks up cholesterol from dying cells and brings it back to liver for excretion. It is therefore referred as 'good' cholesterol.

HDL also blocks oxidation of LDL. Serum HDL of > 50 mg/dl is cardio-protective and < 35 mg/dl indicates increased risk to heart diseases. Women, especially before menopause, have high HDL levels. Exercise and physically active lifestyle are sure ways of maintaining high HDL levels. Looking excess weight and avoiding smoking also maintains or raises HDL. Well-spaced meals keep serum triglycerides low and raise HDL. Serum triglycerides should be kept below 150 mg/dl. Raising HDL is more difficult than lowering LDL. Low fat diets and PUFA rich diets lower both HDL and LDL cholesterol. However, traditional low fat Asian diets result in low LDL and HDL and associated lower risk to heart diseases. More research is needed to validate to long term implications. HDL/LDL ratio has been considered to be crucial in determining risk to heart disease. We will learn more about this aspect in the Clinical and Therapeutic Course (MFN-005) in Unit 12.

The discussion above was quite exhaustive. We hope having gone through this section and the unit on Lipid metabolism in the Nutritional Biochemistry Course, you would be quite clear about the mechanism of digestion, absorption and transport of lipids. Now, let us focus our attention on the functions of lipids in our body.

5.5 FUNCTIONS OF FATS AND OILS

In above sections, we have covered types and sources of fats and fatty acids. We have also understood how it is digested, absorbed and transported. Let us now know ts routes of utilization and why body needs fats.

Let us enumerate

1) Fats contribute to texture, flavour; taste and increases palatability of the diet. They provide an effective medium of heat transfer in deep-frying and transfer of flavours from Indian spices.

2) Fats have highest heat energy density of 9 Kcal/g. It is the major storage fonn of energy in body requiring least space and minimum water of hydration as compared to protein in muscle or glycogen. Adipose cells are 80% lipid and only 20% water and protein.

   In children's diet, cereals and pulses make their diet bulky. Fats are concentrated sources of energy. In adult's diet, use of visible fats should be minimum. Excessive fat intake is not recommended in any age, including children. The following section will detail on visible fat requirements, keeping in mind the invisible fat contents of Indian diets in all age group.

3) Fats are essential for meeting nutritional needs of essential fatty acids like linoleic acid (n-6) and alpha linolenic acid (n-3). These essential fatty acids are needed for the synthesis of important eicosanoids, as already covered in sub- section 5.3. l. Saturated fatty acids, monounsaturated fatty acids and cholesterol can be synthesized in the body, hence the diet only adds-on to their total amount available in the body. Excessive intake of SFA and cholesterol in diets can therefore be harmful. Excess n-6 impairs desaturation and elongation of linol.enic acid to EPA and DHA.

4) Fats promote absorption of fat-soluble vitamins lik vitamin A, D, E and K. Patients of cystic fibrosis often absorb fat poorly and are at-risk for fat-soluble vitamin deficiency. Water miscible preparations of these vitamins are therefore prescribed.

Patients who are given mineral oil laxatives are at-risk of fat-soluble Vitamin deficiency. The mineral oils carry these vitamins into large intestine which are lost in stool. Such laxatives should not be given at mealtime or for long periods.

5) Fat intake ensures satiety. It imparts feeling of fullness and satisfaction and thus delays onset of hunger. In low fat diets, satiety can be ensured by high fibre and fluid intake

6) Fats along with proteins constitute structural components (f cell membrane and some body fluids. Lipoproteins also have an important role in transport of lipids in blood.

7) Fats serve as thermal insulator in the subcutaneous tissues and certain organs. Some lipids act as electrical insulators allowing rapid propagation of depolarization waves along the myelinated nerves. The fat content of the nervous tissues is particularly high.

In anorexia nervosa, the body fat falls dangerously low (< 5%) shows problems in insulation. Body hair stands erect to trap air and simulate insulation.

Assessment: Write body fat % of 10 subjects — 5 underweight and 5 overweight, from a health clinic which has facilitates to measure body fat %.

8) Some dietary fats contain antioxidants. Most of them contain antioxidants which confer stability to the oil and prevent rancidity. Palm oil contains tocotrienols, tocopherols and beta-carotenes. Sesame oil contains lignins. Rice bran oil contains tocotrienols, tocopherols, oryzanol, phytosterols and squalene. Oryzanol (1.2-1.7%) in physically refined rice bran oil helps to elevate HDL, decrease plasma cholesterol, treat nerve imbalance, menopause disorders, retard ageing and acts as anti-dandruff and anti-itching agent. Tocotrienols, tocopherols and squalene are antioxidants

conferring oxidative stability to the oil.

Unsaturated fats are susceptible to oxidation and rancidity. Most oils have natural antioxidants but food manufacturers have an option to add synthetic antioxidants like butylated hydroxyanisol (BHA) and butylated hydroxyl toluene (BHT) to prevent rancidity. One thing is for sure that vitamin E requirements of man are linked to PUFA intake. ICMR recommends vitamin E (toc%pherol) at 0.8 mg/g PUFA intake.

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Before we move on to our next section on nutritional requirements of fats and:oils, let us recapitulate whatever we learnt till now.

5.6 NUTRITIONAL REQUIREMENTS OF FATS AND OILS

As with the other macronutrients, we do compute requirements of visible fats too for all age groups and give guidelines for selection of fats. For this, we must consider total fat intake, which includes both visible and invisible fat in food.

A daily intake of 2400 Kcal Indian diet contains 40 g of fat where 25 g is invisible and 15 g is visible fat. This works out to be that invisible fat is 10 en % (=25 g x 9 Kcal + 2400, where, lg fat gives 9 Kcal). The upper income group, especially in urban areas tends to consume as high as 50 g of visible fat. Their invisible fat content also is about 30-50 g/d due to consumption of fat rich foods, whole milk and ItiJ< products. This urban group may exceed fat intake of more than 30 en% and show several risk factors of an early onset of heart disease. Let us look of fat requirements to meet minimum essential fatty acid requirements in all age groups. Let us start with adults.

5.6.1 Adults

A desirable amount of a linoleic acid to be consumed by a normal adult is 3 en% (ICMR, 1990). The invisible fat present in the usual Indian foods is high in linoleic acid content (rice, wheat, bengal gram, red gram). Hence average, not so rich, Indians have sufficient linoleic acid. Linolenic acid is also present in these foods upto 3% and in spices upto 5%. In an Indian study, even the blood status was satisfactory even if visible fat content of the diets were low. EFA requirement has been computed by ICMR (1990) and depicted in Table 5.3. It seems cereal-based Indian diets can Lipids meet more than half the linoleic acid requirement of adults. It has been recommended to select a visible fat which contains at least 20% linoleic acid.

Viewing 10 en% from invisible fat in diet, the remaining 5 en% can come from visible fat, which has more than 20% linoleic acid. This 5 en% in 2400 Kcal diet works out to be 12 g/day. This implies even 3 tsp of cooking oil/table fat a day meets adult requirements.

Table 5.3: Fat requirements of Indians

Group	EFA Requirement en%	Invisible Fat [a] en%	Minimum Visible Fat		Suggested Desirable Visible Fat Intake	
			en%	g/day	g/day	en%
Adults [c]	3	10	5	12 [c]	20 [c]	9
Older children [c]	3	10	5	12	22	9
Young children	3	10	5	8	25	15
Pregnant woman	4.5	10	12.5	30	30	12.5
Lactating woman	5.7	10	17.5	45	45	17.5

5.6.2 Pregnancy and Lactation

ICMR (1990) recommends that linoleic acid requirements should be raised to 4.5 en% during pregnancy as highlighted in Table 5.3. This can be met from 30 g/d of oil which has >20% linoleic acid. Similarly, linoleic acid requirement during lactation rises to 5.7 en% (Table 5.3) which corresponds to 45 g oil intake which has > 20% of linoleic acid).

5.6.3 Infancy

Adequate breast-feeding ensures 30 g fat intake by infants, of which 10% is linoleic acid and 1% is linolenic acid, Breast milk thus meets EFA needs of infants of 6 en%. Infants who are weaned completely or partially should be given enough vegetable oil with a high linoleic acid content to ensure 6 en% of linoleic acid.

Recent studies have indicated the essentiality of n-3 fatty acids, and the need for the inclusion of docosa-hexaenoic acid (DHA) in food for infants. DHA and arachidonic acid are particularly important for brain development. DHA, in particular has an important role to play in myelination and brain development.

5.6.4 Young and Older Children

Young children need 3 en%, which would be easily met from 8-10 g of oil. However, more visible oil is needed to improve energy density of diets otherwise cereal based diets become bulky. ICMR (1990) recommends 20 g/d in children's diet from oil which has at least 20% linoleic acid.

Finally, having gone through the discussion presented above, you must be thinking which oil should we select and consume on a daily basis i.e., what should be the ideal cooking medium. Let us read and find out for ourselves.

5.6.5 Choice of Cooking Medium in the Context of n-3 and n-6 Fatty Acid Ratio in Indian Diets

A cooking medium should meet EFA needs. Some EFA will come from invisible fat. Selecting an oil with at least 20% linoleic acid is not the only criteria. ICMR (1998) has given dietary guidelines to maintain n-6/n-3 ratio of 5-10, which ensures long-term health. However, most oils are rich in linoleic acid (n-6). Consumption of PUFA rich oils lead to a very high ratio. Excess n-6, impairs desaturation and elongation of linolenic acid to EPA and DHA, which is best avoided, It is, therefore, important to promote linolenic acid (n -3) intake to balance the ratio. For ensuring the appropriate balance of fatty acids in cereal-based diets and in the diets of those who do not eat fish and are primarily vegetarians like in the case of many Indian diets, we need to depend on plant foods rich in linolenic acid. Table 5.2 depicts sources of linolenic acid as wheat, bajra, blackgram, cowpea, rajmah, soyabean, green leafy vegetables, fenugreek and mustard seeds (spices) apart from fish. (American guidelines therefore recoinmend 2 servings of fish per week).

Linolenic acid can also be obtained from oils like mustard, soyabean, canola and rice bran oil (Table 5.2). ICMR (1998) recommends for n-6/n-3 ratio of 5-10 and PUFA/ SFA of 0.8-1.0, hence, the choice of cooking oil should be: -

a) moderate linoleic acid content oils like groundnut oil, rice bran oil or sesame oil

OR

Soyabean oil (containing both linoleic and alpha linolenic acid), and

b) combination of two oils in approximately equal proportion:

Use high linoleic acid oils like sunflower oil, safflower oil and cottonseed oil with palm oil (low linoleic acid)

OR

Mustard Oil. (containing alpha-linolenic acid) along with any other cooking oil (this will reduce erucic acid from mustard oil and thereby its undesirable health effects)

Soyabean oil, rapeseedl mustard oil and rice bran oil, you may have noticed, has both n-3 and n-6 fatty acids but not necessarily in best proportion to be recommended as a single oil except rice bran oil.

It is strongly recommended that more than one source of cooking oil should be used in every household, For this reason, blending of oil is not the best option.

Recently, blending of oil has been popularized for healthful gains, acceptability and equalizing SFA: MI-JFA: PUFA to 1:1:1. Blending rice bran oil with safflower oil in ratio of 7:3 is very promising, since it magnifies the hypocholesterolaemic effect than effects of individual oils. Similarly, blending of palm oil with rice bran oil in a ratio of 3:1 ensure SFA:MUFA:PUFA of 1:5:1 which is effective in preventing heart disease according to Atnerican Heart Association and Japanese Ministry of Health and Welfare.

Let us rake a break here aud recall what we have learnt so far

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5.7 EXCESSIVE FAT INTAKE

Although minimum amount of fat is essential as calculated above but upper limit of fat should be drawn due to its link with an increased lisk of developing obesity, heart diseases and cancer. The fact that these diseases are on a rise can be attributed to the changing dietary and lifestyle practices coupled with stress. Let us look closely at these factors.

5.7.1 Changing Trends in Dietary Intake

As a practicing dietitian, you must be sensitive to the society as a whole. The fat requirements have been worked out with a premise of traditional moderate cost Indian diet. Contemporary society showing nutritional transition and access to fast foods and fried snacks while eating out is in vogue. This leads to an increased intake of saturated fatty acid, milk and milk products, flesh foods and sugar at the cost of whole cereals, millets and pulses. This is likely to decrease EFA intake from invisible sources and raise SFA. The total calories are also high, especially if alcohol consumption is also on a rise. Check out the facts by doing the following assignment/ exercise.

5.7.2 Eating Out

This is emerging as the most common factor associated with obesity, excessive fat intake and total caloric intake. When we closely look at the selection of foods while eating out, they are mostly flied snacks and dishes, like South Indian dosa, vada, or North Indian chole-bhature or fried Chinese. Fried snacks like samosa, bread roll, bread pakora, paneer pakora, and aerated beverages are usually supplied in all canteens. Namkeens and chips also contain 20-70% fat. These foods could be best avoided. Table 5.4 suggests some tips in food selection.

We have already discussed that fried foods and baked products could be a source Lipids of trans-fatty acids (sub-section 5.3. l). Further, quality and source of frying oil is not known. May be the oil used is highly reused and abused. Rice bran oil and palm oil gives a slightly lower oil uptake than other oils. Yd it is better to select dishes prepared ly other cooking methods than frying for lesser oil intake. Dish selection and behaviour modifications are the key words in commercial business of weight reduction clinics.

Excessive consumption of fat can lead to various harmful health effects. What are these? The next sub-section focuses on these health effects.

5.6.3 Diseases: Association and Preventive Measures

By now, you must have realized that excessive consumption of fat can lead to

various harmful health effects.. Well, three diseases have shown close link to excessive dietaty fat intake: obesity, heart diseases and cancer. Let us see how are these related and their onset can be prevented.

1) *Obesity*

In obesity, cutting down total energy intake or increasing output to ensure energy balance is the basic principle of prevention. Fat being energy dense is always on the hit list. This will help you to counsel all such patients. Selection of foods and modified cooking methods further prevent excessive fat intake. Low fat diets should be given with high fibre and fluid diet to ensure compliance and satiety.

2) *Heart Diseases*

Heart diseases show strong links to fat and cholesterol intake. Foods rich in cholesterol are of animal origin and given in Table 5.5. Higher dietary cholesterol increases blood cholesterol but high blood cholesterol with family history does not necessarily gain on cholesterol-free diet. Both chug and low cholesterol diet is recommended. Vegetable oils have no cholesterol, as cah be noted from Table 5.5. The reference of 'good' and 'bad' cholesterol to dietary fats is in reference to the effect in blood lipids and HDL/LDL ratio. The significance of n-6/n-3 ratio has been already covered in previous sections. High intakes of n-6 polyunsaturated fats have been associated with the reduced total cholesterol and LDL cholesterol concentrations that are associated with low risk of CHD. In general, epidemiological studies have demonstrated an inverse association between n-6 polyunsaturated fatty acid intake and risk of CHD n-3 polyunsaturated fatty acids (particularly, eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) have been shown to reduce the risk of CHD and stroke by a multitude of mechanisms: by preventing arrhythmias, reducing atherosclerosis, decreasing platelet aggregation, lowering plasma triacylglycerol concentrations,decreasing proinflammatory eicosanoids, modulating endothelial function and decreasing blood pressure in hypertensive individuals.

American Heart Association (AHA) and ICMR (1998) guidelines broadly suggest:

- Total fat intake should not exceed 30 en%.
- SFA fat intake should be 7-10 en%.
- Dietary cholesterol intake should not exceed 300 mg/d. Intake less than 200 mg/d is advisable,

Table 5.5: Cholesterol content of foods (in descending order)

Food	Cholesterol (mg/100 g)
Egg yolk	1500
Egg whole	550
Kidney	375
Liver	300
Butter	250

Lobster	200
Shrimp	125
Crab	125
Cheese, Cream	120
Cheese, Cheddar	100
Milk powder (whole)	85
Pork	70
Lamb	70
Fish	70
Cheese spread	65
Mutton	65
Ice cream	45
Cheese, cottage	15
Milk, whole	11
Milk, skim	3
Vegetable oils	0

ICMR (1998) further suggests:

- Just take enough fat (as per the RDA),
- Use more than one source of cooking oil,
- Limit use of ghee, butter and vanaspati,
- Eat linolenic acid rich foods like green leafy vegetables, spices like fenugreek seeds and mustard seeds in a predominantly cereal pulse diet,
- Eat fish more frequently than meat and poultry,
- Limit and avoid organ meats like liver, kidney and brain,
- Skimmed milk and low fat milk is preferred instead of whole milk.

3) Cancer

Role of fat in cancer is debatable. High fat intake is indicated as a risk factor to cancer of breast, colon etc. Saturated fat intake has been implicated more in cancer events. Abused oil intake (re-used oil) and oils with high peroxidative potential producing free radicals in body also promote carcinogenesis. Look up Unit 9 in the Nutritional Biochemistry Course (MFN-002) for more informationon free radicals. The unsaturated fatty acid consumption should not be indiscreetly promoted in absence of relevant research data. The PUFA intake should not exceed 10 en%.

With this, we come to an end on our discussion on lipids, its types and sources. We hope that this unit will have brought up issues related to fats and oils which will definitely help you out as a dietitian.

5.8 LET US SUM UP

In this unit, we learnt about the classification of fats, the major difference between fats and oils and and the concept of visible and invisible fats. We saw that man primarily consumes triglycerides. Diets also provide cholesterol, which is present

only in foods of animal origin.

We then learnt about lipid digestion and absorption, where we discussed that long chain fatty acids, cholesterol and phospholipids are absorbed through the lymphatic vessels only after emulsification by bile. Short and medium chain fatty acids are absorbed directly into blood. We also get to know about 'good' and 'bad' cholesterol. The good cholesterol or HDL is cardio-protective and can be raised by exercise, avoidance of smoking, maintaining normal weight and eating pattern, Consumption of fruits and vegetables inhibits LDL oxidation and in turn, prevents cholesterol deposition.

Fats have an important role in human nutrition and some amount of it should be present in daily diet. Use of 2-3 different oils per household is recommended. Eating out often must be avoided as it leads to an increase in consumption of fats especially trans-fatty acids.

Finally, we learnt that excessive fat intake could lead to major health diseases such as obesity, heart diseases and cancer. Hence, a judicious fat intake with a healthy life style and correct eating habits must be chosen to prevent the risk of these diseases.

5.9 GLOSSARY

Chylomicrons : water miscible lipoprotein molecules.

Compound lipids : simple lipids which combine with other molecules such as proteins, carbohydrates and phosphates.

Derived lipids : fatty lipids, glycerol, cholesterol and other derived compound.

Essential Fatty Acids (EFA) : those fatty acids that cannot be synthesized in body and are needed in daily diet. Linoleic acid and linolenic acids are two essential fatty acids.

Pats : triglycerides made up of saturated fatty acids which are liquid at room temperature.

Invisible fats : fats that are present as an integral component of different foods such as milk, meat, egg, cereals, pulses etc.

Linoleic acid : an EFA; also called Lin or LA content of fats. Chemically, it is omega-6 (n-6); C18:2, cis-9, 12 octadecenoic acid.

Linolenic acid : an EFA also, called Len content of fats or ALNA

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(alpha linolenic acid). Chemically, it is omega-3 (n-3), C18:3; cis 9, 12, 15 octadecenoic acid.

Lipoprotein : any particle in blood containing a core of lipids with a shell of protein. It can freely move in an aqueous medium of blood.

Simple lipids : fatty acid esters of glycerols or higher alcohols.

Trans-fatty acid : all naturally occurring fats in the body are cis isomers; Trans-isomers differ in structure and properties but have same fonnula.

Triacylglycerol : also called triglyceride. Acyl stands for fatty acids hence three fatty acids esterify three alcohol groups of aglycerol molecule lo form triglyceride or triacylglycerol. ,2-monoacyl : has single 'fatty acid which esterify only second carbon glycerol of glycerol.

Visible fats : fats that are used as such at the table or for cooking. ,!They are of both plant and animal origin.

5.10 CHECK YOUR PROGRESS

1) Explain the relevance of measuring body fat. Name the methods that are used to measure body fat. Give the equation for calculating BF %.

2) What do you mean by visible and non-visible fats? Give examples.

3) Classify lipids, giving examples.

4) What are EFAs? Give examples and enumerate their functions in our body.

5) How are trans-fatty acids produced? What are its sources?

UNIT

6

WATER

STRUCTURE

6.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

enumerate the functions of water in the human body,
discuss the factors influencing water content of the human body,

explore the most basic nutrition task of water balance and, the mechanisms involved in regulating this,

appreciate the requirements of water for different age groups,

explain the disturbances in fluid balance and consequences, and

describe the importance of averting fluid imbalance and methods of correcting fluid imbalance when it occurs.

6.2 INTRODUCTION

Units 3, 4 and 5 in this course covered the macronutrients. Macronutrients, you know, are those nutrients which are required in large amounts by our body namely, carbohydrates, fats and proteins. We studied about their functions, role and food sources. Other than the macronutrients, we do require certain other nutrients, some of which are required in very small amounts, but these are extremely important. We shall learn about these nutrients, i.e. the micronutrients in the next few units. Now in this unit, we shall focus on water, the most important nutrient of all the essential nutrients required by the body.

The absence of water affects us more quickly than the absence of any other nutrient. Meeting our need for a continuous supply of life-sustaining water and maintaining the body water in different compartments are major nutritional and physiologic tasks.

What is the role of water in the body'? How is the water distributed and held in the body? What is meant by water balance'?
What is our water requirement'? What do the disturbances in fluid balance lead to? You will find a detailed discussion on these important aspects in this unit.

6.3 WATER: AN ESSENTIAL BUT OVERLOOKED NUTRIENT

You may already know that the total body water (TBW) constitutes 50-60% of the body weight. A 70 kg 'standard male' contains 42 litre water — 60% of his body weight while an adult female contains 55% of body weight as water. Why is there a difference in TBW content between males and females? This decrease is due to a higher fat content found in females. The proponion of water in the body, however, varies in individuals depending on body composition. Let us see how.

For example, you will find that muscular people have a higher proportion of water than the less muscular or obese people. Can you say why? Well, simply because the striated muscle contains more water than any other body tissue (except blood). While water content of the muscles is 65-75%, it amounts to less than 25% of the weight of fat. Consequently, the differences in body water between individuals are largely due to the variations in body composition i.e. differences in lean tissues vs. fat. Similarly, males have a higher proportion of water in their bodies than do females because they have a higher proportion of lean tissue and a lower proportion of fat.

An athlete will have a greater proportion of body water than a non-athlete as he/she has developed a relatively larger proportion of lean body mass. You would notice that there is a steady fall in the proportion of water as we age, which is due to an increased deposition of fat in the body, as wcl! as, loss of muscle mass with age. Table 6.1 presents the percentage of total body water at different stages of lifecycle.

Subjects	Total Body Water (%)
Infants and children	
At Birth	75
At 1 year	58
6 - 7 years	62

Males	
16 - 30 years	58.9
31 - 60 years	54.7
61 - 90 years	51.8
Females	
16 - 30 years	50.9
31 - 90 years	45.2

Table 6.1: Percentage of TBW in infants, children and adult

6.3.1 Functions of Water in the Body

Because of its unique chemical and physical characteristics, water plays several key roles in our life processes. These functions are described herewith:

- Water as a neditm and solvent: Water is the medium of all cell fluids, including digestive juices, lymph, blood, urine, and perspiration. All the physiochemical reactions that occur in the cells of the body take place in the precisely regulated environment of the body fluids. Water enters into many essential reactions, such as hydrolysis, that occurs in digestion. Water is an end-product in the oxidation of energy-yielding nutrients.

- Water is a solvent for the products of digestion, holding them in solution and pennitting them to pass through the absorbing walls of the intestinal tract into the blood stream. Due to its ability to dissolve the nutrients and cellular waste products, it carries nutrients to the cells and removes the waste products to the lungs, kidneys, gut and skin.

- Water as a lubricant: All fluids have lubricating propenies as they can make it easier for the solid materials to slip over one another. Water-based fluids act as lubricants in various parts of the body, most notably within joints where synovial fluid makes movements easier and minimizes wear and tear in cartilage and bone. The lubricant action of saliva and mucus in the mouth and the oesophagus is not so obvious.

- Water as a temperature regulator: Water plays an important role in the distribution of heat throughout the body and the regulation of body temperature. Heat is generated in the body due to hard work, exposure to heat, fever or merely by the metabolism of energy-yielding nutrients. The most effective route of heat loss from the body is via the evaporation of water as perspiration from the surface of the skin. When perspiration evaporates, the heat is largely drawn from the body. Under nonmal circumstances, the body is continuously

cooled by the evaporation of perspiration froin the surface of the skin, known as insensible perspiration.

- Water as a source of dietary minerals: Allhough water is coinposed of only oxygen and hydrogen, the water we drink or use in food preparation can contain significant amounts of minerals, such as calcium, magnesium, zinc, copper and fluoride; the amount will vary based on the source of water and any treatment the water has been put through. While hard water will contain magnesiuln and calcium, the soft water may contain sodium.

  Being an effective solvent, water may carry significant amounts of toxic compounds of lead or cadmium, pesticides and also industrial waste products. Regular monitoring of water supply to check for such contamination is essential to safeguard the public health.

The discussion above highlights the significance of water. Within the body, the water is held in the compartments. What are these compartments? What are the forces that control the water distribution in the body? Read the next section to understand these concepts.

6.4 WATER DISTRIBUTION AND COMPARTMENTS OF BODY WATER

Each one of us has a ve itable 'sea within', held in place by multiple membranes and our protective envelope of skin. Within this envelope, water diffuses freely to all parts and is controlled by its own chemical potential. There are various compartments of fluid in our body, separated by membranes. The quantity of water contained in every compartment is beautifully balanced by the forces that maintain equilibrium among the parts.

There are electrolytes and other solutes in the water, the concentration and distribution of which determine internal shifts and balances in the body water. All these aspects, including the water distribution in the body are described in this section. We begin by getting to know the body water compartments.

6.4.1 Compartments of Body Water

Within the body, water is found in two major compartments. These are:

The intracellular compartment (inside the cell)

The extracellular compartment (outside the cell).

The water containing varied concentrations of biochemicals in these compartments is, therefore, referred to as intracellular fluid (ICF) and extracellular fluid (ECF). Intracellular fluid compartment constitutes two-thirds of the total body water.

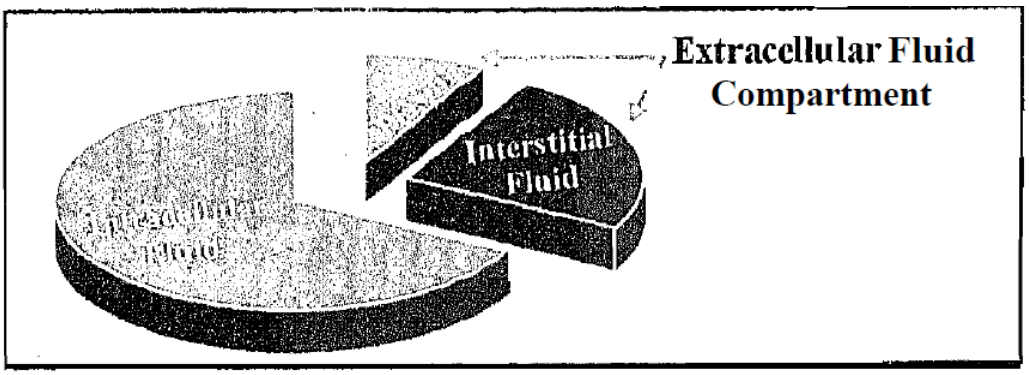

Figure 6.1: Intracellular fluid compartment: two-thirds of the total body water

Figure 6.2 diagramatically represents the two fluid compannents of the body

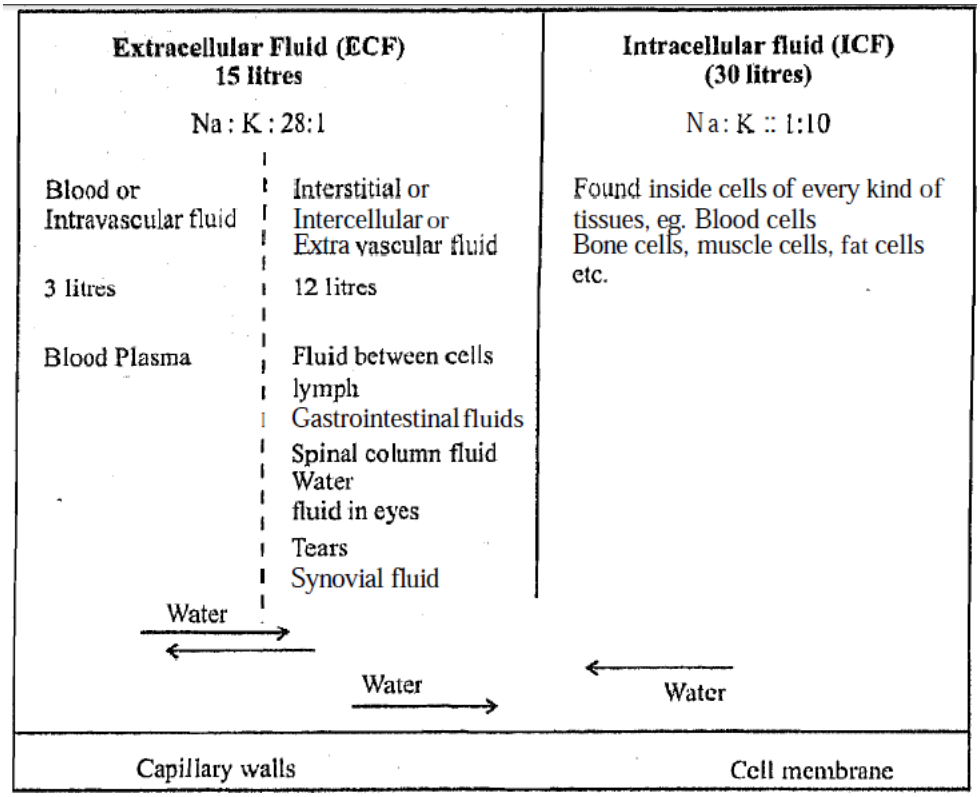

Figure 6.2: The two major fluid compartments of the body

The chemical composition of these fluid compannents varies from place to place in the body, depending on the type of cells the fluid within and around it. The intracellular and extracellular fluid compartments are separated by the semi-permeable membranes of the body's cells. These membranes allow water to pass through them but fonn a selective barrier to other chemicals, allowing them to diffuse or to be carried readily and restricting the passage of many others. Let us learn about ICF and ECF in more details.

NOTES

A) The intracellular fluid or the water within the cells makes up about 40-45% of the total body weight. Because the body cells are the sites of vast metabolic activity, it is of no surprise that the total water inside the body cells is about twice the amount outside the cells. These are high in potassium and magnesium and low in sodium and chloride ions. B) The extracellular fluid compartment is further subdivided into several smaller Water compartments as you may have noticed in Figure 6.2. These include:

- Plasma
- The intravascular fluid compartment, and
- The intercellular [interstitial or extravascular fluid (ISF)] compartment.
- The transcellular fluid compartment

Let us get to know a little more about these compartments.

Plasma is the only major fluid compaftment that exists as real collection of fluid all in one location. It differs from ISF in its much higher protein content. Blood contains suspended red and white cells so plasma has been callecl the interstitial fluid of the blood. The fluid compartmen called the blood volume is interesting in that it is a composite compartment containing ECF and ICE

The extracellular fluid compartment is sub-divided into the intravascular fluid compartment (fluid within the blood vessel) and intercellular/interstitial/ extravascular fluid compartment (fluid between the body cells but outside of the blood vessel).

The intravascular fluid comprises of all the fluid within the blood vessels of the "vascular" system — namely, the arteries, veins and capillaries. The intercellular compartment, on the other hand, contains the fluid around and between the cells of the body, which carries nutrients to the cells and collects waste products for eventual excretion.

The intravascular fluid is separated from the intelcellular fluid by the walls of the blood vessels, which also form a semipermeable barrier that allows the water to pass through it but exerts a strict selective control over the passage of other chemicals. The transcellular fluid is a small compartment that represents all those body fluids which are formed from the transport activities of cell. These do not readily exchange water with the bulk of the extracellular compartment and includes cerebrospinal fluid and secretions of the gastrointestinal tract.

The fluids in the eyeball (vitreous humor), around joints (synovial fluid), and within the digestive tract, as well as, a few specialized fluids are outside the cells and thus are exrtracellular, but do not readily exchange water with the bulk of the extracellular compartment. These fluids are called transcellular fluid compartment. So we have looked at the various water compartments of our body. How is water distribution controlled in these compartments'? The next sub-section focuses on this aspect.

6.4.2 Forces Influencing Water Distribution

"IWo major types of solute particles control body water distribution by their varying ücentrations in body fluids and the forces these concentrations create. These solute particles are of two kinds — electrolytes, that include the positively charged sodium and potassium inns and the negatively charged chloride ions, commonly known as electrolytes and the plasma protein. The concentration of sodium inside the cells is about 5 mEqL (miliequivalents) compared with 140 mEqL outside while for chloride ions, concentration is 96-106 mEq/L. The normal range for potassium is 3.7 to 5.2 mEgfL. The specific electrolytes and the plasma proteins are, therefore, the main players in the balancing act in our "sea within".

The movement of water is controlled mainly by osmotic pressure generated by the inorganic ions in solution in the body. Osmotic pressure is directly proportional to the number of particles in solution and usually refers to the pressure exereted by water or solvents flowing into a solution at the cell membrane. The osmotic pressure of the intracellular fluid, is the function of its content of potassium, the predominant cation in the intracellular fluid, as illustrated in Figure 6.3.

By contrast, the osmotic pressure of extracellular fluid may be considered relative to its content of sodium, the major cation present in extracellular fluid. Although variations in the distribution of sodium and potassium ions are the principal causes of water shifts between the various compartments, chloride and phosphate ions also influence the water balance.

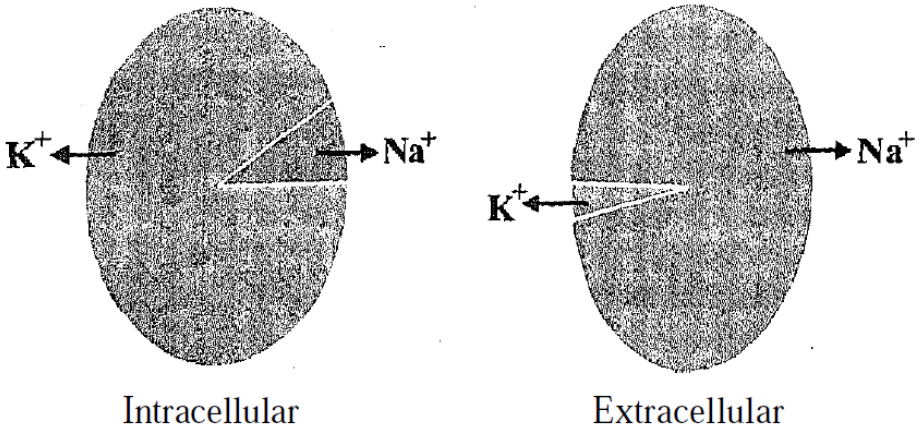

Figure 6.3: Relative levels of and K" in the intracellular and extracellular fluid

The plasma proteins, which are non-diffusible because of their large molecular weight, also play an important role in maintaining osmotic equilibrium. Oncotic pressure, or what is also known as Colloidal Osmotic Pressure (COP), is the pressure at the capillary membrane cuused by dissolved proteins in the plasma. Oncotic pressure helps to retain water within the blood vessels, thus maintaining the integrity of the blood volume in the vascular compartment.

With the understanding of water distribution and the forces which come in play, let us next study the concept of water balance. But before that, let us review what we have learnt so far.

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6.5 WATER BALANCE

The amount of fluid in the body is tightly controlled because imbalance can be devastating. In a normal individual, the maintenance of water balance is achieved by adjusting both water intake and excretion as needed. What are the major sources of water intake and excretion? Read further to find out

6.5.1 Water Intake

The,major sources of water are:

1) The preformed water that we consume as water or as beverage. This will include both preformed water in fluids and in foods.

   The amount of fluids that we consume as beverages, including water depends on climatic conditions and habit. People living in tropics, where there are greater losses of water due to evaporation from the skin, consume more water than do those in temperate climates, and people who engage in strenuous physical activity drink more than do people leading a sedentary lifestyle. This may amount to as much as 1-2 L/ day.

   This mgy also be referred to as prefomed water in fluids. Foods (other than water and beverages) are the second most important sources of water for the body. Most foods contain 50% water, but li.l]c has the highest amount of water. Fmits and vegetables rank next to milk, while fats and oils do not contain any water, The water contained in cookies, cakes and chocolates are relatively low. This entire group contributes to 25-30% of daily water intake. This may also be referred to as preformed water in foods.

2) Water that arises from oxidation of foods within the body, which is referred to as water of oxidation or metabolic water. Water which comes from the oxidation of food is the last source of water. 1 g of starch yields 0.6 g of water; I g of protein 0.41 g; and I g of fat gives 1.07 g of water. This source contributes only about 10% of the total water input. This is also known as water of oxidation / metabolic watej: The water embedded in the network of glycogen molecules in muscle and liver is made available to the body when it is used as a source of energy. Therefore, in case of athletes using glycogen reserves as a source of energy during intense physical activity, this serves as an additional source of water.

Next, what are the routes of water loss from our body? Let us find out

6.5.2 Water Output (Losses of body water)

Water is lost from the body by the four routes, namely kidneys (renal system), skin, lungs and intestine. Let us discuss each of these routes.

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A) Renal loss: Normal adult kidneys excrete about 1-2 liters of urine daily. The water in this total volume is made up of two portions: obligatory and facultative.

i) Obligatory water excretion: The kidney is 'obligated' to excrete some water to rid the body of its daily load of urinary solutes; the body's excretory system is designed to maintain the necessary balance through its filtering and selective reabsorbing system in the kidneys. About 15 ml of water is required to dissolve 1 g of solute materials arising out of the metabolism. The quantity of obligatory water excretion depends on the load on the metabolic products — chiefly urea and sodium chloride. The average adult obligatory water excretion is about 900 ml.

ii) Facultative water excretion: In addition to obligatory water loss, an additional 500 ml, more or less water is excreted for maintaining water balance.

B) Skin: The water loss from the skin is through perspiration, which could be insensible and/or visible.

i) Insensible perspiration accounts for a relatively constant amount of water loss that is proportional to the surface area of the body. It is so called because the evaporation takes place from the skin immediately and the water loss is not noticeable.

As we have already seen, this evaporation is an important means by which body temperature is maintained. Infants have a much greater surface area relative to body weight than do adults; consequently, they are much more vulnerable to water loss from the skin and rapid changes in body temperature.

ii) The water losses by visible perspiration are highly variable; the amount could be as high as 4L in hot climate or during strenuous physical activity. Whenever a great deal of water is lost by perspiration, body water is conserved by the elimination of much more concentrated urine.

C) Intestine: A small quantity of water (about 100-200 ml) is normally lost in faeces, but this can exceed 5 L in diarrhoeal episodes.

D) Lungs: The air expired from the lungs also contains water. Any condition that would increase the rate of respiration — for example, fever-increases the water loss by this route. An individual engaged in the vigorous activity will loose more water by this route as compared to one who is sedentary.

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The details of input and output in a cool environment are shown in Table 6.2.

Table 6.2: Daily water balance in man

Source	Input (ml)	Source	Output (ml)
Food	800 - 1000	Insensible loss	800 - 1000
Oxidation of Food	300 - 400	Sweat	200
as water	1000 - 2000	Faeces	100 - 200
		Urine	1000 - 2000
Total	2100 - 3400		2100 - 3400

Source: Weq J B. (1990).

Now, we have a good idea about the water intake and output. It is interesting to note that, inspite of the water output, the total body water is maintained. How is the water balance maintained in the body? Let's learn about this concept next.

6.5.3 Regulation of Water Balance

The input of water, as well as, its loss can be highly variable due to individual habits and environmental factors; in spite of this, the total body water needs to be maintained constant to achieve normal osmolality for physiological functions. The osnqolality is a measure of the osmoles of solute per kilogram of solvent. In chemistry, the osmole (Osm) is a unit of measurement that defines the number of moles of a chemical compound that contribute to a solution's osmotic pressure.

Although the sources of water to the body and the loss of water from the body are in balance, the fluid exchanges that take place in a 24 hour period are of tremendous magnitude and impressive in precision and regulation. Regulatory steps operate which control water input by thirst and urinary output by kidneys. This regulation of water balance by digestive system, kidneys, hormonal control and thirst is discussed herewith.

A) For the digestive process alone, the estimated daily volume of fluid that enters and leaves the gastrointestinal (GI) tract is estimated to be about 9 litres (consisting of saliva, gastric juice, bile, pancreatic and intestinal juice and water intake). The fluid exchange between the GI tract and the blood circulation are variable from hour to hour; yet they are so balanced that the volume of blood and the fluids within the tract are in equiliböum. The daily losses from the bowel are only around 100-200 ml. Almost all of the fluid is reabsorbed from the gut.

B) The kidneys are highly efficient conservators of body water. Although the kidneys filter 180 L of blood per day (125 ml / min), the urinary output is in the range of 1-2 L for 24 hours. Before the urine leaves the kidneys, variable amount of water and various solutes are reabsorbed by the renal tubules.

This ability plays a major role in maintaining blood volume within normal limits. The eventual urine produced after reabsorption has occurred, is collected in the bladder and excreted periodically,

C) Hormonal control of fluid balance: When water intake is insufficient or water loss is excessive, the kidneys compensate by conserving water and excreting more concentrated urine. The renal tubules increase water reabsorption in response to the hormonal action of ADH (anti-diuretic hormone) released by the pituitary glands under the stimulation of the hypothalamus, and this helps to restore the blood volume. Water balance is critical in maintaining the blood volume, which in turn influences blood pressure.

Cells in the kidneys respond to low blood pressure by releasing an enzyme called rennin, which in turn causes the kidneys to reabsorb sodium through a series of events. Sodium reabsorption in turn is accompanied by water retention thus helping to restore blood volume and the blood pressure.

Renin activates a protein called angiotensinogen in the blood to its active form, angiotensin. Being a powerful vasoconstrictor, angiotensin nasrows the blood vessel, thereby raising the blood pressure. Angiotensin also mediates the release of the hormone aldosterone, which causes the kidneys to retain more sodium and thus the water. Again, the effect is that when more water is needed, less is excreted. In summary, the following three mechanisms effectively restore homeostasis by responding to low blood volume or highly concentrated blood, as illustrated' in Figure 6.4.

* ADH causes water retention.
* Angiotensin constricts blood vessels.
* Aldosterone causes sodium retention.

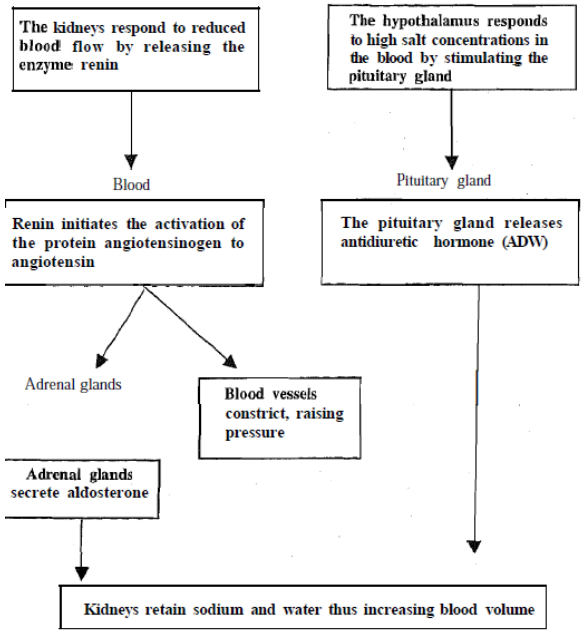

Figure 6.4: How the body regulates water excretion

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D) Thirst and satiety influence water intake, apparently in response to changes sensed by the mouth, hypothalamus and nerves. When the blood is too concentrated (having lost water, but not the dissolved substances within it), the mouth becomes dry, and the person responds by drinking . When the hypothalamus detects that the blood is too concentrated, it also initiates the drinking behaviour. Besides stimulating the thirst sensation, the hypothalamus stimulates the pituitary gland to release ADH. This hormone increases the reabsorption of water.

Thirst drives a person to seek water, but it often lags behind the body's needs. A water deficiency that develops slowly can switch on the drinking behaviour in time to prevent dehydration, but a deficiency that develops quickly may not. Also, thirst itself may not always remedy a water deficiency; a person must notice the thirst signal, pay attention, and take time to get a drink. The long distance runner, the gardener in hot weather, the child busy playing, and the elderly person whose thirst sensation may be blunted can experience serious dehydration if they fail to drink promptly in response to their need for water. So then how much water does the body need? Let us find out. But after the check your progress exercise

6.6 REQUIREMENTS FOR WATER

The body has no provision for water storage; therefore the amount of water lost every 24 hours must be replaced to maintain health and body efficiency. The precise need for water depends on a person's body weight and lifestyle. The requirements in relation to body weight varies in a general way with age; the younger the individual, the greater his/her requirements for water per unit body weight. Under ordinary circumstances, a reasonable allowance based on recommended energy intake is 1.0 ml/Kcal for adults and 1.5 ml / Kcal for infants. This translates into:

35 ml/ kg in adults
50 - 60 ml/kg in children
150 ml / kg in infants

Infants have an increased need for water because of the limited capacity of their kidneys to handle the renal solute load, their higher pe centage of body water and large sulface area per unit of body weight. Exercise, high temperature, low humidity, high altitude and a high fibre diet increase fluid needs. Alcoholic beverages and those containing caffeine such as coffee, tea and sodas, however, are not good substitutes for water; both alcohol and caffeine act as diuretics, causing

the body to lose fluids.

What are the consequences of disturbances in fluid balance? We assume you know! Read the next section and refresh your memory.

NOTES

6.7 DISTURBANCES IN FLUID BALANCE

The correct functioning of cells and tissues depends on appropriate concentrations of nutrients; so any abnormal loss or accumulation of jluid can cause a variety of problems. These problems may be caused by:

a) water loss from diarrhoea, nausea, excessive perspiration, or fever, resulting in dehydration, and

b) undesirable changes in the distribution of fluid within the body

Let us learn about these problems in more details.

6.7.1 Dehydration

Dehydration is defined as the excessive loss of body water. It may occur because of inadequate intake, or abnormal loss of body water or a coinbination of both. The fall in the level of body water associated with dehydration is associated with a fall in blood volume with a consequent fall in blood pressure. The symptoms of dehydration are:

Thirst
Loss of appetite
Decreased urination
Impaired physical performance
Nausea
Impaired temperature regulation
Muscle spasms
Increased pulse rate
Increased respiration rate
General debilitation

Symptoms of severe dehydration appear when fluid .levels fall by more than 10%, whereas a 20% reduction is fatal. With water loss in excess of 10% of body weight, there is a possibility of cardiovascular failure caused by a reduction in blood pressure and a compensating increase in the heart rate as highlighted earlier in Figure 6.2. Abnormal loss of water occurs from prolonged vomiting, haemorrhage, diarrhoea, protracted fevers, burns, excessive perspiration, drainage from wounds, and so on. Athletes loose considerable amounts of water through the skin as a result of their strenuous physical activity.

People for whom water losses may be accompanied by significant losses of

sodium include those engaged in strenuous physical activity of any sort, those exposed to high environmental temperatures at work, and visitors to tropical regions who are unaccustomed to heat. Such people, and in general anyone loosing in excess may need small amounts of salt along with the fluid they drink to make up their sodium loss. The Indian tradition of serving mildly salted watery buttermilk, panna, salted lime juice on a hot afternoon are all examples of replenishing the fluid and salt loss through skin. Children who are ill, especially those with fever, diarrhoea, and increased perspiration, need to be reminded to drink plenty of fluid. One other situation that demands extra fluid for the body is a long airplane flight; a traveler can lose approximately 1.5 litres of water during a 3-hour flight chiefly due to increased in sensible perspiration. Tlle dehumidified air in the airplane is so dry that excessive 'insensible' perspiration and evaporation occur.

Athletes in good physical condition experience a reduction in athletic performance if they lose 3% of body water. Studies investigating the factors limiting our efficiency at work suggest that a lack of adequate water intake has a much more significant effect than does a lack of food. Reduction of as little as 2% of total body water causes a decline of 20 to 30% in efficiency at work.

During starvation or a high-protein and low- carbohydrate diet, excessive loss of body water, sodium, potassium is lost in the urine. This accounts for the rapid initial weight loss and weakness often reported by people on starvation-like diets.

The discussion above focused on dehydration, the condition when the water output is more resulting in imbalance. Opposite to this condition, when intake of fluid is greater, the condition caused is called oedema. Let us get to know about this condition.

6.7.2 Oedema

In some pathological conditions the body is in a positive water balance; that is the intake of fluids is greater than the excretion, and the patient is said to have oedema. Oedema results when the body water- is increased to the levels of 10% or more above normal. We had learnt in the earlier section that plasma proteins exert oncotic pressure that helps to retain water within blood vessels, thus preventing its leakage from plasma into the interstitial spaces. In certain disease states as in Kwashiorkor, the protein content of the plasma is exceptionally low, water leaks into the interstitial spaces causing oedema.

Oedema is one of the classical symptoms of kwashiorkor, and this has already been covered in the unit on Proteins. Dietary treatment with proteins of high biological value should be initiated to correct this. In contrast to the oedema arising due to a dietary protein deficiency in PEM, the oedema noticed in Nephrotic syndrome results due to an increased permeability of the glomerular capillary; the plasma proteins, which are normally retained in the blood, escape into the urine causing proteinuria. With a loss of plasma proteins in the urine, blood proteins fall sharply, giving rise to oedema.

Congestive cardiac failure (CCF) and cirrhosis of the liver are examples of conditions with a disturbance in sodium excretion, namely sodium excretion is reduced thereby contributing to the retention of water. Treatment will involve restriction in the amount of salt with/ without fluid restriction in the diet. At times, diuretics may be used to facilitate fluid excretion

Fluid loss secondary to diarrhoea has been responsible for thousands of deaths of children in developing countries. Oral rehydration therapy (ORT) with a simple mixture of water, salts and sugar has been highly effective in reducing the number of deaths. No wonder water has been appropriately described as the most forgotten and taken- for-granted nutrient.

6.8 LET US SUM UP

In this unit, we learnt that water inspite of being ignored, is an essential nutrient required for life. Though the content of total body water varies from individual to individual, it plays a key role in the body. You would recall that these involve carrying several nutrients and waste products throughout the body, serves as the solvent for minerals, vitamins, amino acids, glucose and a multitude of other small molecules, and acts as lubricant and cushion around joints, aids in body's temperature regulation, serves as a shock absorber inside the eyes, spinal cord and in pregnancy, the amniotic sac surrounding the foetus in the womb and actively panicipates in many chemical reactions.

Then we saw that water is a constituent of every cell of the body intracellular fluid. spaces between cells (interstitial space), and also within the blood (intravascular fluid). Water, is obtained from various sources such as beverages, solid foods and energy-yielding nutrie»ts within the body. On the other hand, water is eliminated from the body through urine, skin, lungs and faeces. We, then, learnt about a variety of sensitive physiological control systems. Finally, we came to know that in order to be adequately hydrated, the average adult should consume about two litres of fluid per day, in the form of clean water and in addition consume non-caffeinated, non-alcoholic beverages, soups, milk, butterinilk, and other beverages. The disturbances in fluid balance, is of two types: dehydration and oedema.

6.9 GLOSSARY

Biological value : a measure of protein quality determined by comparing the amount of nitrogen retained in the body with the arnount absorbed frorn diet.

Cirrhosis : a serious liver condition characterized by irreversible scarring of the liver that can lead to liver failure and death. Scarring results in loss ofliver cells and impairs liver function.

Congestive Cardiac Failure : the inability of the heart to pump blood effectively to the body or requiring elevated filling pressures in order to pump effectively.

Dehydration : depletion of body fluids.

Diuretics : a substance or drug that tends to increase the urine discharge.

Insensible perspiration : water given off by the intact skin as vapour by simple evaporation from the epidermis or as sweat.

Kwashiorkor : severe malnutrition caused by a lack of proteins especially in young children.

Lean Body Mass : everything in the body except for fat, including bone, organs, skin, nails and all body tissues including muscles.

Vitreous humor : the colourless mass of gel that lies behind the transparent, lens and in front of retina and fills the center of eyeball.

6.10 CHECK YOUR PROGRESS

1) What proportion of TBW constitutes in our body weight? What are the factors influencing it

2) Define the following terms

   a) Intracellular flui

   b) Transcellular flui

   c) Osmotic Pressure

3) Why is it essential to maintain water balance in the body? How is it done?

4) What are the routes by which our body looses water?

5) What is the role of the following in regulating water balance?

   a) Kidneys

   b) Hormones

UNIT

7

FAT-SOLUBLE VITAMINS: VITAMIN A, D, E AND K

STRUCTURE

7.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- describe the structure and functions of fat-soluble vitamins,
- identify their food sources, bioavailability and consequences of deficiency
- recognize the recommended amount needed during various physiological stages, and
- appreciate their importance in relation to other nutrients.

7.2 INTRODUCTION

Vitamins are the organic substances that act as coenzyme and/or regulator of metabolic processes. There are 13 known vitamins, most of which are present in foods while some are produced within the body. You would recall from your study in Nutritional Biochemistry Course that depending on the property of solubility, vitamins are divided into two groups, namely, water-soluble and fat-soluble. Water-soluble vitamins include vitamin B-complex, which is a group of B Vitamins, and vitamin C or ascorbic acid while the fat-soluble vitamins comprise of 4 vitamins-A, D, E and K. In this unit, we shall focus on the fat-soluble vitamins. The next unit shall deal with the water-soluble vitainins.

Fat-soluble vitamins A, D, E and K, are termed so because they are found in nature in close association with fatty foods such as butter, cream, vegetable oils, meat, poultry and fish and their products. Though these four vitamins have quite different properties, this unit discusses low they all share some commonalities such as mechanism of absorption from intestines, storage of the excess intake and development of deficiency with inadequate intakes, as well as, toxicity at intakes far in excess of the requirements. The unit also provides information on their requirements, status assessment and interaction with other nutrients.

7.3 FAT-SOLUBLE VITAMINS-AN OVERVIEW

What are fat soluble vitamins? As we already know, there are four fat-soluble vitamins — A, D, E and K. The presence of fat is required for the assimilation of these vitamins in the body. All of these, though quite different from each other in their structures, sources and physiological roles, are significant to us during different life stages. In Chis unit, therefore, we shall focus on understanding the following aspects for each of the vitamin:

- **Structure:** You would recall reading about the structures of these vitamins and their forms in the Nutritional Biochemistry Course (MFN-002) in Unit 3. Therefore, we are not going into the details in this unit and suggest you refer back to unit 2 in the Nutritional Biochemistry Course and refresh your understanding. For your convenience, however, we have given the structures of these vitamins here in the text. Look at Figure 7.1 which illustrates the fat-soluble vitamins. As you go through these structures, you would have noticed that all these fat-soluble vitamins have certain common features such as an aromatic ring structure with an aliphatic side chain, one or more double bonds either in the lång or in the side chain and a functional group such as an aldehyde (CHO : in vitamin A), ketone (C = O : in vitamin K), methyl (CHO or hydroxyl groups (OH : in vitamin D)

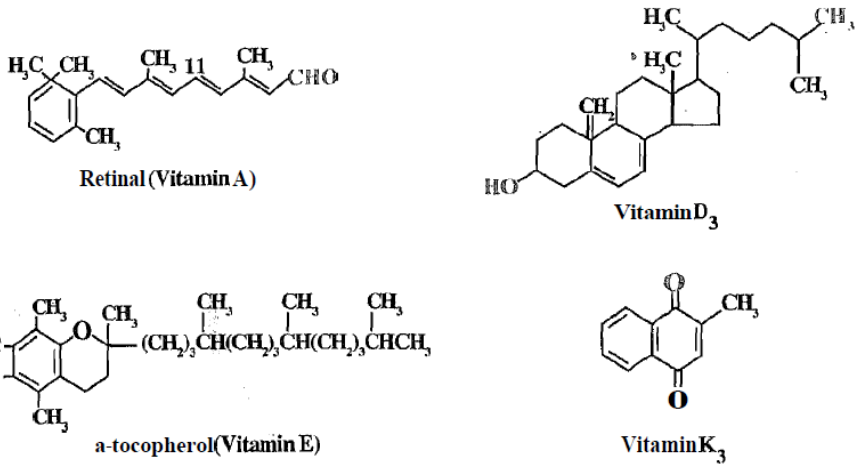


Figure 7.1: Fat-soluble vitamins

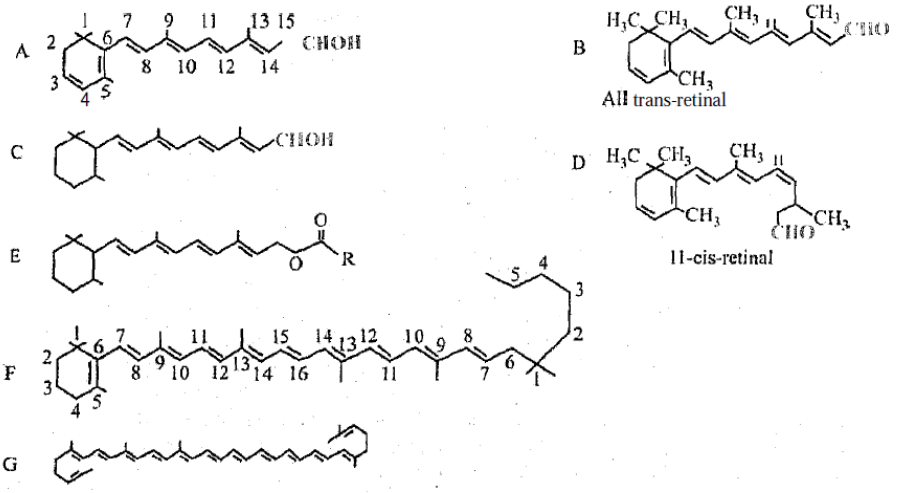
- **Food sources:** Under this sub-section, you will get to know the various food sources of these vitamins in our diet. As a student of dietetics, it is essential for you to know the foods that are rich in these vitamins. Absorption, Storage and Elimination: Reading through this section you would realize that all fat-soluble vitamins undergo similar metabolic fate. They are absorbed along with fats from the small intestine. Bile is essential for the effective absorption of fats and therefore fat-soluble vitamins. The salts of bile ac;ds (tmnine and glycine deiivatives of cholic acid) are the digestion promoting of bile. They are surface active agents (i.e. they lower the surface tension and emulsify fats) and also activate the enzyme lipases. They combine with fat-soluble vitamins to forrn molecular components which are then absorbed. Further, all fat-soluble vitamins are stored in concentrated amounts in the liver. The main pathway of excretion is through the bile into small intestine and consequently faecal excretion. A detailed discussion on absorption, storage of each vitamin is presented later, within this section.
- **Bioavailability:** The term bioavailability refers to the overall efficiency of utilization, including physiological and biochemical processes involved in intestinal absorption, transport, metabolism and excretion of the nutrients. In other words, it is the fraction of ingested vitamins absorbed and utilized for normal physiological functions or storage. Therefore, under this section we shall study the factors which affect the bioavailability of these vitamins.
- **Requirements and Recommended Dietary Allowances (RDA):** What do we mean by requirements and RDA? The requirement level is the amount of nutrient needed to be absorbed to maintain adequate nutritional status in an individual. It differs with body size, age, rate of growth and special physiological situations such as pregnancy and lactation and some pathological conditions that accelerate usage, wastage or destruction as in certain acute or chronic diseases (diarrhoea/constipation). RDA, on the other hand, is the amount of a nutrient that will meet the needs of practically all individuals in a defined physiological category. We shall get to know about the requirements and RDA of the fat-soluble vitamins in this section.
- **Hypo and Hypervitaminosis:** This section shall describe the adverse affects associated with deficient or excessive intake.
- **Criteria fur assessing vitamin status:** The ability to accurately assess vitamin status requires criteria which are "unique to the vitamin and will provide valid results fundamental to clinical and research settings. Such criteria are used to assess the nutliture of fat soluble vitamins, which are discussed here in this section.

So let us get started with our discussion on fat-soluble vitamins. We shall begin with vitamin A.

7.4 VITAMIN A

Vitamin A, one of the fat soluble vitamins, refers to a sub-group of retinoids that

possess the biological activity of all-trans-retinol. The term 'retinoids' includes both naturally-occurring forms of vitamin A (rctinol and retinyl esters) and its synthetic analogues which possess the biological activity of the most active geometric isomer, all-trans-retinol. You would recall reading about the structure of all-trans-retinol in the Nutritional Biochemistry Course in Unit 3. Look at Figure 7.2, which illustrates the different forms of vitamin A. Retinol (an alcohol) (refer to Figure 7.2A) can only be found in animal sources, Retinol is referred to as pre-formed vitamin A, as it is present in foods already in the active form and does not require any conversion. Retinol is oxidized reversibly to retinal (Figure 7.2B), which exhibits all the biological activities of retinol, or fulther oxidized to retinoic acid (Figure 7,2C), which is active in animal growth, but not in vision or reproduction. The form of vitamin A involved in vision is II-cis-retinal (refer to Figure 7,2D), whereas the primary storage forms are retinyl esters (refer to Figure 7.2E), the most common of which is retinyl palmitate.



A: all-trans retinol; B: all-trans retinal; C: all-trans retinoic acid; .
D: 11-cis retinal; E: retinyl esters, mainly retinyl palmitate; F: all-trans β carotene; G: Lycopene

Figure 7.2: Different forms of vitamin A

The major source of vitamin A, as you may be aware, is the carotenoid pigments which are synthesized by plants. Several carotenoids possess vitamin A activity and include alpha, beta and gama carolene, lycopene (refer to Figure 7.2G) and cryptoxanthin to name a few. The primary and most efficient pro vitamin A or carotenoid is the beta-carotene (molecular weight 536.9) which has two molecules of retinal attached tail to tail.

Unlike retinol, most carotenoids can quench singlet oxygen and act as antioxidants because of their long chain of conjugated double bonds, as can be seen in Figure 7.2F. Upon hyd101ysis, each inolecule of beta- carotene theoretically yields two molecules of vitamin A. The other casotenoid precursors are about half as active as O-carotene.

Next, let us study about the food sources of vitamin A.

Food Sources of Vitamin A

Vitamin A or retinol (prefornuecl vitamin A), as you may already know, is found only in foods of animal origin, such as milk, cheese, cream, butter, ghee, egg, fish, kidney and liver, liver oils of fish such as halibut, cod and shark. Provitamin A (so called because it is a precursor and has to be chemically transformed into retinal) or "-carotene is found primarily in plant foods, which contain orange or yellow-coloured pigments called carotenoids. O-carotene is the most widely distributed carotenoid in plant foods. Palm fruit and red palm oil are the richest source of beta-carotene and dark green leafy vegetables, ripe Fruits such as mango, papaya, apricots and yellow/ orange vegetables like carrot, pumpkin and sweet potato are rich in [3-carotene. Figure 7.3 illustrates the sources of vitamin A and betn-carotene.

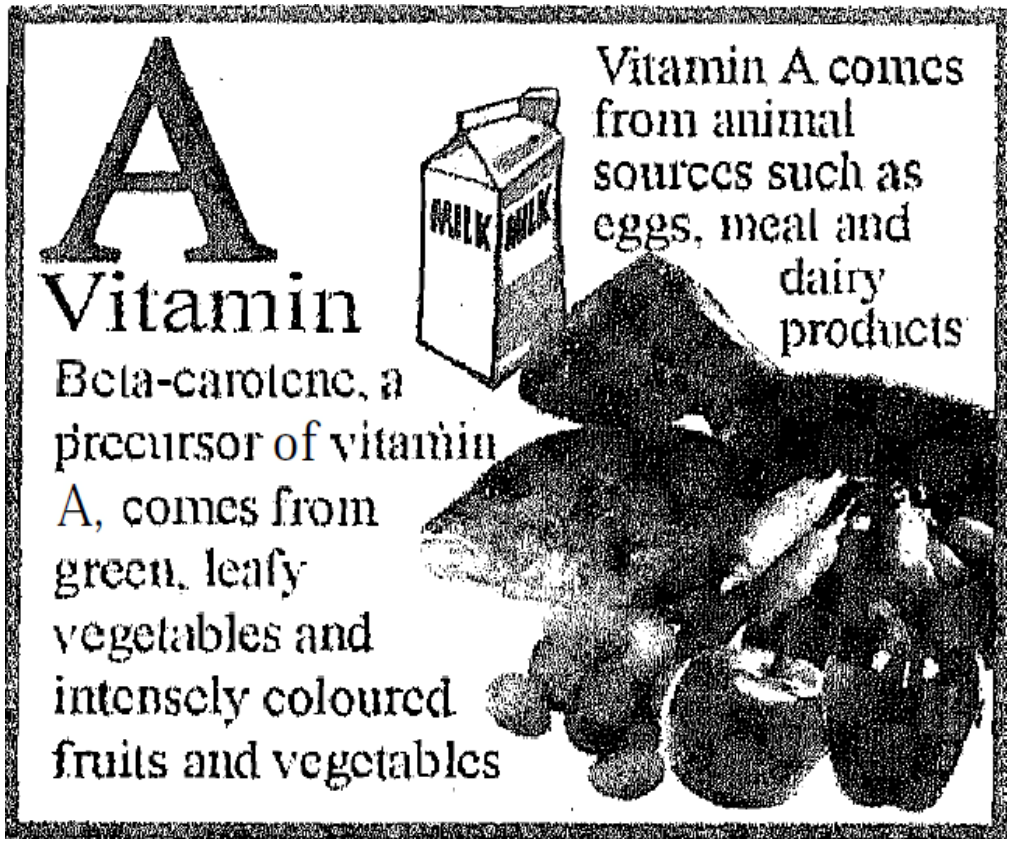


Figure 7.3: Food sources of vitamin A and beta-carotenes

Now that we have looked at the sources, let us understand how vitamin A is absorbed and stored in our body.

Absorption, Storage and Excretion

From our discussion above, it is clear that the dietary supply of vitamin A consists of retinoids (retinol and rétinyl esters in annual tissues) and carotenoids (13-carotene and other carotenoid pigments from plants). Let us see how these are absorbed.

Absorption

Vitamin A and carotenoids tend to aggregate with lipids into globules, which then pass into the small intestine. Dietary vitamin A (retinol) is absorbed as such in the intestines. Retinyl esters (mainly palmitate) arc hydrolyzed by the combined action of bile salts and the esterases in the small intestine. The released carotenoids and retinol in the small intestine are solubilized into miscelles i.e., small aggregates of mixed lipids and bile salts suspended within the gastric bolus (material taken into the body by way of. the digestive tract) solution. The micelles are absorbed into the intestinal mucosal cell. Approximately 70 to 90% of retinol from the diet is absorbed as long as the diet is adequate in fat. Carotenoid absorption from the diet ranges from about 20% to 50%, but carotenoid absorption may be as low as 5%.

Transport and Utilization

The efficacy of the intestines to facilitate absorption and utilization of retinoids and carotenoids depends upon the cellular uptake of these compounds into the intestinal mucosal cell, bioavailability or passage of the molecules beyond the intestinal mucosa into the body with the potential for storage or use in tissues and bioconversion i.e., production of active retinoid from pmvitamin A carotenoids. Inside the intestinal cells, ß-carotene is cleaved I-y a cytosolic enzyme 15—15' o.rygenase to form retinaldehyde, which is then reduced by the microsomal enzytne retinal reductase to retinal. Thus, the ultimate product fanned in the intestines is retinol, which is then re-esterified with long chain fatty acids by intra cellular retinol-binding proteins (CRBP) and packed into chylomicron containing cholesterol esters, phospholipids, triacylglycerol etc. What happens to this chylomicra? Let's see this in the next paragraph how arc thcsc transported via circulation.

Transport

The chylomicra and retinal-binding protein play an important role in the transport of retinol. This chylomicra complex enters the lymphatic system via the thoracic duct and into systemic circulation. Chylomicrons deliver retinyl esters, some unesteritied retinol and carotenoids to many extrahepatic tissues such as bone marrow, spleen. blood cells, lungs, kidney. Chylomicron remnants deliver retinyl ester and a portion of the casotenoids not taken by peripheral tissue to the liver.

For carotenoids reaching the liver, a small portion can be cleaved to form retinol, some may be incorporated into the very low-density lipoprotein (VLDLs) synthesized in the liver, and then be released as part of VLDLs for circulation to various tissues in the body and some may be stored in the liver.

As for the retinyl esters,leaching the liver, hydrolysis of retinyl esters occurs. Within the cells, retinol binds with 'a cellular retinol-binding protein (CRBP), CRBP is thought to function both to help control concentration of free retinol within the cell cytoplasm and thus prevent its oxidation, and to direct the vitamin to specific enzymes of metabolism. The enzymatic metabolism of retinol includes esterification by enzymes such as lecithin retinol acyl transferåse (LRAT) or acyl

CoA retinol acyl transferase (ARAT), oxidation of retinol to retinal by NAD(P) H-dependent retinol dehydrogenase, and phosphorylation of retinol to retinyl phosphate by ATP for glycoprotein function. Retinol not metabolized or transported from the liver may be stored in small cells called stellate cells (along with lipid droplets) following re-esterification.

Retinol mobilization from the liver and delivery to €arget tissue are dependent on the synthesis and secretion of retinol-binding protein (RBP). It would be interesting to note that RBP is a 183 amino acid residue, has a molecular weight of about 21,000 and is present in concentsation at 3-4 mg/dl RBP. in turn, joins the binding site on a larger protein, transthyretin (TTR). Thus the hepatic parenchymal cell is involved in the uptake and storage of vitamin A in the liver and its release into circulation as the retinol-RBP-TTR complex. The retinol-RBP-TTR complex circulates in the plasma with a half-life of about II hours. Some tissues that take up retinol from the RBP-TTR complex include the adipose, skeletal, kidney, white blood cells and bone marrow.

Next, let us get to know about the storage of vitamin A in the body.

The primary organ for storage of vitamin A is the liver. Reserves are found in the stellate cells, as mentioned above. The average liver weighs 1.5 kg and when replete, contains 450 mg of vitamin A stores. Hepatic tissue concentrations of < 30 mcg / g is considered marginal. Total body stores of vitamin A range from 300-900 mg witll 20% found in peripheral organs and tissues.

So far we have discussed about the absörption, transpolt, storage of vitamin A. It was mentioned in the text above that the bioavailability of vitamin A is a determinant of its absorption and hence excretion. Let us now understand the key aspects related to the bioavailability of vitamin A.

Bioavailability Vitamin A

By now it is clear that vitamin A is supplied in two forms. One form is retinol, from animal foods such as liver, fatty fish, eggs, and milk, and from fortified foods. Retinol is considered pre-]brmed vitamin A. The other form is the carotenoids from plant foods (P-carotene, a-carotene and 13-ctyptoxanthin). These convert to vitamin A in the body and are called provitamin A carotenoids. Retinol and carotenoids have different vitamin A activity. You would realize that it takes greater amounts of carotenoids to equal the activity of retinol. Different conversion factors have been therefore developed to address this aspect while developing the RDA for vitamin A.

You may come across recommendations for vitamin A expressed as International Unit or as retinol equivalent (RE) or as retinol activity equivalent (RAE). To express the vitamin A activity of carotenoids in diets on a common basis, a joint FAO/ WHO Expert Group in 1967 introduced the concept of the retinol equivalent (RE) and established the following relationships among food sources of vitamin A:

1 pg retinol	= 1 RE
1 pg p-carotene	= 0.167 pg RE
I pg other pro-vit:lmin A carolenoids	= 0.084 yg RE

NOTES

More recently, vitamin A recommendations are in mg/day as RAE. The term RAE was introduced to replace the term retinol equivalent (RE) to take into account new research on the vitamin A activity (bioefficacy) of carotenoids. The conversions in terms of RAE, retinol, carotene are presented herewith:

1 pg RAE = 1 pg retinol (vitamin A)
= 12 pg p-ciuotenc in mixed foods
= 24 pg other provitarniil A carolenoids in nlixed foods

Hence, with the RAE system, we can see that the relative proportion of retinol, beta carotene and other carotenoids is 1:12:24. The RAE system helps to account for the differences between carotenoids and retinol. It takes about 12 units of bela-carotene and 24 units of other carotenoids to make I unit of retinol in the body. In Retinol Equivalents (RE), retinol, beta carotene and other carotenoids proportion is 1:6:12. Many food and supplement labels still list vitamin Ain International Units (II-Js)l This measure can be converted to RAEs with some calculations. If all the vitamin A activity is from retinol, then 3.33 IU vitamin A (retinol) = I RAE. Otherwise, we can use these conversions:

I IU vitamin A activity = 0.3 mg retinol
= 3.6 mg -carotene
= 7.2 mg a-carotene or ß-cryptoxanthin

Let us understand this conversion with the help of an example. For example, a dessert prepared from carrots and milk supplies 10,000 IU vitamin A (20% as carotene). The calculation includes:

1) 10,000 IU x = 2000 IU (thus 8000 IU as retinol, 2000 IU as ß-carotene)
2) 8000 x 0.3 (or 8000/3.33) = roughly 2400 mg as retinol 2400 RAE)
3) 2000 x 3.6 = roughly 7200 ing as (3-carotene (7200 mg/ 12 = 600 mg RAE)
4) 2400 mg RAE + 600 mg RAE = 3000 mg RAE supplied by this supplement

With the International Units (IU) system, therefore, the relative proportion of retinol, beta carotene and other carotenoids is 1:2:4.

Having understood the concept of bioavailability of carotenoids, now let us look at the factors which influence the bioavailability of carotenoids.

Factors Affecting Bioavailability of Carotenoids

Factors affecting bioavailability of carotenoids can be classified under the following two headings:

1) Factors influencing uptake from lumen to intestinal cell

inhibition by intrinsic matrix,
inhibition by dietary fiber sources,
differential crowding by stereo isomeric forms,
inverse relationship between ingested amount and uptake,
intraluminal oxidative destruction,
enhancement by presence of fat and oil, and
enhancement by cooking and processing.

2) Factors influencing the efficiency of bioconversio

amount of pro vitamin A presented to the 'cell,
differential conversion by stereoisomeric form, and
vitamin A status of the host.

With a brief review of the factors, we end our discussion on bioavailability of vitamin A. Next, let now move on to the functions of vitamin A.

Functions Vitamin A

Vitamin A (retinol) is an essential nutrient needed in small amounts by humans for the normal functioning of the visual system, growth and development, and maintenance of epithelial cellular integrity, immune function, and reproduction. While we discuss the major functions of vitamin A, it is important to note that primary vitamin A deficiency (VAD) may give rise to more than one secondary effects which can often be recognized in the form of clinical signs and symptoms most important being ocular manifestations grouped under 'xerophthalmia'. In addition to the specific signs and symptoms of xerophthalmia and the risk of irreversible blindness, nonspecific symptoins include increased morbidity and mortality, poor reproductive health, increased risk of anaemia, and contributions to depressed growth and development.

Let us then review the functions of vitamin starting with the most critical function of vitamin A i.e., its role for maintaining vision.

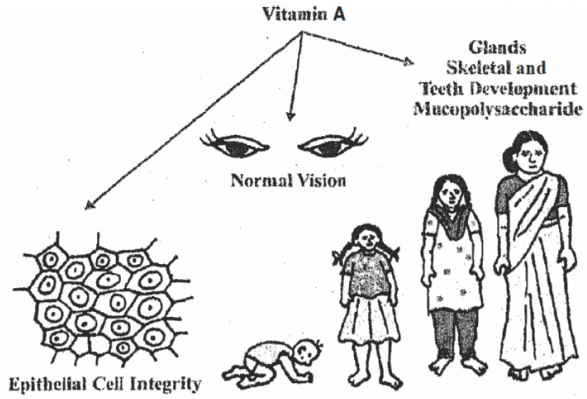


Figure 7.4: Functions of vitamin A

1) Role in visual perception and function: Vitamin A plays a critical role for maintaining normal vision. This function is of critical importance both from clinical relevance, as well as, public health point of view, as you may already be aware. Vitamin A deficiency is the leading cause of preventable severe visual impairment and blindness, and the most vulnerable are preschool children and pregnant women, particularly in our country. It is ironical that a small amount of less than 10 gm of fresh leaves can meet the days requirement of vitamin A of preschool children. Yet an estimated 2,50,00 to 5,00,000 to VAD children world over become blind every year, and about half of them die within a year. Administration of large doses of vitamin A to children at-risk has been the most popular approach to control nutritional blindness.

But, how is vitamin A involved in the maintenance of vision? Our subsequent discussions will focus on this aspect.

The key component which interlinks vision with vitamin A is rhodopsin which is the photosensitive pigment of the eye and is also referred to as visual purple. In the visual system, as described above, carrier bound retinol is transported to ocular tissue and to the retina by intracellular binding and transport proteins. Rhodopsin, the visual pigment critical to dim-light vision, is formed in rod cells after conversion of all-trans- retinol to retinaldehyde, isomerization to the 1 1 -cis-form, and binding to opsin. Alteration of rhodopsin through a cascade of photochemical reactions results in the ability to see objects in dim light.

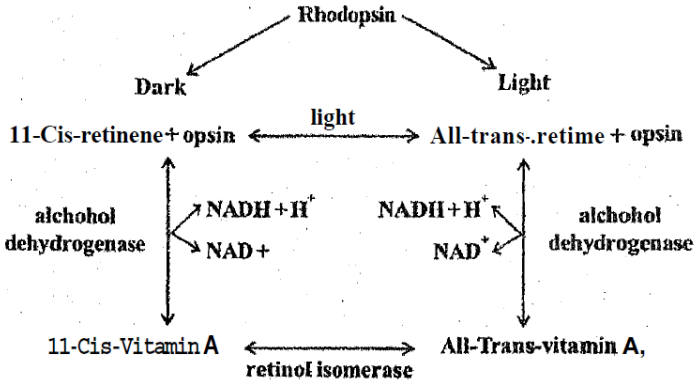


Figure 7.5: Rhodopsin cycle

Rhodopsin consists of the protein opsin bound 10 a pigment cis-isomer of retinal (vitamin A aldehyde) formed by the oxidation of retinol in the epithelium of the rods in the retina of the eye by alcohol dehydrogenase in the presence of NAD. The action of light bleaches the visual purple or dissociates rhodopsin to opsin and retinene. During the regeneration of rhodopsin in the dark, the sequence of evenls gets reversed? i.e., retinyl palmitate is hydrolyzed to retinol, which is transported to the outer segment of the rod. There it is oxidized and isomeiized to 11-cis retinal, which then reacts with opsin to form rhodopsin. Thus, the re-synthesis of rhodopsin is isomer specific i.e. it can be regenerated only after retinol is rearranged to the

11-cis form. The rearrangement is possible both as a photochemical reaction and an oxygen-dependent dark reaction. These cyclic changes in which vitamin A plays a critical role in vision in dim light is called Rhodopsin cycle (vitamin.A visual cycle).

The speed at which rhodopsin is regenerated is related to the availability of retinol. Night blindness is usually an indicator of inadequate available retinol. Deficiency of vitamin A in the diet leads to impairment in the vision particularly at night or when dark. This is referred to as 'night blindness', when the individual cannot see in dim light. Difficulty in reading or driving a car in dim light, progresses to inability to see the objects in dim light. We shall read about the progressive stages of visual impairment with respect to vitamin A status in the human body later in this section. The next function of great significance is the role of vitamin A in differentiation of cells.

2) Role in growth and cellular differentiation: The growth and differentiation of epithelial cells throughout the body are especially affected by vitamin A deficiency. In addition, goblet cell numbers are reduced in epithelial tissues and as a consequence, mucous secretions diminish. Cells lining protective tissue surfaces fail to regenerate and differentiate, hence they flatten and accumulate keratin. Classical symptoms of xerosis (drying or non-wetability) and desquamation of dead surface cells as seen in ocular tissue (i.e. xerophthalmia) are the external evidence of the changes also occurring to various degrees in internal epithelial tissues. Current understanding of the mechanism of vitamin A action within cells outside the visual cycle is that cellular functions are mediated through specific nuclear receptors. Binding with specific isomers of retinoic acid (i.e.all trans- and 9-cis-retinoic acid) activates these receptors. Activated receptors bind to DNA response elements located upstream of specific genes to regulate the level of expression of those genes. These retinoid-activated genes regulate the synthesis of a large number of proteins vital to maintaining normal physiologic functions. There may, however other mechanisms of action that are as yet undiscovered.

3) Role in immune response: Vitamin A is essential to normal immune function and regulation. As discussed above, during vitamin A deficiency the goblet cell numbers are reduced in epithelial tissues and as a consequence, mucous secretions (with their antimicrobial components) diminish. Cells lining protective tissue surfaces fail to regenerate and differentiate; hence they flatten and accumulate keratin. Both factors — the decline in mucous secretions and loss of cellular integrity— reduce the body's ability to resist invasion from potentially pathogenic organisms. Pathogens can also compromise the immune system by directly interfering with the production of some types of protective secretions and cells.

4) Integrity of epithelial tissues: Vitamin A is essential for the integrity of the mucous-secreting cells. In fact vitamin A maintains the health of epithelial

cells that line internal and external surfaces of the lungs, intestines, stomach, vagina, urinary tract and bladder, eyes and skin. These cells act as important barriers to bacteria. Certain epithelial cells secrete mucous to keep the skin, eyes and Fat-Soluble Vitamins: other mucous membranes moist. In deficiency, the epithelial tissues are keratinized. The tissues affected are salivary glands, respiratory tract, eyes, skin and sex organs.

5) Role as antioxidant: Some carotenoids, in addition to serving as a source of vitamin A, have been shown 10 function as 'antioxidants. Studies show that lycopene (the pigment which gives tomatoes the red colour) is a scavenger of single-oxygen, offering powerful antioxidant activity. Antioxidants protect our cells against the effects of free radicals, which you may recall reading in the Nutritional Biochemistry Course, are polentially damaging compounds produced as by-products of metabolism, as well as, through exposure to toxins and pollutants (e.g. smoking).

   Free radicals, as you may be aware, can cause cell damage that may contribute to the development of cardiovascular disease and cancers. Thus, vitamin A and related nutrients may collectively be important in protecting against conditions related to oxidative stress, such as aging, air pollution, arthritis, cancer. cardiovascular disease, cataracts, diabetics mellitus and infection. However, this role has not been consistently demonstrated in humans.

6) Bone and nerves: The role of vitamin A in bone formation and the association of its deficiency with the degeneration of myelin sheath is currently being explored.

7) Role in protein metabolisms and growth: Severe vitamin A deficiency results in abnormal RNA metabolism and protein synthesis and hence interferes with growth. Hence vitamin A is also called growth vitamin. Conversely, absorption and mobilization of vitamin A is impaired in protein malnutrition.

8) Role in the synthesis of mucoproteins and macropolysaccharides: Vitamin A is vital for the synthesis of mucoproteins and glycoproteins and incorporation of inorganic sulphate in mucopolysaccharides and their synthesis.

9) Role in reproduction: Deficiency of vitamin A leads to infertility in the male and failure of the female to conceive or resorption or abortion of the foetus, chiefly in animals.

Deficiency and Toxicity of Vitamin A

WHO defines VAD as tissue concentrations vitamin A low enough to have adverse health consequences even if there is no evidence of clinical xerophthabnia. Vitamin A deficiency (VAD), as you may already know, leads to impairment in the vision, severe infections and even death. It encompasses the full spectrum of clinical

consequences associated with sub optimal vitamin A status. These disorders are known to include reduced immune competence resulting in increased morbidity and mortality (largely from increased severity of infectious diseases), night blindness, corneal ulcers, keratomalacia and related ocular signs and symptoms of xerophthalmia, exacerbation of anaemia through sub optimal absorption and utilization of iron and other conditions not yet fully identified or clarified (e.g. retardation of growth and development).

Xerophthalmia (dryness of the eye) is the hallmark feature of clinical vitamin A deficiency and is characterized by abnormalities of the conjunctiva and cornea of eye. It has been classified into stages according to specific ocular manifestations as described herewith:

One of the earliest manifestations of xeropthalmia is night blindness (Stage XN). Individuals suffering from night blindness cannot see in dim light or around dusk. Subsequently, the conjunctiva, which is the thin transparent membrane that covers the cornea and lines the inside of the eyelid, becomes discoloured (muddy coloured), dry and loses its brightness. This stage is known as conjunctival xerosis (Stage XI A). In addition to xerosis, dry, foamy, triangular spots may appear on the conjunctiva. These are known as the Bitot's spot (Stage XI B). Though conjunctival changes in xetopthalmia do not lead to blindness, they should be Considered as warning signs. If neglected, the changes may progress affecting the cornea causing corneal xerosis (Stage X 2). In this condition, the cornea becomes dry and dull and appears like ground glass. This condition must be treated as an emergency. If it is not treated immediately with vitamin A, the individual can develop ulcers (sores) in the cornea (Stage X3A - corneal ulceration) leading to the liquefication of cornea, a condition called keratomalacia (Stage X 3B). Increasing softening of the corneas may lead to corneal infection, rupture (perforation) and degenerative tissue changes.

This condition inevitably leads to irreversible blindness. Past involvement causing corneal ulcers (Stage XS) when healed leave white scars on the black portion of the eye which can interfere with normal vision. A globe destroyed by advanced keratomalacia is xerophthalmic fundus (XF). In addition, thickening of the hair follicles (follicular hyperkeratosis) is a cutaneous manifestation of vitamin A deficiency. You may have already studied about this classification in the Public Nutrition Course in Unit 3. Conditions and populations associated with increased need for vitamin A includes young children particularly the pre-schoolers, pregnant and lactating mothers as already highlighted earlier, as well as, clinical conditions such as malabsorptive disorders (steatorrhoea), pancreatic, liver or gallbladder diseases. Patients with chronic nephritis, acute protein deficiency, intestinal parasites, or acute infections may also become vitamin A deficient.

Toxicity

Because vitamin A is fat-soluble and can be stored, primarily in the liver, routine consumption of large amounts of vitamin A over a period of time can result in toxic

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symptoms, including liver damage, bone abnormalities and joint pain, alopecia, headaches, vomiting and skin desquamation. In fact, symptoms that occurs due to intakes in excess of those recommended over a prolonged period are referred to as symptoms of hypervitaminosis.

Hypervitaminosis A appears to be due to abnormal transport and distribution of vitamin A and retinoids caused by overloading of the plasma transport mechanisms. Very high single doses can cause transient acute toxic symptoms that may include bulging fontanelles in infants, headaches in older children and adults, and vomiting, diarrhoea, loss of appetite and irritability in all age groups. Rarely does toxicity occur from ingestion of food sources of preformed vitamin A.

When this occurs, it usually results from very frequent consumption of liver products. Toxicity from food sources of provitamin A, chiefly carotenoids, is not reported, except lor the cosmetic yellowing of skin.

Most children aged 1-6 years tolerate single oral doses of 60,000 µg (2,00,000 IU) vitamin A in oil at intervals of 4-6 months without adverse symptoms. Occasionally diarrhoea or vomiting is reported but these symptoms are transient with no lasting sequence. Older children seldom experience toxic symptoms unless they habitually ingest vitamin A in excess of 7,500 µg (25,000 IU) for prolonged periods of time. When women take vitamin A at daily levels of more than 7,500 µg (25,000 IU) during the early stages of gestation, foetal anomalies and poor reproductive outcomes are reported.

Women who are pregnant or might become pregnant should avoid taking excessive amounts of vitamin A.

A careful review of the latest available information by a WHO Expert Group recommended that daily intakes in excess of 3,000 µg (10.000 IU) or weekly intakes in excess of 7,500 µg (25,000 IU) should not be taken at any period during gestation.

From our discussions above, it is clear that both deficient and excess intakes of vitamin A can be harmful. So then what are the requirements of vitamin A by our body and what should be the most optimum intake to maintain good health?

Requirement and Recommended Dietary Allowance (RDA) for Vitamin A

Recommendations for adequate vitamin A intake arc based on the amounts needed to correct night blindness among vitamin A deficient subjects and to raise plasma levels in vitamin A deficient individuals to a normal level.

This is due to the fact that human milk, particularly colostrums is a rich source of vitamin A. It is also evident that the intake recommended for pre-scholars and older children are equal to that recommended for adult man and woman. This high level has been suggested keeping in mind the high prevalence sate of clinical vitamin A deficiency in this segment of the population.

Table 7.1(a): Recommended allowances for vitamin A

Group		Vitamin A (µg/day)	
		Retinol	β-Carotene
Man		600	2400
Woman		600	2400
Pregnancy		950	3800
Lactation			
Infancy	0-6 months	350	1200
	6-12 months	350	1200
Children	1-3 years	400	
	4-6 years	400	1600
	7-9 years	600	2400
Boys	10-12 years	600	2400
Girls	10-12 years		
Boys	13-15 years	600	2400
Girls	13-15 years		
Boys	16-18 years	600	2400
Girls	16-18 years		

Table 7.1(b): Estimated mean requirement and safe level of intake for vitamin A

Age Group	Mean Requirement (µg RE/day)	Recommended Safe Inlake (µg RE/day)
Infants and children		
0 - 6 months	180	375
7 - 12 months	190	400
1 - 3 years	200	400
4 - 6 years	200	450
7 - years	250	500
Adolescents,		
10-18 years	330 - 400	600
Adults		
Females,19 - 65 years	270	500
Males, 19 - 65 years	300	600
65+	300	600
Pregnant women	370	800
Lactating women	450	850

The recommendations discussed above, have been based on the fact that what level of vitamin A is required to prevent deficiency and also maintain health. In calculating the safe intake, a normative storage requirement equivalent to 434 mg RE/day was taken into consideration. However, when vitamin A deficiency or toxicity is anticipated, it is necessary to assess the existing vitamin A status. This provides vital information regarding the future course of nutrition and

medical action which would be necessary to restore back good health. Therefore, we shall now review the criteria for assessment of vitamin A status. Criteria for Assessment qf Vitamin A Status Various parameters/criteria can be used for the assessment of vitamin A status. Some of these have been described herewith: 1) Clinical Assessment Clinical features of deficiency occur as ocular and extra ocular lesions. Ocular lesions affect the posterior segment of the eye initially with impairment of dark adaptation and night blindness (twilight blindness). Xerosis of the conjunctiva is the first sign seen on clinical examination. This leads to Bitot's spots. Keratomalacia is the last stage. Extra-ocular lesions include dry scaly skin (follicular hyperkeratosis), toad skin or phrynoderma. There is increased susceptibility to infections.

Table 7.2: WHO classification for assessment of vitamin A statu

Classificatiou	Primary Signs
·XI A	Conjunctival Xerosis
XI' B	Bitot's Spots
X 2	Corneal Xerosis
X 3A	Corneal Ulceration
X3B	Keratomalacia
	Secondary signs
X N	Night blindness
X F	Fundal changes
X S	Corneal scarring

2) Conjunctival Impression Cytology (CIC)

Conjunctival impression cytology (CIC) is a simple, rapid and inexpensive method which is suitable for a field survey. By touching with a filter paper the lower temporal portion Of the conjunctiva for about 3-5 seconds, as illustrated in Figure 7.6, the desquamated layers of cells are transferred to the filter paper. This strip is then stained and examined. CIC is a useful test for the assessment of subclinical VAD. It detects the progressive loss of goblet cells in tile conjunctiva and the appearance of enlarged, partially keratinized epithelial cells.

Figure 7.6: Conjunctival impression cytology

CIC provides an early measure of the histological changes in the eye i.e. changes in the conjunctional epithelium with eventual keratinization. These changes are used to differentiate between normal children and those with mild xerophthalmia. Diagnosis is based on the absence or rare appearance of goblet cells or mucin spots in sufficient quantity. The CIC technique is modified to another method in which cells are immediately transferred to a glass slide. This method is called conjunctival impression cytology with transfer.

3) Dietary Assessment Criteria

Several methods can be adopted for the dietary assessment of vitamin A such as food frequency, weekly or 3 day food weight record, and 3 day or 1 week food recall method.

4) Serum Vitamin A Content

Assessment of serum vitamin A content is the most reliable criterion for assessing vitamin A status. Serum levels indicative of various degrees of deficiency are as follows:

Status	Serum vitamin A levels (mcg/dl)
Normal	≥ 25
Deficiency	< 12
Sub clinical	12 - 25

Circulating vitamin A concentrations becoine elevated (>200 nlcg 1 dl) owing to vitamin A overload.

5) Liver Biopsy Assays

These are used to measure the total vitamin A stores, as well us, the response in levels of vitamin A relative to different dosages of the vitamin. This method has an unacceptably high level of risk.

6) Dark Adaptation

In the early stages of VAD, the individual cannot see objects in dim light. This phenomenon is used as a criterion for assessment in the dark adaptation test. The subject is either kept in a dark room for some time and asked to identify an object which is dimly illuminated, the intensity of light being increased till the subject is able to see the object is exposed to bright light for some time, by which the visual purple is bleached. The time required for the rhodopsin to be regenerated is measured by the ability to see a dimly illuminated object. Longer time taken to identify the objects is indicative of variable stages of vitamin A deficiency.

7) Interaction with Other Nutrients

Of the various nutrients, the interaction of vitamin E, proteins, zinc and iron with

vitamin A is of significance. How? Let's proceed with our discussion and find out

- Vitamin E: Vitamin E is required for the cleavage of ß-carotene into retinal and to protect the oxidation of these compounds.

- Proteins: The protein status of an individual influences vitamin A status and transport because an inadequate protein intake depresses the activity of the enzyme that cleaves ß-carotene. Also, vitamin A metabolism is closely related to protein status as vitamin A transport is dependent on several vitamin A-binding proteins synthesized in our body as discussed earlier.

- Zinc: Its deficiency interferes with vitamin A metabolism. It leads to a reduction in the synthesis of plasma proteins, particularly, RBP, made in the liver. Thus, plasma retinol concentrations decrease and liver retinol concentrations increase. Also, zinc deficiency decreases hepatic mobilization of retinol from its storage form as retinyl esters.

- Iron: Iron status of an individual correlates with vitamin A. The deficiency of vitamin A has been found to be associated with microcytic anaemia. While the exact mechanisms underlying the impact of vitamin A on iron and anaemia are unknown, several hypothesis exist to explain this phenomenon. One prevalent hypothesis is that vitamin A increases levels of serum iron, which allows haematopoesis to thrive, increasing haemoglobin and erythrocyte production. In vitamin A deficiency, iron would not be available for erythropoesis, and anaemia would result.

7.5 VITAMIN D

Vitamin D is a generic term and indicates a molecule of the general structure with rings (A, B, C, D). The ring structure is derived from the cyclopentanoper hyclrophenenthrene ring structure for steroids. Ergocalsiferol (D_2), cholecalciferol (D_3) are the forms of vitamin D.

Vitamin D, can either be made in the skin from a cholesterol-like precursor (7-dehydrocholesterol) by exposure to sunlight or can be provided pre-formed in the diet.

The version made in the skin is referred to as vitamin D_3 whereas the dietary form can be either vitamin or a closely-related molecule of plant origin known as vitamin D_2. The synthesis of vitamin 133 from its pro vitamin, 7-dehydrocholesterol, occurs by UV in addition and proceeds from the pro vitamin to the pre vitamin and finally to the vitamin. The first main step of the reaction is the photochemical conversion of 7-dehydrocl—olesterolto previtamin D. This reaction yields up to 85% of previtamin m. The next and final step is accomplished by the thermal conversion of previtamin D_3 to vitamin D_3.

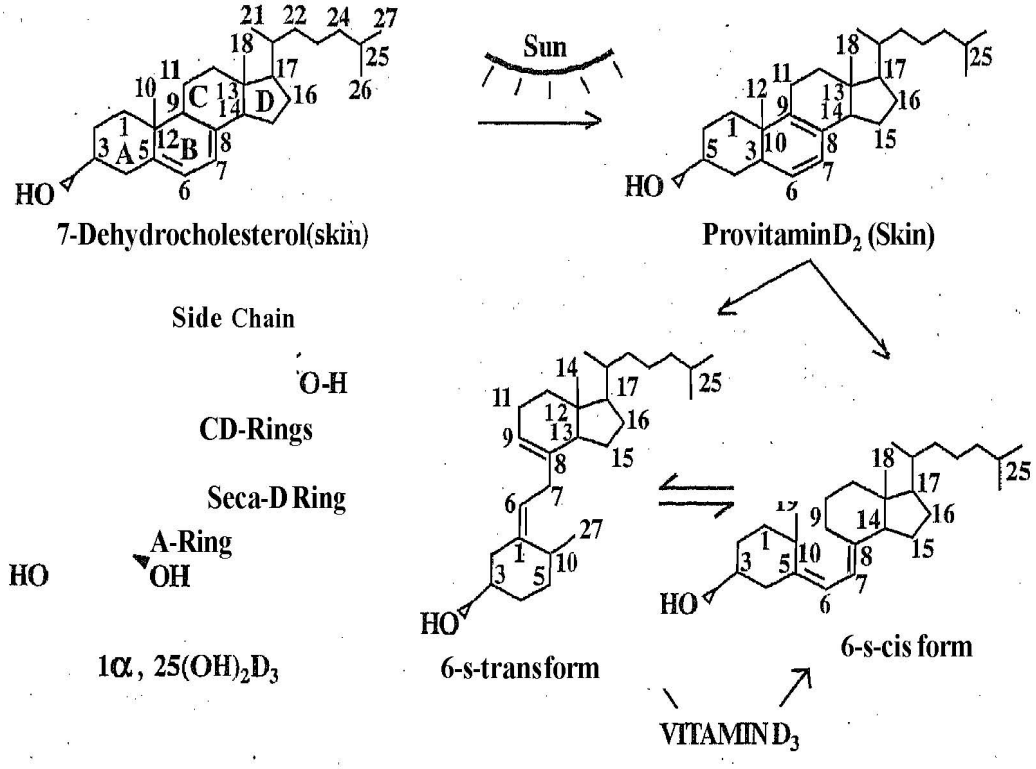

Figure 7.7: Pathway for the production vitamin

Next, let us review the food sources. of vitamin D.

Sources of Vitamin D Vitamin D, also called the sunshine vitamin is easily manufactured in the skin from 7-dehydro cholesterol on exposure to sunlight. Small amounts are present in dairy products such as milk, cheese, butter, margaline and cream, egg yolk, liver, oysters and certain varieties of fish. So we have seen that it is not just through diet, sunlight can also help us to manufacture vitamin D. We just read that the form of vitamin D present in food is different from that required by our body.

Absorption, Storage and Elimination

As we have already mentioned earlier, all fat-soluble vitamins share a common metabolic fate. Vitamin D is absorbed along with fats from the duodenum and jejunum. Bile too is essential for the effective absorption of fats and therefore of vitamin D.

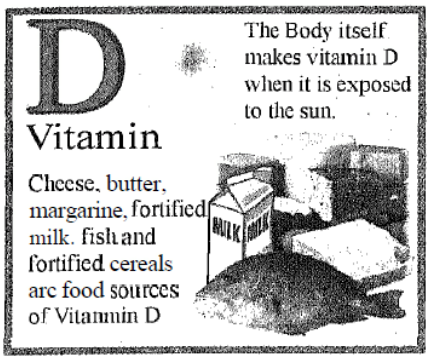

Figure 7.8: Vitamin D sources

Conditions unfavorable to fat absorption such as lack of bile, disorders such as sprue and celiac disease results in poor absorption of vitamin D. Once absorption is complete, vitamin D enters the blood as a part of the chylomicrons. Vitamin D formed in the skin by the direct irradiation of the pro vitamin present in the skin is directly absorbed into the blood stream. The vitamin is stored in concentrated quantities in the liver and to a lesser extent in the skin, spleen, lungs, brain and kidney. The main pathway of excretion of vitamin D is through the bile into the small intestine and consequent faecal excretion. Only less than four per cent of the intake of the vitamin is excreted by the urinary pathway.

Functions Vitamin D

Vitamin D is required to maintain normal blood levels of calcium and phosphate, which are in turn needed for the normal mineralization of bone, muscle contraction, nerve conduction and general cellular functions in all cells of the body. Vitamin D also modulates the transcription of cell cycle proteins, which decrease cell proliferation and increase cell differentiation of a number of specialized cells of the body (e.g. osteoclastic precursors, enterocytes, keratinocytes). This property may explain the actions of vitamin D in bone resorption, intestinal calcium transport and skin. Vitamin D also possesses immunomodulalory propertics that may alter responses to infections in vivo.

1) Mobilization of bone calcium and phosphorous: It is now firmly established that vitamin D3 is metabolized first in the liver to 25-hydroxyvitamin D (25-OH- D) (calcicliol) and subsequently in the kidneys to 1,25 dihydroxycholecalciferol or (calcitriol) to produce a biologically active hormone. The functions of vitamin D are mediated by this vital vitamin D hormone by a homeostatic mechanism which involves the hormone acting on the intestines, kidney and bone to increase serum calcium and phosphorus levels. stimulates intestinal absorption of calcium and phosphate and mobilizes calcium and phosphate by stimulating bone resorption. These functions serve the common purpose of restraining blood levels of calcium and phosphate to normal when concentrations of the two ions are low. This helps to achieve a normal blood calcium concentration and maintenance of

calcium homeostasis.

In calcium homeostasis, works in conjunction with pa a thyroid hormone (PTH) to produce its beneficial effects on the plasma levels of ionized calcium and phosphate. The physiologic loop (Refer to Figure 7.9) starts with the calcium receptor of the parathyroid gland. When the level of ionized calcium in plasma falls, P TH is secreted by the parathyroid gland and stimulates the tightly regulated renal enzyme 25-0H-D-1-a-hydroxylase to make more from the' large circulating pool of 25-OH-D. The resulting increase in (with the rise in PTH) causes an increase in calcium transport within the intestine, bone and kidney. All these events raise plasma calcium levels back to normal, which in turn is sensed by the calcium receptor of the parathyroid gland. The further secretion of P TH is turned off not only by the feedback action of calcium, but also by a short feedback loop involving 1,25-(OH)2D directly suppressing PTH synthesis in the parathyroid gland.

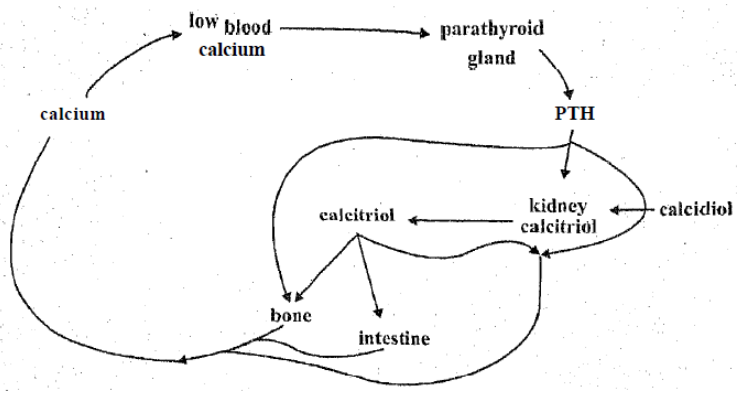

Figure 7.9: Calcium homeostasis

2) Mineralization and formation of new bone: Vitamin D plays a role in the synthesis of a prominent non collagenous protein, osteocalcin, a vitamin K- dependent protein found in the bone matrix and dentine — which is associated with new bone formation.

3) Bone growth and development—calcification of osteoid tissue: Vitamin D participates in metabolic processes associated with bone growth and development. It is involved in calcification of osteoid tissues. Osteoid is a protein mixture which is secreted by osteoblasts. When it mineralizes, it becomes bone.

4) Modulation of the transcription of cell cycle proteins: The compound (calcitriol), is present in the blood complexes to the vitamin D-binding protein, a specific a-globulin. Calcitriol is believed to act on target cells in a similar way to a steroid hormone. Free hormone crosses the plasma membrane and interacts with a specific nuclear receptor known as the vitamin D receptor, a DNA-binding, zinc-finger protein with a relative molecular mass of 55,000. This ligand-receptor complex binds to a specific

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vitamin D-responsive element and, with associated transcription factors (e.g. retinoid X receptor), enhances transcription of mRNAs which code for calcium-transporting proteins, bone matrix proteins, or cell cycle-regulating proteins.

5) Formation of enzymes: Vitamin D is essential for the formation of two enzymes- alkaline phosphatase in the intestinal lining (involved in calcium transport) and adenosine triphosphatase, (for collagen formation in bone matrix).

6) Regulation of amino acid levels in the blood: Vitamin D helps to prevent loss of amino acids through the kidney and thus regulate the amino acid level and also regulate the level of citric acid in tissues and bones.

7) Participation in muscle formation and metabolism: Vitamin D takes part in muscle function and metabolism.

8) Inhibition of cancer cell proliferation and growth: Vitamin D diminishes proliferation of abnormal intestinal, lymphatic, mammary and skeletal cells and provides a potential for the treatment of skin diseases such as psoriasis (a disorder in which there is proliferation of the keratinocytes and a failure to differentiate rapidly).

9) Role in the immune system: Immune responses that are mediated by T-cells can be inhibited by the large doses of calcitriol i.e. 1,25 dihydroxycholecalciferol. It is a natural steroid hormone formed in the healthy body as the biologically active form of vitamin D. A deficiency of vitamin D also interferes with the T-cell mediated immunity. 10) Regulation of blood pressure: The renin-angiotensin system regulates the blood pressure. The synthesis of renin is decreased by calcitriol through its interaction with the vitamin D regulator (VDR). Inappropriate activation of the renin- angiotensin system is thought to play a role in some forms of human hypertension and adequate vitamin D levels may be important for decreasing the risk of high blood pressure. So, now we have a good idea about the role of vitamin D in our body. Next, let us study the factors which affect the bioavailability of vitamin D.

Bioavailability of Vitamin D

The nutritional availability of vitamin D is less significant because it can be endogenously produced and retained for long periods by the tissues. Factors that affect availability are the duration of exposure to sunlight, seasonal variation, skin pigmentation, cultural practices like purdah system associated with clothing that covers the entire body and face.

You might have seen small children with bow legs, who are unable to walk normally and have enlarged bone joints. These, along with many other symptoms, are associated with vitamin D deficiency.

Deficiency and Toxicity of Vitamin D

Infants constitute a population at-risk for vitamin D deficiency because of relatively large vitamin D needs brought about by their high rate of skeletal growth; Breast-fed infants are particularly at-risk because of the low concentrations of vitamin D in human milk. This problem is further compounded in some infants fed human milk by a restriction in exposure to ultraviolet (UV) light for seasonal, latitudinal, cultural or social reasons. Dietary absence of vitamin D or lack of UV (sunlight) exposure causes the bone disease called rickets in infants/children and osteomalacia in adults. Let us first study the characteristic features of rickets in children.

Rickets: The following characteristics are seen in fully developed cases of rickets:

1) In case of young infants, delayed closure of the fontanelles i.e. a soft membranous gap between the cranial bones, softening and reduced mineralization of the skull (craniotabes).

2) While in older infants, sitting and crawling are delayed and there is bossing of skull. Also there are soft, fragile bones, bow legs, enlargement of the costochondral junction (a cartilage that attaches the front of the ribs to the breastbone) with rows of knobs or beads forming the Rachitic Rosary, pigeon chest and spinal curvature.

3) Enlargement of wrist, knee and ankle joints.

4) Poorly developed muscles, lack of muscle tone, pot belly being the result of weakness of abdominal muscles, weakness with delayed walking.

5) Restlessness and nervous irritability.

6) High serum alkaline phosphatase, low inorganic blood phosphorus, normal or low serum calcium.

7) Tetany characterized by low serum calcium, muscle twitching, cramps and convulsions.

8) Delayed dentition and malformation of the teeth, permanent teeth more' subject to decay.

Let us now discuss the symptoms of 'adult rickets' i.e. osteornalacia.

Osteomalacia: It occurs when there is a lack of vitamin D and calcium, in women who have had many pregnancies, who subsist on a meagre cereal diet with little exposure to sunshine. In osteomalacia, the following changes are seen:

1) Softening or demineralization of the bones leading to deformities of legs, spine, thorax and pelvis. As the bones soften, weight may cause bowing of the long bones, vertical shortening of the vertebrae and flattening of pelvic bone.

2) Rheumatic pain in bones of the legs and back.

3) General weakness with difficulty in walking.

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4) Spontaneous multiple fractures.

5) Normal parturition difficult since sacrum convexity is increased, ribs of the iliac bone are flattened and the inlet becomes asymmetrical and narrowed.

Toxicity

The adverse effects of high vitamin D intakes include hypercalciuria (excessive urinary calcium excretion) and hypocalcaemia (high concentration of calcium in blood). Excessive amounts of vitamin D are not normally available from dietary sources, and hence cases of vitamin D intoxication are rare. Nevertheless, toxicity may occur in individuals on excessive amounts of supplemented vitamins, for example, drinking milk fortified with inappropriately high levels of vitamin D3. The signs and symptoms associated with it are anorexia, nausea and vomiting, followed by polyuria, polydipsia, weakness, nervousness and pruritis (itchiness). Renal function is impaired and metastatic calcifications may occur, particularly in the kidneys. So, what should be the safe level of intake? For this, recommendations have been made.

Recommended Dietary Allowances for Vitamin D

The recommendations of vitamin D are expressed as IU. 1 IU is defined as the activity contained in 0.025 mcg cholecalciferol. The recommended allowances for vitamin D as suggested ly the Indian Council of Medical Research (ICMR) for Indians are 200—400 IU, as highlighted in Table 7.3. A vitamin D supplement providing 400 to 800 IUs may be essential for the elderly, panicularly consume less milk and are totally home bound.

Table 7.3: Recommendations for vitamin D according to age groups

Age Group	FAO/WHO 2004 µg/day*	ICMR (IU/day)
Infants		
0 - 6 months	5 (200 IU)	
7 - 12 months	5 (200 IU)	
Children		200-400
1 - 3 years	5 (200 IU)	
4 - 6 years	5 (200 IU)	
7 - 9 years	5 (200 IU)	
Adolescents, 10 - 18 years	5 (200 IU)	
Adults		
19 - 50 years	5 (200 IU)	
Older adults, 51 - 65 years	10 (400 IU)	
Elderly adults, 65 + years	15 (600 IU)	
Pregnant women	5 (200 IU)	
Lactating women	5 (200 IU)	

Criteria for Assessment of Vitamin D Status

You may recall the events involved in calcium homeostasis described earlier in this section. We studied that sufficient 25-OH-D must be available to provide adequate steroid hormone 1, 25-dihydroxycholecalciferol (1,25-(OH)2D) synthesis and hence an adequate level of plasma calcium. It becomes evident therefore, that vitamin D status can be assessed by measuring the circulating level of the steroid hormone 1,25-dihydroxycholecalciferol. Plasma levels of 3-6 mg/dl are considered normal.

Interaction of Vitamin D with other Nutrients

Vitamin D metabolism is inter-related with calcium, phosphorous, vitamin K and iron.

Calcium: The interaction of vitamin D with calcium has already been discussed earlier. Vitamin D initiates calcium absorption, as well as, activation of protein kinase.

Phosphorous: Vitamin D increases the activity of brush border alkaline phosphatase, which hydrolyzes phosphate ester bonds allowing phosphorous absorption.

Vitamin K: An inter-relationship exists between vitamin D and K based on their relationship to the mineral calcium. Vitamin D has an impact on calcium metabolism and vitamin K-dependent proteins bind calcium. The two sites of action of vitamin D .are bone and kidney tissues, where vitamin K-dependent calcium- binding proteins have been identified which regulate the production of crucial enzymes.

Iron: A decrease in vitamin D has been observed as a result of iron deficiency. With this, we end our study of vitamin D.

7.6 VITAMIN E

Vitamin E is the generic term for tocopherols and tocotrienols that have a phenolic functional group on a chromane ring system with an isoprenoid side chain. Isoprene, as you can see, is a branched chain unsaturated hydrocarbon of five carbon atoms (C-C-C-C-C). This carbon skeleton forms the basis of carotenoids, steroids and tocopherols. The tocopherols and tocotrienols occur as homologues — a,ß and y— that differ in the number or location of methanyl substituents in the chromanol.

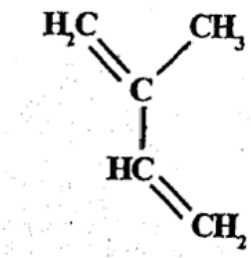


Figure 7.11: Isoprene unit

Having looked at the structure of tocopherols and tocotrienols, let us study about the food sources of vitamin E.

Sources Vitamin E

Vitamin E is present in alinost all foodstuffs. It is found in wheat germ, corn, nuts, seeds, olives, spinach, asparagus and other green leafy vegetables and vegetable oils like groundnut, soy, cotton seed and safflower are rich sources. The vitamin E content of edible oils is usually proportional to the amount of polyunsaturated fatty acid content of the oils.

Table 7.4: Vitamin E content of vegetable oils

Oil	a-tocopherol	γ-tocopherol	6-tocopherol	a-tocotrienol
Coconut	0.5	0	0.06	0.5
Maize (corn)	11.2	60.2	1.8	0
Palm	25.6	31.6	7.0	14.3
Olive	5.1	Trace	0	0
Peanut	13.0	21.4	2.1	0
Soybean	10.1	59.3	26.4	0
Wheat germ	133.0	26.0	27.1	2.6
Sunflower'	48.7	5.1	0.8	0

We may need to understand here that there may be a variation in the α-tocopherol levels or intake, the variation being ascribed mainly to the type and quantity of dietary oils used and the proportion of the different homologues in the oils. For example, sunflower seed oil contains approximately 50 mg α-tocopherol /100 g in contrast to soybean oil that contains only 10 mg/100ml. Because vitamin E is naturally present in plant-based diets (whole grain cereals, dark green leafy vegetables, pulses, nuts and oilseeds as highlighted in Figure 7.12) and animal products (such as egg yolk, butter and liver) and is often added by manufacturers to vegetable oils and processed foods, intakes are probably adequate to avoid overt deficiency in most situations.

Exceptions may be during ecologic disasters and cultural conflicts resulting in food deprivation and famine. So we have a large variety of foods which can help us meet our vitamin E needs.

Next, once inside the body, what is the fate of vitamin E? Let us find out next.

Absorption and Storage of Vitamin E

1) *Fat-Soluble Vitamins:*

Absorption of vitamin E from the intestine depends on adequate pancreatic function, biliary secretion and micelle formation. Conditions for absorption are like those for dietary lipid, that is, efficient emulsification, solubilization within mixed bile salt micelles, uptake by enterocytes, and secretion into the circulation via the lymphatic system. Emulsificationtakes place initially in the stomach and then in the small intestine in the presence of pancreatic and biliary secretions. The resulting mixed micelle aggregates the vitamin E molecules, solubilizes the vitamin E, and then transports it to the brush border membrane of the enterocyte, probably by passive diffusion.Within the enterocyte, tocopherol is incorporated into chyloinicrons and secreted into the intracellular space and lymphatic system and subsequently into the blood sl-ream. Tocopherol esters, present in processed foods and vitamin supplements, must be hydrolyzed in the small intestine before absorption.

Vitamin E is transported in the blood by the plasma lipoproteins and erythrocytes. Chylomicrons carry tocopherol from the enterocyte to the liver, where they are incorporated into parenchymal cells as chyloinicron remnants. The catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein, lipase. During this process, tocopherol can be transferred to high-density lipoproteins (HDLs). The tocopherol in HDLs can transfer to other circulating lipoproteins, such as low-density lipoprotein (LDL) and very low-density lipoproteins (VLDLs). During the conversion of VLDL to LDL in the circulation, some a-tocopherol remains within the core lipids and is thus incorporated in LDL. Most a-tocopherol then enters the cells of peripheral tissues within the intact lipoprotein through the LDL receptor pathway, although some may be taken up by membrane binding sites recognizing apolipoprotein (A-I and A-II) present on HDL. Although the process of absorption of all the tocopherol homologues in the diet is similar, the a-form predominates in blood and tissue. From a nutritional perspective, the most important form of vitamin E is a-tocopherol. It is absorbed faster and retained better than other forms. This is due to the action of binding proteins that preferentially select the a form over other forms.

Vitamin E is mainly stored in muscles and adipose tissue. Vitamin E content of elythrocytes is about 20 percent of that in plasma and there is an efficient exchange between these pools. The vitamin is most concentrated in cellular fractions that are rich in membrane lipids such as mitochondria.

2) *Elimination*

The primary oxidation product of a-tocopherol is a-tocopheryl quinone that can be conjugated to yield the glucuronate. This glucnronide is excreted in the bile as such or further degraded in the kidneys to u-tocopheronic acid glucuronide and

hence excreted in the bile. Those vitamin E homologues not preferentially selected by the hepatic binding proteins are eliminated during the process of nascent VLDL secretion in the liver and probably excreted via the bile. Some vitamin E may also be excreted via skin sebaceous glands.

3) *Functions of Vitamin E*

Vitamin E is the major lipid-soluble antioxidant in the cell antioxidant defense system and is exclusively obtained from the diet. The main role of vitamin E and the biological activity of tocopherols are due to its antioxidant property. This antioxidant property of vitamin E is useful for various body processes and substances which is enumerated herewith.

1) Protection of poly unsaturated fatty acids (PUFA) from oxidative damage:

The major biological role of vitamin E is to protect PUFAs and other components of cell membranes and low-density lipoprotein (LDL) from oxidation free radicals. Vitamin E is located primarily within the phospholipid bilayer of cell membranes. It is particularly effective in preventing lipid peroxidation — a series of chemical reactions involving the oxidative deterioration of PUFAs. Elevated levels of lipid peroxidation products are associated with numerous diseases and clinical conditions.

The PUFAs, you may recall studying in the Nutritional Biochemistry Course, have methylene (-CH2-) groups located between two double bonds. This type of functionality makes PUFA particularly sensitive to the flameless oxidation in air that is called autoxidation, because the doubly allelic hydrogen atoms in these methylene carbons are very mpidly abstracted ly peroxyl radicals. Free radicals are produced in normal metabolism and ly the effects of toxins on tissues.

These free radicals (eg. superoxide produced endogenously by many processes like phagocytosis) can cause the formation of lipid free radicals as shown in the initiation sequence reactions 1 and 2. In reaction 2, initiation produces the lipid free radicals and a conjugated dienyl radical (L). The lipid radical L then undergoes the propagation sequence reaction 3 and 4 leading to the formation of lipid hydroperoxides, COOH.

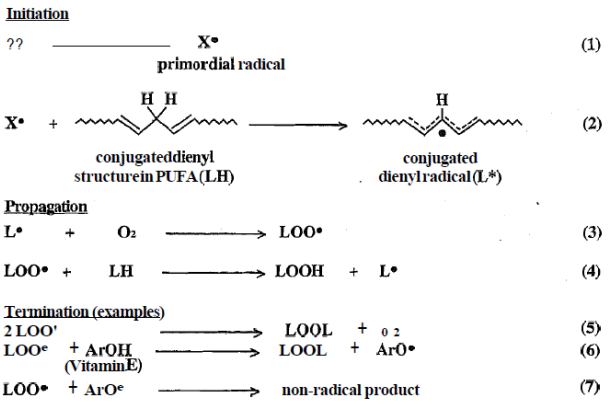


Figure 7.13: The autoxidation of PUFAs

Lipid hydroperoxides produced in autoxidation processes are also fomed in enzyme-catalyzed reactions. For example, the enzymes in cyclooxygenase pathway which convelts arachidonic acid to several types of hydroperoxides. These have potent biological properties.

Autoxidation is a chain process. Reactions 3 and 4 continue to altemate until a termination occurs in which two radicals combine to form a new two-electron bond. When vitamin E is absent, from five to twenty five LOOH molecules are formed in reaction 4 for each primordial X radical formed in reaction 1. If vitamin E is present, it traps peroxylradicals to give stable LOOH molecule and a vitamin E radical. The vitamin E radical is stable enough to seek another LOO* radical as in reaction 7 and complete the termination sequence. In absence of vitamin E, however, each primordial radical produces <l molecule LOOH. Thus, vitamin E effectively stops the autoxidation chain reaction which converts PUFA to lipid hydroperoxides, LOOH. One molecule of tocopherol can effectively protect 100 or more PUFA molecules from autoxidative damage. Biological membranes generally contain one percent as Bat-Soluble Vitamins: many molecules of vitamin E as molecules of PUFA. Vitamin A, D, E and K

2) Protection of erythrocytes: Vitamin E protects erythrocytes from haemolysis by the production of oxidizing agents e.g. dialuric acid and hydrogen peroxide.

3) Protection of cell membrane: It protects the cell membrane from getting damaged from naturally occurring peroxides and toxic free radicals formed from fatty acids and oxidative tissue damage as described above.

4) Protection against poisoning: It protects liver from injury due to carbon tetra chloride poisoning.

5) Protection of both vitamin A and carotene: It protects vitamin A and ß-carotene from destruction by oxidation, especially in the alimentary tract, thus sparing the supply of vitamin A available to the body.

6) Synthesis of enzymes and proteins: It serves as a co-repressor in the synthesis of certain enzymes and plays a specific role in the synthesis of haem proteins.

7) Protection of mitochondria: It protects the mitochondrial function of the muscles and cardiac tissue. Tocopherol acts as an electron acceptor in the electron transport system and prevents the disruption of mitochondria.

8) Reduction in free radical generation: Vitamin E acts synergistically with selenium thereby reducing susceptibility of LDL to oxidation, free radical generation and membrane damage. This antioxidant role of vitamin E together with selenium protects against cardiovascular diseases especially atherosclerotic lesions.

NOTES

9) Regulation of the enzyme activities: Vitamin E regulates the activity of enzymes, δ-amino levulinic acid (ALA) synthetase in bone marrow and ALA dehydrase in liver,

10) Prevention of diseases: Because of its anti-oxidant function and its role in Inhibiting cell proliferation of smooth muscles, vitamin E can be used for prevention/ treatment of diseases. Epidemiological studies suggest that dietary vitamin E influences the risk of cardiovascular disease. It has also been suggested that vitamin E supplementation (200-400 mg/ day) may be appropriate therapeutically to moderate some aspects of degenerative diseases such as Parkinson disease, reduce the severity of neurologic disorders such as tardive dyskinesia (potentially irreversible and involuntary movements), prevent periventricular haemorrhage in pre-term babies, reduce tissue injury arising from ischaernia and reperfusion during surgery, delay cataract development, and improve mobility in arthritis sufferers. From our discussion above, it must be clear that the major role of vitamin E lies in its antioxidant property. Next, let us get to know about the bioavailability of the tocopherols and the resulting diseases. Bioavailability

For dietary purposes, vitamin E activity is expressed as α-tocopherol equivalents (α-TEs). One α-TE is the activity of 1mg a-tocopherols. To estimate the α-TE of a mixed diet containing natural forms of vitamin E, the number of milligrams of ß-tocopherols should be multiplied by 0.5, y-tocopherol by 0.1, and a-tocotrienol by 0.3. The bioavailability of tocopherols varies inversely with the uptake. This meals that ingesting four times the amount of the vitamin raises tissue levels by only two-fold. A high correlation exists between the total fat and tocopherol concentrations in blood serum. Thus, diseases associated with high serum lipids (hypothyroidism, diabetes, and hypercholesterolemia) produce high plasma vitamin E levels and those associated to low serum lipids produce low vitamin E levels.

Deficiency and Toxicity of Vitamin

Fortunately, vitamin E deficiency in human is extremely rare. This may probably be due to its wide occurrence, in natural foods as highlighted above. Evidence of deficiency is however seen in individuals with chronic fat absorption e.g. sprue and fibrocystic disease of pancreas. Changes occurring in severe deficiency include disorders of reproduction, abnormalities of muscle, liver, bone marrow and brain function, defective embryogenesis, increased haemolysis of red blood cells, creaünuria and deposition of brownish ceroid pigment in smooth muscle. Skeletal muscle dystrophy may occur and, in certain species, is accompanied by cardiomyopathy.

Recent evidence has established that vitamin E deficiency is a cause of the impaired neuromuscular function, sometimes seen in patients with disorders that interfere with absorption or transport of the vitamin. Symptoms include poor reflexes, impaired locomotion, decreased sensation in the hands and feet, and changes in the retina. Disorders provoked by traces of per oxidized PUFAs in the diets of animals

with low vitamin E status include cardiac or skeletal myopathies, neuropathies and liver necrosis. Muscle and neurological problems are also a consequence of human vitamin E deficiency. Early diagnostic signs of deficiency include leakage of muscle enzymes such as creatine kinase and pyruvate kinase into plasma, increased levels of lipid peroxidation products in plasma and increased erythrocyte haemolysis. We read about the consequences of low intake of vitamin E on the human body. A very high intake of vitamin E can also elicit severe adverse reactions, as described next.

Toxicity

Vitamin E is relatively non-toxic. Adults tolerate doses as high as 100 to 1,000 IU per day. However, adverse effects such as muscle weakness, fatigue, nausea, diarrhoea, double vision, elevation of serum lipids, impaired blood coagulation and reduction of serum thyroid hormones occur due to indiscriminate ingestion of excessive amounts of vitamin E over long periods of time. Evidence of pro-oxidant damage has been associated with the feeding of supplements but usually only at very high doses (e.g. >1000 mg/ day). Next, let us get to know about the requirements for vitamin E.

Recommended Dietary Allowance of Vitamin E

The requirements for the vitamin E are expressed in terms of tocopherol equivalents (TE) as mentioned earlier — 8 mg for females and 10 mg for males. It has been seen that the adequacy of RDA varies with PUFA content significantly; increased intakes necessitate larger amounts of vitamin E in the diet. FAO/ WHO 2004 committee has suggested that when the main PUFA in the diet is linoleic acid, a α-tocopherol—PUFA ratio of 0.4 (expressed as mg tocopherol per g PUFA) is adequate for adult humans. This ratio has been recommended in the United Kingdom for infant formulas, Use of this ratio to calculate the vitamin E requirements of men and women with energy intakes of 2550 and 1940 Kcal/day, respectively, and containing PUFAs at 6% of the energy intake (approximately 17 g and 13 g, respectively), Fat-Soluble Vitamins: produced values of 7 and 5 mg/ day of u-TEs, respectively. Vitamin A, D, E and K The criterion for assessment of vitamin E status in our body is presented, next.

Criteria for Assessment of Vitamin Status

Vitamin E is assessed by determining the plasma lipid fraction levels. 0.8 mg of total tocopherol/g total plasma lipids indicates adequate nutritional status. The interaction of vitamin E with other nutrients is enumerated finally

Interaction with other Nutrients

Vitamin E is directly related to selenium, other fat-soluble vitamins and PUFA. Let us study this relationship.

- Selenium: An inter-relationship exists between vitamin E and selenium, as selenium functions as an integral part of glutathione peroxides—an enzyme—that converts lipid peroxide into a lipid alcohol.

- Vitamins A, D and K: A high intake of vitamin E interferes with the functions of other fat-soluble vitamins such as vitamin K absorption and vitamin D in terms of bone mineralization while in case of vitamin A deficiency. It lowers the rate of vitamin A depletion from the liver. It protects the cleavage products and substrate from oxidation. However, large doses of vitamin E inhibit ß-carotene absorption or conversion to retinol in the intestine.
- Polyunsaturated Fatty Acid (PUFA): A relationship between vitamin E and dietary P UFA is strong, as we have already studied earlier, because the requirement for the vitamin increases or decreases as the dietary intake of PUFA rises or falls.

We now end our study about vitamin E. Do answer the questions given in check your progress exercise 3'and check your understanding on the topic.

7.7 VITAMIN K

Vitamin K is an essential fat-soluble micronutrient; the only unequivocal role in health is in the maintenance of normal coagulation. Vitamin K is the family name for a series of fat-soluble compounds which have a common 2-methyl-1 ,4-naphthoquinone nucleus but differ in the structures of a side chain at the 3-position. They are synthesized by plants and bacteria. In plants, the only important molecular form is phylloquinone (vitamin K1, which has a phytyl side chain. Bacteria synthesize a family of compounds called menaquinones (vitamin K2), which have side chains based on repeating unsaturated 5-carbon (prenyl) units.

Menaquinones are designated menaquinone-n. (MK-n) according to the number (n) of prenyl units. The compound 2-methyl1,4-naphthpquinone (common name menadione) may be regarded as a provitamin because vertebrates can convert it to MK-4 by adding a 4-prenyl side chain at the 3-position. What are the food sources of vitamin K? Let us find out.

Sources of Vitamin K.

As mentioned above, in plants, the only important molecular 'form of vitamin K is phylloquinone. Phylloquinoneis distributed ubiquitously throughout the diet, and the range of concentrations in different food categories is very wide.

The next best sources are certain vegetable oils (e.g. soybean, rapeseed and olive), which contain 50-200 mg/100g, other vegetable oils, such as peanut, corn, sunflower and safflower, however, contain much lower amounts of phylloquinone (1-10 mg/100 g). The great differences between vegetable oils with respect to vitamin K content obviously present problems for calculating the phylloquinone contents of oil containing foods when the type of oil is not known. Other good sources include animal foods such as egg yolk, milk and organ meats like liver.

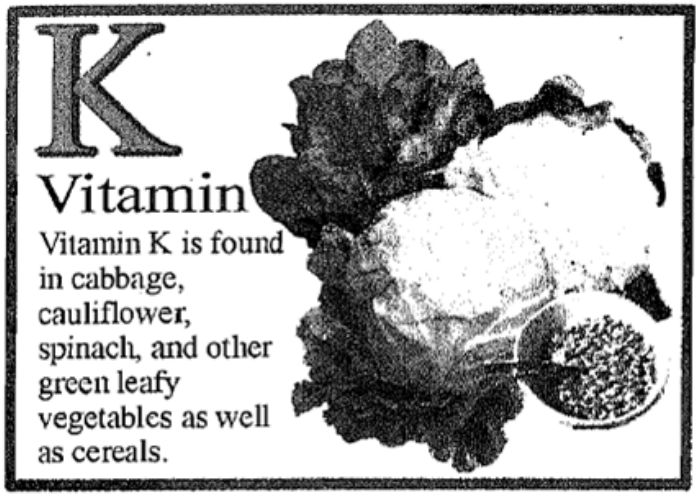


Figure 7.14: Food sources of vitamin K

Importance of Intestinal Bacterial Synthesis as a Source of Vitamin K

Intestinal microflora synthesize large amounts of menaquinones, which are potentially available as a source of vitamin K. Quantitative measurements at different sites of the human intestine have deinonstrated that most of these menaquinones are present in the distal colon. Major forms produced are MK-I and MK-II by Bacteroides, MK-8 by Enterobacter, MK-7 by Veillonella, and MK-6 by Eubacterium lentum etc.

However, the balance of evidence suggests that the bioavailability of bacterial menaquinones is poor because they are for the most part tightly bound to the bacterial cytoplasmic membrane and also because the largest pool is present in the colon, which lacks bile salts for their solubilization.

Bioavailability of Vitamin K

Very little is known about the bioavailability of the K vitamins from different foods. It has been estimated that the efficiency of absorption of phylloquinone from boiled spinach (eaten with butter) is no greater than 10% compared with an estimated 80% when phylloquinone is given in its free form. This poor absorption of phylloquinone from green leafy vegetables may be explained by its location in chloroplasts (organelles in plant cells that conduct photosynthesis) and tight association with the thylakoid membrane (a phospholipid bilayer memberane-bound compartment internal to chloroplasts). In comparison, the bioavailability of MK-4 from butter artificially enriched with this vitamin was more than two-fold higher than that of phylloquinone from spinach. The poor extraction of phylloquinone from leafr vegetables, which as a category represents the single greatest food source of phylloquinone, may place a different perspective on the relative importance of other foods with lower concentrations of phylloquinone (e.g. those containing soybean and rapeseed oils) but in which the vitamin is not tightly bound and its bioavailability is likely to be greater.

Vitamin K availability varies directly with fat intake and any condition of fat malabsorption reduces its bioavailability. In healthy adults, absorption of phylloquinone has been estimated to be 80 percent when phylloquinone is administered in its free form as discussed above, but decreases significantly when absorbed from foods. Cooking has no effect, but addition of fat increases absorption multifold.

Absorption, Storage and Elimination of Vitamin K

Dietary vitamin K, mainly phylloquinone, is absorbed chemically unchanged from the proximal intestine after solubilization into mixed micelles composed of bile salts and the products of pancreatic lipolysis. In healthy adults, the efficiency of absorption of phylloquinone in its free form is about 80%. Within the intestinal mucosa, the vitamin is incorporated into chylomicrons, is secreted into the lymph, and enters the blood via the lacteals (minute intestinal lymph-carrying vessels). Once in the circulation, phylloquinone is rapidly cleared at a rate consistent with its continuing association with chylomicrons and the chylomicron remnants, which are produced by lipoprotein lipase hydrolysis at the surface of capillary endothelial cells. Although phylloquinone is the major circulating form of vitamin K, MK-7 is also present in plasma, at lower concentrations and with a lipoprotein distribution similar to phylloquinone. Vitamin K is stored in the liver — the site of synthesis of coagulation proteins—and consists of 90 percent menaquinones. PhyLloquinones and menaquinones are also found in extra hepatic tissues. Phylloquinonelevels are high in liver, heart and pancreas. Vitamin K is extensively metabolized in the liver and excreted in the urine and bile. About 60-70% of the amount of phylloquinone absorbed from each meal will ultimately be lost to the body by excretion. This, therefore, suggests that the body stores of phylloquinone are being constantly replenished. .

Functions of K

The functions of vitamin K are both physiological and biochemical. These include:

1) Blood coagulation:

The primary function of vitamin K in the body is in the maintenance of normal blood coagulation. The vitamin K-dependent coagulation proteins are synthesized in the liver and comprise Factor II (prothrombin), Factor VII (proconvertin), Factor iX (Christmas factor) and Factor X (Stuart factor), which have a haemostatic role i.e. they are procoagulants that arrest and prevent bleeding. Let us get to know how this mechnism works. Prothrombin is converted to its active form, thrombin, which in turn, is necessary for the formation of fibrin, a protein that is the basis for a blood clot.

Vitamin K also acts as a cofactor for an enzyme in the liver which converts glutamic acid residues in a precursor process to gamma-carboxy glutamic acid. This reaction is necessary before prothrombin can function in blood coagulation.

2) Vitamin K-dependent carboxylation:

Vitamin K acts as a cofactor in the Fat-Soluble Vitamins: synthesis of Y-carboxyglutamic acid (Gla) from glutamic acid residues required VitaminA, D,E and K for the normal coagulation of blood.

The biological role of vitamin K, therefore, is to act as a cofactor for a specific carboxylation reaction that transforms selective glutamate (Glu) residues to Y- carboxyglutamate (Gla) residues. The reaction is catalyzed by a microsomal enzyme, Y-glutamyl, or vitamin K-dependent carboxylase, which in turn is linked to a cyclic salvage pathway known as the vitamin K epoxide cycle. The hydroquinone (reduced form of vitamin K), C02 and 02 are required for the reaction. During the catalysis, hydroquinone is oxidized to vitamin K 2,3-epoxide and the energy derived from the oxidation drives the carboxylation.

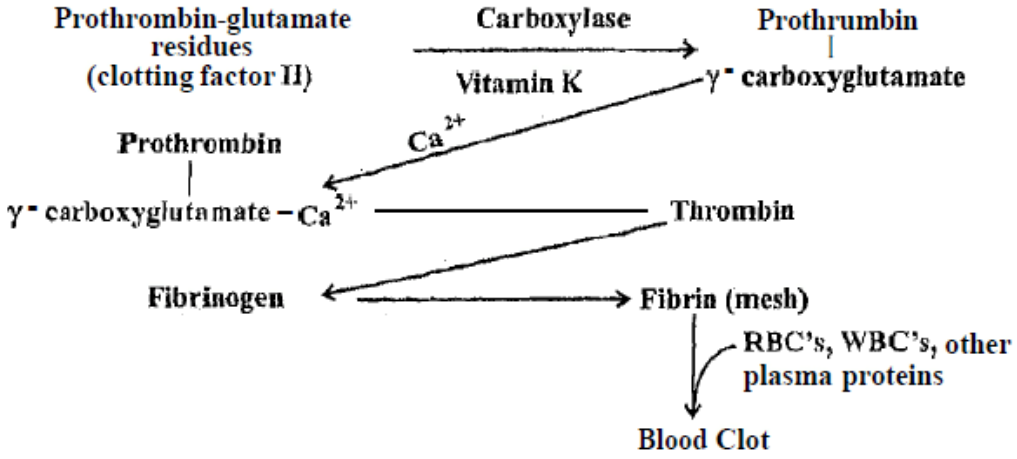


Figure 7.16: Vitamin K cycle

3) Vitamin K dependent proteins:

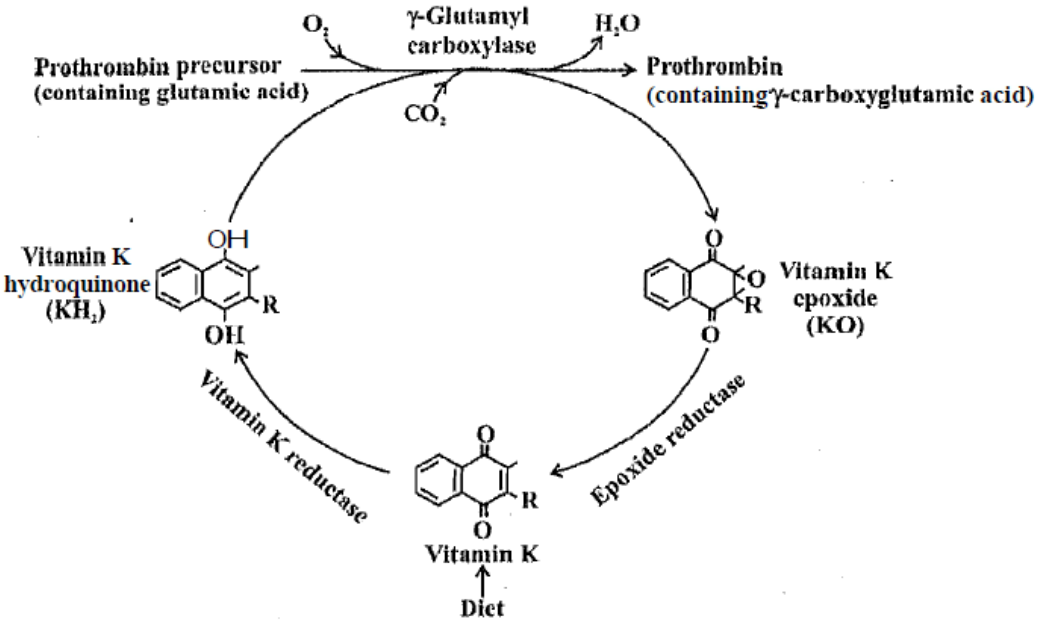
The four vitamin K-dependent procoagulants (factor II or prothrombin, and factors V II, IX, and X), about which we studied above, are serine proteases that are synthesized in the liver and then secreted into the circulation as inactive forms (zymogens). Their biological activity depends on their normal complement of Gla residues, which are efficient chelators of calcium ions. In the presence of Gla residues and calcium ions, these proteins bind to the surface membrane phospholipids of platelets and endothelial cells where, together with other cofactors, they form membrane-bound enzyme complexes. When coagulation is initiated, the zymogens of the four vitamin K-dependent clotting factors are cleaved to yield the active protease clotting factors.

Two other vitamin K-dependent proteins, protein C and protein S, play a regulatory role in the inhibition of coagulation. The ftmction of protein C is to degrade

phospholipid- bound activated factors V and VIII in the presence of calcium. Protein S acts as a synergistic cofactor to protein C by enhancing the binding of activated protein C to negatively charged phospholipids. There is an evidence that protein S is synthesized by several tissues including the blood vessel wall and bone and may have other functions besides its well-established role as a coagulation inhibitor. Yet another vitamin K-dependent plasma protein (protein Z) is suspected to have a haemostatic role but its function is currently unknown.

Apart from the coagulation proteins, several other vitamin K-dependent proteins have been isolated from bone, cartilage, kidney, lungs and other tissues. Only two, osteocalcin and matrix Gla protein (MGP), have been well characterized. Both are found in bone but MGP also occurs in cartilage, blood vessel walls, and other soft tissues. One function of MGP is to inhibit mineralization. Thus far, no clear biological role for osteocalcin has been established despite its being the major noncollagenous bone protein synthesized osteoblasts. Nephrocalcin has been isolated from kidney and urine. Atherocalcin, plaque Gla protein,proline rich Gla proteins have been identified from atheromatous plaques, spinal and thyroid tissues

Table 7.5: Vitamin K dependent proteins mid their functions



4) Sphingolipid metabolism: Vitamin K

Spingolipids, as you would recall from your Biochemistry Course, are a class of membrane lipids that are composed of one molecule of the long-chain amino alcohol sphingosine (4-sphingenine) or one of its derivatives, one molecule of a long-chain

acid, a polar head alcohol and sometimes phosphoric acid in di-ester linkage at the polar head group.

5) Prevents bone loss:

Vitamin K is known to inhibit bone loss through inhibiting effect on osteoclast formation. Thus, adequate levels of vitamin K must be maintained in the human body. From functions, we move on to study about the deficiency and toxicity of vitamin K.

Deficiency and Toxicity Vitamin K

Both excess and low intakes can have serious implications on human health. Although such conditions arise rarely, these can often be life-threatening. subsequent discussions are pertaining to excess and deficient intake. Adults are usually protected from a lack of vitamin K because vitamin K is widely distributed in plant and animal tissues, the vitamin K cycle conserves the vitamin, and microbiological flora of the normal gut synthesizes menaquinones. Also, a normal diet contains about 300 to 500 mcg vitamin K daily and therefore supplies at least three times the amount of recommended vitamin K. Vitamin K deficiency leads to a lowered prothrombin level and increased clotting time, and thereby hemorrhages.

The factors that lead to vitamin K deficiency include: .

1) Marginal dietary intake if one undergoes trauma and extensive surgery etc.

2) Inadequate intake of vitamin K by the mother leads to hemorrhagic disease in the newborn, with low prothrombin level.

3) Inadequate intestinal absorption (disease of liver and intestine such as biliary obstruction, malabsorption and parenchymal liver disease leads to deficiency in adults. Large amounts of vitamin A and E may interfere with the absorption or metabolism of vitamin K. In severe disease of the liver, the synthesis of the clotting factors is impaired even though the source of vitamin K is adequate.

In infants up to around age 6 months, vitamin K deficiency, although rare, represents a significant public health problem throughout the world. The deficiency syndrome is traditionally known as hemorrhagic disease of the newborn. More recently, in order to give a better definition Of the cause, it has been termed vitamin K deficiency bleeding (VKDB).

Epidemiological studies worldwide have identified two major risk factors for VKDB viz; exclusive human-milk feeding and the failure to give any vitamin K prophylaxis. The increased risk for infants fed human milk compared with formula milk is probably related to the relatively low concentrations of vitamin K (phylloquinone) in breast milk compared with formula milks.

Toxicity

Vitamin K1 does not produce any toxic effects in doses (10-20 mg) normally used for the treatment of subjects suffering from disorders of liver or intestines. Vitamin K analogues (menadione and water soluble forms of menndione), administered to premature infants produce toxicity attributed to increased breakdown of red blood cells (haemolytic anaemia), hyperbilirubinaemia and inhibition of glilcouronide formation.

Table 7.6: Recommended nutrients intakes for vitamin K

Proteins	Physiological Function
Blood coagulation	
Prothrombin	Procoagulant
Factor VII	Procoagulant
Factor IX	Procoagulant
Factor X	Procoagulant
Protein C	Anticoagulant
Protein S	Anticoagulant
Protein Z	undetermined
Bone	
Osteocalcin	Negative regulator of bone formation
Matrix γ-carboxy glutamic acid (Gla) protein	Calcification inhibitor
Protein S	Undetermined
Others	
Nephrocalcin	Undetermined
Atherocalcin	Undetermined
Proline rich Gla proteins 1 and 2	Undetermined

Criteria for Assessment Vitamin K Status

The parameters of blood clotting and prothrombin time are used as criteria to assess vitamin K status as this vitamin is vital for the formation of the factors involved in blood coagulation especially prothrombin. A normal prothrombin time is considered to be between 11 and 13 seconds, while a duration greater than 25 seconds is associated with major bleeding. In addition, maintenance of plasma prothrombin concentrations in the range 80-120 mg/ml suggests adequate vitamin K status.

Finally, let us get to know about the interaction of vitamin K with other nutrients.

Interaction with other Nutrients

Vitamin K absorption is inter-related to other fat-soluble vitamins (A and E) and calcium.

- **Vitamins A and E:** Excess vitamin A interferes with vitamin K absorption while the a-tocopherol or vitamin E, as we have already studied earlier, also affects absorption, function and metabolism of vitamin K. It may block the

regeneration of the reduced form of vitamin K and/or may affect p10thrombin formation.

- **Calcium:** Since vitamin D functions have an impact on calcium metabolism, an inter-relationship exists between vitamin K-dependent proteins and vitamin D, as well as, calcium. In the tissues of the bones and kidney, vitamin D plays a major role, vitamin K-dependent calcium-binding proteins have been identifie and shown to regulate the production of crucial enzymes.

With a discussion on vitamin K, we end our study on fat-soluble vitamins. The next unit will focus on the water-soluble vitamins.

7.8 LET US SUM UP

This unit focused on the fat-soluble vitamins. Fat-soluble vitamins are vital to health. They can be obtained from inexpensive, readily available plant: foods and sunlight. A summary of the important functions and sources of fat-soluble vitamins is presented herewith. We learnt that the deficien y of vitamin A is a nutritional disorder of public health significance in India.

Summary of Fat Soluble Vitamins

Vitamins	Sources	Functions
Vitamin A	• Retinol: liver, egg yolk, cream, butter, ghee, milk β-carotene: yellow and orange vegetables, green leafy vegetables	• Maintenance of health of epithelial tissues Vision in dim light Growth of skeletal and soft tissues • Resistance to infections
Vitamin D	Action of sunlight on the skin • Animal foods like eggs, butter, fish liver oil	Absorption of calcium and phosphorous Deposition of calcium and phosphorous in bones
Vitamin E	• Vegetable oils, whole grains, deep green leafy vegetables, pulses, nuts and oilseeds.	• Protection of unsaturated fatty acids, vitamin A and C from destruction in the body/food.
Vitamin K	• Dark green leafy vegetables, egg yolk, liver. • Bacterial synthesis	• Clotting of blood.

7.9 GLOSSARY

Abetalipoproteinemia : a rare inherited disorder of fat metabolism characterized by severe deficiency ß-lipoproteins and abnormal RBCs and abnormally low cholesterol levels.

Arthralgias : neuralgic pain in a joint or joints.

Beta carotene : a fat-soluble carotenoid pigment present in plants which is a precursor of vitamin A.

Bioavailability : the fraction of ingested vitamins utilized for normal physiological functions and storage.

Blepharitis : an inflammation of the eyelid margins.

Differentiation : the growth of cells into a specific type of cell.

Isoprene : a branched chain composed of unsaturated hydrocarbon of five carbon atoms.

Myalgias : pain in the muscles.

Osteocalcin : a protein responsible for the deposition of calcium salts in the bone.

Rhodopsin : a pigment formed by the combination of a specific form of vitamin A with a protein.

Seco-steroids : the steroids in which one of the rings have been broken.

Sprue : a chronic disorder that occurs in children and adults in which nutrients are not absorbed. Symptoms include foul-smelling diarrhoea and emaciation.

Vitamins : organic compounds (other than carbohydrates, fats and protein) which are needed only in small amounts by the body.

7.10 CHECK YOUR PROGRESS

1) What are retinoids? How do ß-carotene differ from retinoids.

2) Discuss the role of vitamin A in visual perception.

3) List any five factors that affect bioavailability of carotenoids

4) What level of intake elicits acute vitamin A toxicity'? What are the signs and symptoms of acute hypervitaminosis A?

5) Explain the synthesis of vitamin D_3 from its provitamin.

6) Explain the inter-relationship of vitamin D metabolism with vitamin K.

UNIT

8

WATER - SOLUBLE VITAMINS : B COMPLEX VITAMIN & VITAMIN C

STRUCTURE

8.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

describe the structure and functions of water soluble vitamins,

identify the food sources, bioavailability, consequences of deficiency and toxicity,

recognize the recomnlended amount needed during various physiological stages, and

appreciate their importance in relation to other nutrients.

8.2 INTRODUCTION

Vitamins are essential nutrients found in foods. The requirements are small but they perform specific and vital functions essential for maintaining health. In the

previous unit, we learnt about fat-soluble vitamins. Here in this unit, we shall focus our understanding on the another class of vitamins water-soluble vitamins i.e. vitamin B- complex and vitamin C.

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You would recall that the major group of water soluble vitamins is the B-cotnplex group of vitamins. Examples include thiamin, riboflavin, niacin, pyridoxin, folic acid, cyanocobalamin etc. Vitamin C or ascorbic acid though categorized under water soluble vitamins, is different from the B-complex group due to its different nature and mode of action in the body.

So let us begin our discussion on the similar lines as we had done for fat-soluble vitamins.

8.3 WATER-SOLUBLE VITAMINS: AN OVERVIEW

Vitamins, we already know, are classified by the materials in which they will dissolve. Fat-soluble vitamins —vitarnin A, D, E and K—about which we already learnt in the last Unit, dissolve in fat before they are absorbed in the blood stream to carry out their functions. Excesses of these vitamins are stored in the liver. Because they are stored, they arc not needed every day in the diet. By contrast, water-soluble vitamins dissolve in water and are not stored. They are eliminated in urine. We need a continuous supply of them in our diets. The water-soluble vitamins are the B-complex group and vitamin C.

Vitamin B-complex, as the name suggests, comprises of a group of vitamins which essentially are same in many respects, However, in this unit, we shall focus on six of these— thiamin, riboflavin, niacin, pyridoxin; folic acid and cynacobalamin— which along with other B-complex vitamins are considered to be essential from nutrition point of view.

All water-soluble vitamins have cyclic sing structures with side chains and are alcohols, amines or acids. All of them are enzymes, coenzymes or apoenzymes and have key roles in several metabolic reactions. Vitamin C or ascorbic acid, on the other hand, is a compound that is structurally similar to carbohydrate and plays important physiological roles.

Being water-soluble, the B-complex and C vitamins are readily absorbed from the different regions of the small intestine. Water-soluble vitamins are easily destroyed or washed out during food storage or preparation. Proper storage and preparation of food can minimize vitamin loss.

Clinical manifestations of deficiency of some B vitamins— such as beriberi (cardiac and dry), peripheral neuropathies, pellagra, and oral and genital lesions (related 10 riboflavin deficiency) —were once major public health problems in some parts of the world. These inanifestations have now declined, the decline being

brought about through changes in the patterns of food availability and consequent changes in dietary practices. Although many clinical manifestations of B-vitamin deficiencies have decreased, there is evidence of widespread subclinical deficiency of these vitamins (especially of riboflavin and pyridoxin). These subclinical deficiencies, although less dramatic in their manifestations, exert deleterious metabolic effects.

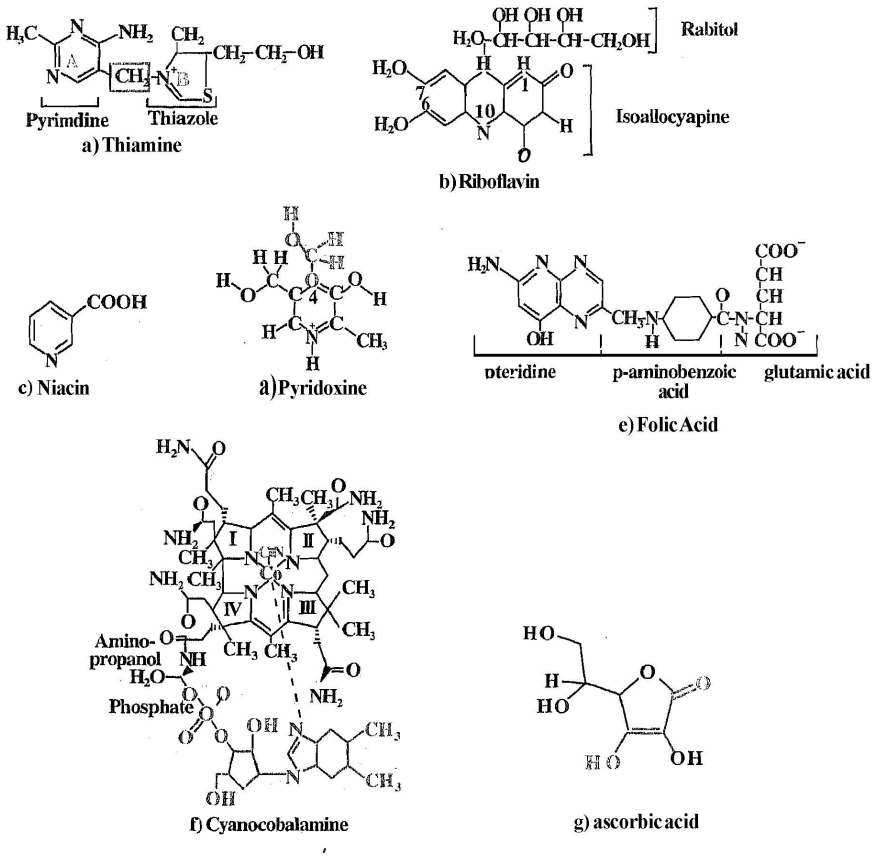


Figure 8.1: Structure of water soluble vitamins

In our discussion in this unit, we shall focus on the food sources, the mechanism of absorption, storage and elimination, innportant physiological roles, deficiency diseases and the concept of bioavailability for each of these vitamins.

Let's begin with thiamin, one of the essential B-complex vitamins.

8.4 THIAMIN (VITAMIN BL OR ANEURIN)

Thiamin is one of the earliest recognized vitamins. The chemical structure of thiamin (Figure 8.1) was established by Williams in 1936. The thiamin molecule consists of two linked organic ring structures: a pyrimidine ring bearing an amino group and a sulphur — containing thiazole ring linked to the pyrimidine by a

methylene bridge (as shown in red in Figure 8.1(a) under the thiamin structure). The thiazole ring bears a primary alcohol side chain that becomes phosphorylated to give the thiamin phosphate esters that have cofactor activity. include thiamin monophosphate (TMP), thiamin pyrophosphate (TPP) and thiamin triphosphate (T TP). TTP is the most abundant form and constitutes almost 80% of total thiamin.

Let next study about the food sources of thiamin.

Food Sources

Thiamin is present in many food products and depending on the amount of vitamin present, we have categorized the foods as rich, good or fair sources as enulnerated herewith:

Rich sources: Rice polishings, wheat germ, dried yeast, yeast extract.

Good sources: Whole cereals, whole wheat, millets, raw and hand-pounded or parboiled rice, pulses, soyabean, dried beans, oilseeds and nuts.

Fair sources: Meat, fish, eggs, milk, vegetables and fruits

Figure 8.2 highlights some of these sources of thiamin. Look up Table 8.2 as well given at the end of the unit which summarizes the rich sources of all water-soluble vitamins.

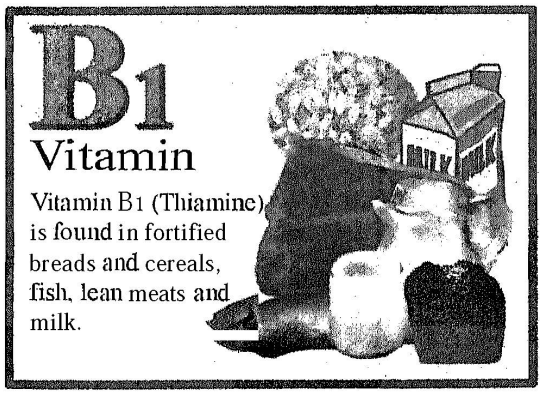


Figure 8.2: Food sources of thiamin

Next, let us leam about the metabolic fate of thiamin.

Absorption, Storage and Elimination

After a meal, thiamin is found in the intestine in the free form. Its absorption involves two mechanisms— both active and passive. At lower intraluminal concentrations (of <1-2 gmol/L), thiamin is absorbed by an active sodium-dependent carrier-mediated system. This mechanism involves phosphorylation. At a higher concentration, passive diffusion occurs. Thiamin is absorbed primarily from the upper jejunum by diffusion and by an active transport mechanism but can also occur in the duodenum and ileum.

After absorption, only a small part passes into circulation as free thiamin while a greater part is converted into thiamin pyrophosphate (TBP) in the liver and

intestinal mucosa with the help of the enzyme thiamin kinase and ATP. A small quantity of thiamin is also converled into thiamin triphosphate (TTP). Thiamin is transported in blood by facilitated diffusion — in erythrocytes in both free and phosphorylated forms and in plasma as free thiamin and TMP. Thiamin or its phosphorylated derivatives are present in negligible amounts in various tissues. Thiamin is excreted in urine.

What is the role of thiamin in our body. Surely, you must be aware of the significant role of thiamin. Read the next sub-section and refresh your knowledge.

Functions Thiamin

Thiamin has a key metabolic role in the cellular production of energy, mainly in glucose metabolism i.e. it helps the body cells convert carbohydrates into energy.

Thiamin is also essential for the functioning of the heart, muscles, and nervous system. All these functions of thiamin are elaborated in this section. This will help you understand the functions of thiamin as an coenzyme better.

So get started. We begin with the regulatory function of thiamin.

1) **Regulator of enzyme activity:** Thiamin regulates the enzymes involved in carbohydrate metabolism. These are:

   a) Pyruvate dehydrogenase, which provides a key link between glycolytic pathway and citric acid cycle.

   b) α-ketoglutarate dehydrogenase in citric acid cycle and transketolase involved in pentose phosphate pathway.

   c) Each enzyme contains a decarboxylase moiety that binds TPP at the active site, a lipoic acid binding moiety, a flavoprotein and one or more regulatory components that toggle the enzylne complex between the active form and the inactive form.

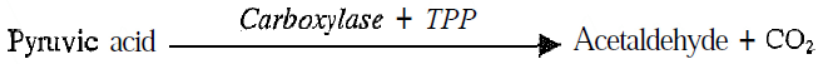
   d) A fourth thiamin requiring enzyme is a branched-chain ketoacid dehydrogenase, which plays a role in the metabolism of branched-chain amino acids.

2) **Coenzyme in enzyme catalyzed reactions:** Thiamin functions as the coenzyine thiamin pyrophosphate (TPP) in the metabolism of carbohydrates and branched- chain amino acids. Specifically the Mg^{2+} coordinated TPP participates in the formation of a-ketols (e.g. among hexose and pentose phosphates as described in the reaction given at point iv below) as catalyzed,by transketolase and in the oxidation of α-keto acids (e.g. pyruvate, α-ketoglutarate, and branched chain α-keto acids) by dehydrogenese complexes. Hence, when there is insufficient thiamin, the overall decrease in carbohydrate metabolism

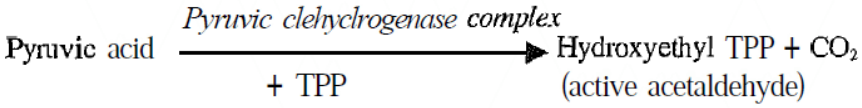
NOTES

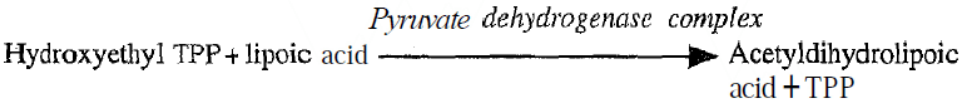
and its interconnection with amino acid metabolism (via α-keto acids) has severe consequences, such as a decrease in the formation of acetylcholine for neural ftmction.

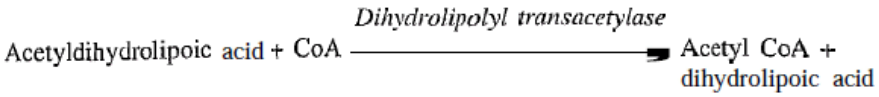
i) *Decarboxylation of pyruvic acid:*



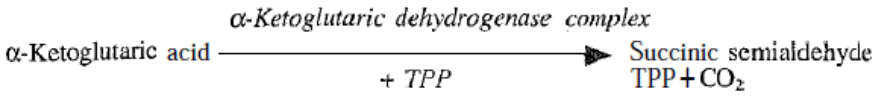
ii) *Oxidative Decarboxylation of Pyruvic acid:*

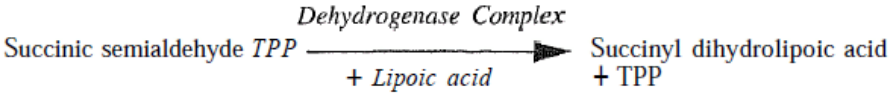


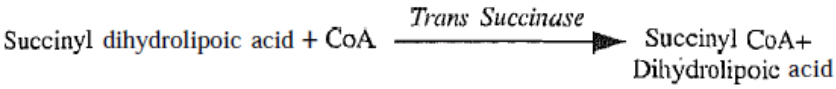




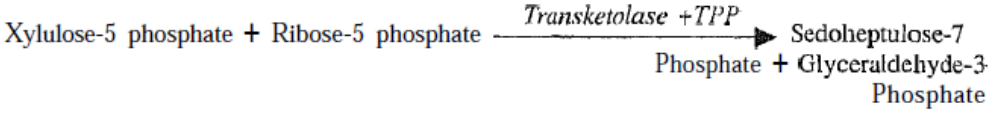
iii) *Oxidative Decarboxylation of a-Ketoglutaric acid:*

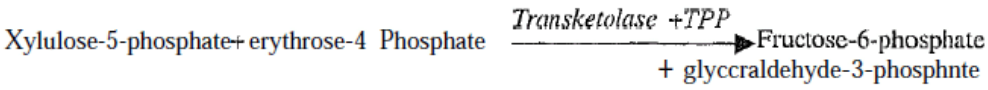






iv) *α-Ketol Fornzation in HMP shunt pathway:*





3) **T PP and TTP are vital for the nerves and cardiac tissues:** TPP and TEP are interconvertible and arc involved in carbohydrate metabolism. As discussed above, when there is insufficient thiamin, the overall decrease in carbohydrate metabolism and its interconnection with amino acid metabolism (via α-keto acids) has severe consequences, such as a decrease in the formation of acetylcholine for neural function. Thus, deficiency in the tissues affects energy Inetabolism in nervous tissue and cardinc muscle.

4) **Role in the conversion of carbohydrate to fats:** Thiamin helps in the initial steps of fatty acid and sterol production. In this way, thiamin also

helps convert carbohydrate to fat for storage of potential energy.

Having looked at the functions, next let: us consider the bioavailability aspect for thiamin.

Bioavailability of Thiamin

Thiamin is readily available from the gut from food sources (as thiamin phosphate esters). Drugs and alcohol abuse may interfere with thiamin absorption and impair thiamin availability. Compared with most other vitamins, thiamin deficiency is seen more rapidly when low intake is encountered. Since thiamin is lost in cooking and is depleted by use of coffee, tannin from black teas, nicotine and alcohol, it is necessary to insure that intake of thiamin is optimal.

What would be the consequences of decreased intake of thiamin? The next sub-section focuses on this aspect,

Deficiency of Thiamin

Thiamin deficiency causes the disease beriberi in human beings, which has been classically considered to exist in dry (paralytic) and wet (oedematous) forms. The early clinical features are anorexia and dyspepsia, associated with heaviness and weakness of the legs. There is tenderness of the calf muscles on pressure with coinplaints of 'pins and needles' pain and numbness in the legs. The knee jerks are usually sluggish but occasionally slightly exaggerated. The subjects feel weak and get easily exhausted while working. If not treated, the subjects may develop polyneuritic beriberi, that is, inflammation of many or all of the peripheral nerves, A detail discussion on the different forms of beriberi follows:

1) **Wet beriberi:** Oedema is the important feature of wet beriberi. It may develop rapidly and involve not only the legs but also the face, trunk and serous cavities. Palpitation and breathlessness are present. The calf muscles are frequently tense, slightly swollen and tender on pressure. The veins of the neck are distended and show visible pulsations. The diastolic blood pressure is low and systolic is high. The pulse is fast and bouncing. The heart becomes weak and death occurs due to heart failure.

2) **Beriberi:** Early symptoms are similar to those found in wet beriberi. The muscles become progressively wasted and weak and walking becomes difficult. The emaciated subject needs the help of sticks to stand and walk and finally becomes bed-ridden. If not treated, the patients will die.

   Beliberi occurs in human-milk-fed infants whose nursing mothers are deficient. Let us get to know about the infantile beriberi

3) **Infantile beriberi:** Infantile beriberi is commonly seen in many South-East Asian countries where the diets consist mostly of "polished rice" and are deficient in thiamin. The occurrence of beriberi is due to:

   a) inadequate thiamin intake, related mainly to poor thiamin content of breast milk, and

b) consumption of over-milled rice, deficient in thiamin by the mother. The disease in infants is generally acute in onset while the chronic forms of the disease are seen in late infancy and childhood. Two types of infantile beriberi are known. These are: (i) cardiovascular type, and (ii) neuritic type.

i) The cardiovascular type (wet): It manifests itself in babies between the ages of 2 and 4 months. The onset is acute with classical signs and symptoms of congestive cardiac failure, tachycardia, dyspnoea, enlargement of the heart, elevated venous pressure, enlarged tender liver, oedema and oliguria. In some infants, cyanosis and pulmonary oedema may develop rapidly and death may ensue in a matter of few hours.

ii) The neuritic type (dry): It is also referred to as Wernicke-Korsakoff syndrome or cerebral beriberi. It shows typical manifestations of peripheral neuropathy, tenderness of calf muscles, diminished tendon jerks. The accent is predominantly on the central nervous system (CNS) with sensorial alteration (irritability, apathy, drowsiness and coma) signs of raised intracranial tension, staring expression and varying degrees of neurologic deficit.

Besides occurring in infants, beriberi also occurs in adults with high carbohydrate intakes (mainly from milled rice) and with intakes of anti-thiamin factors, such as the bacterial thiaminases that are in certain ingested raw fish. Beriberi is still endemic in Asia. In relatively industrialized nations, the neurologic manifestations of Wernicke- Korsakoff syndmme are frequently associated with chronic alcoholism in conjunction with limited food consumption. Some cases of thiamin deficiency have been observeci with patients who are hypermetabolic, are on parenteral nutrition, are undergoing chronic renal dialysis, or have undergone a gastrectomy. Thiamin deficiency has also been observed in people with chronic alcoholism.

We have studied the deficiency symptoms of thiamin so far. What about toxicity related to excess ingestion of thiamin? Let us find out

Toxicity Thiamin toxicity is not a problem because renal clearance of the vitamin is rapid. Since the body stores of thiamin are very low, we must ensure adequate daily intake. What are the requirements for thiamin then? Let us get to know this next.

Recommended Dietary Allowance (RDA)

Thiamin, as it must be clear by now, is needed mainly for the metabolism of carbohydrate, branch-chained amino acids, fat and alcohol. Because the requirements increase as energy expenditure increases, thialnin requirements are expressed as ratios to food energy. Look at Table 8.1, which presents the ICMR and the FAO/ WHO 2004 recommendations for thiamin requirement for different age and physiological groups.

Table 8.1: ICMR and FAO/WHO recommended dietary intakes for thiamin by groups

Recommended Thiamin Intake					
Group		**ICMR (mg/day)**	**Group**		**FAO/WHO 2004 RNI (mg/day)**
Man	Sedentary work	1.2	*Adults* (19+ years)		
	Moderate work	1.4	Males		**1.2**
	Heavy work	16			
Women	Sedentary work	0.9	*Adults* (19+ years)		
	Moderate work	1.1	Females		**1.1**
	Heavy work	1.2			
Pregnancy		+0.2	Pregnancy		I.4
Lactatinn			Lactalion		1.5
	0 - 6 months	+0.3			
	7 - 12 months	+0.2			
Infants	0 - 6 months	55 mcg /kg	*Infants*	0 - 6 months	0.2
	6 - 12 months	50 mcg /kg		7 - 12 months	0.3
Children	1 - 3 years	0.6	*Children*	1 - 3 years	0.5
	4 - 6 years	0.9		4 - 6 years	0.6
	7 - 9 years	1.0		7 - 9 years	0.9
Adolescent			*Adolescents*		1.0
	Boys 10 - 12 years	1.1	Males	(10 - 18 years)	1.2
	Girls 10 - 12 years	1.0	Females	(10 - 18 years)	1.1
	Boys 13 - 15 years	1.2			
	Girls 13 - 15 years	10			
	Boys 16 - 18 years	**1.3**			
	Girls 16 - 18 years	1.0			

Because thiamin facilitates energy utilization, its requirements have traditionally been expressed on the basis of energy intake, which can vary depending on activity levels. Therefore, the RDA as recoinmended by ICMR for adults is 0.5 mg/1000 Kcal, however, an intake of no less than 1 mg/day is advised. The individual intake for thiamin, hence for an adult man is 1.2 mg/day and adult woman is 0.9 mg/day as indicated in Table 8.1. You may have noticed that the requirements increase in case of pregnancy and lactation owing to increased energy demands.

Criteria for Assessment of Thiamin Status

Thiamin status has been assessed by ineasuring urinary thiamin excretion under basal conditions or after thiamin loading, transketolase activity, and free and phosphorylated fonns in blood or serum. Let us understand these assessment criterias.

1) **Determination of Erythrocyte Transketolase (ETK) Activity:** The enzyme transketolase requires T PP for its activity, for the metabolism of

pentose phosphate sugars as described under the functions earlier. ETK activity is expressed as basal (without TPP) activity (ETKA) or as the difference between stimulated and basal activity us a percentage of basal activity. In thiamin deficiency, the enzyme activity is reduced (decreased ETKA) and a small part of the added pentose phosphate disappears. When TPP is added, ETK activity is increased. The percent increase in ETK activity due to added TPP, as indicated in the Table 8.2, is an index of the degree of thiamin deficiency.

Table 8.2: Determination of erythrocyte translietolase activity

Thiamin Status	Increased due to Added TPP (%)
Normal	0 - 15
Marginal deficiency	15 - 25
Moderate deficiency	> 25

2) **Urinary Excretion Test:** The urinary excretion of thiamin is an index of recent dietary intake of the vitamin. Hence, determination of thiamin in urine samples, 4 hours after the administration of a 5 mg dose of the vitamin, for a period of 24 hours, is a reliable index of thiamin status. An excretion value <20 nzcg is indicative of thiamin deficiency.

3) **Estimation of blood thiamin levels:** The levels of free thiamin and its phosphoesters in whole blood and erythrocytes is measured using high-performance liquid chromatography methods. This measure gives a good indication of thiamin status.

We end our study of thiamin now. The interaction of thiamin with other nutrients is another aspect we would like to review in this unit. The interaction of all the water-soluble vitamins me taken up in general.

So now we move on to the next water soluble vitamin i.e. riboflavin

8.5 RIBOFLAVIN

Riboflavin (vitamin B_2, a water-soluble vitamin, was discovered in milk as a pigment possessing a yellow green flourescence as early as in 1879. However, its role in our body was identified much later. The name 'riboflavin' was given to this vitamin in view of the similarity of a part of its structure to that of the sugar ribose and because of its relation to the general group of flavins.

Riboflavin and its coenzyme derivatives are isoalloxazines i.e. they contain a pteridine ring with a benzene ring fused on to it. The side chain is a C5 polyhydroxy group, a derivative of ribitol, a pentaliydroxy compound, as illustrated in Figure 8. 1(b). You would recall studying that riboflavin has two major coenzyme derivatives, namely flavin mononzicleotide (FMN) and flavin adenine

dinucleotide (FAD) which is formed by the combination of FMN with one molecule of adenosine triphosphate (ATP). Let us begin study of riboflavin by recapitulaing our knowledge about food sources of riboflavin

Food Sources

The food sources of riboflavin include:

Rich sources: Liver, dried yeast, egg powder, milk powder.

Good sources: Whole cereals, millets, pulses, green leafy vegetables, oilseeds and nuts, meat, fish, eggs and milk.

Fair sources: Milled cereals and cereal products, roots and tubers, other vegetables and fruits.

Figure 8.3 illustrates some important sources of riboflavin. Look up the Table given at the end of the unit which summarizes the rich, good and fair sources of all water soluble vitamins.

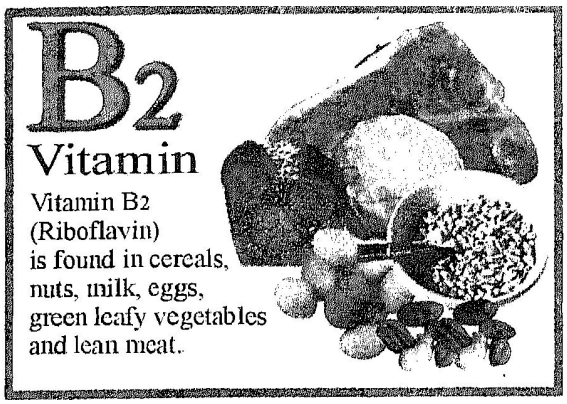


Figure 8.3: Foods rich in Riboflavin

Absorption, Storage and Elimination

Riboflavin is absorbed from the small intestine through tlie portal vein and is passed to all tissues via general circulation. Absorption occurs in the upper part of the gastrointestinal tract by specialized transport involving a phosphorylation-dephosphorylalion mechanism more than by diffusion. This process is sodium-dependent and involves an ATPase active transport system. Delaying intestinal transit time may result in an increase in the total amount of riboflavin absorbed from the intestine. Intestinal uptake is increased in cellular riboflavin deficiency and decreased with a high riboflavin status. Riboflavin is also synthesized by intestinal bacteria and then absorbed by the colon.

This riboflavin produced by bacterial synthesis also contributes to overall riboflavin nutrition. Transport of riboflavin involves loose binding to albumin and tight binding to a number of globulins —several classes of immunoglobulins (IgA, IgG and IgM). Riboflavin is not stored in the body. A major part is excreted in urine and the rest is broken down in the tissues.

Next, let us learn what is the role of riboflavin in our body.

NOTES

Functions

The role of riboflavin in human metabolic processes and in maintaining good health is highlighted herewith.

1) **Precursor of co-enzymes:** The major function of riboflavin is to serve as the precursor of the coenzymes FMN and FAD and of the covalently bound flavins. These coenzymes are widely distributed in metabolism. The role of FMN and FAD as part of enzymes or as coenzymes are shown in

Table 8.3: Role of FMN and FAD

Enzyme	Coenzyme	Reaction
NADH dehydrogenase	FMN	NADH → NAD
Succinate dehydrogennse	FAD, Fe	Succinate → Fumarate
L-Glycero-P-dehydrogenasc	FAD	Glycero-P 3 Dihydroxyacetone-P
Choline dehydrogeiiase	FAD	Choline → Betaine aldehyde
Acyl-CoA-dehydrogenase	FAD (ETK)	Acyl-CoA → Dehydroacyl-CoA
Sarcosine dehydrogenase	Fe, Flavin (ETK)	Sarcosine → Glycine + HCHO
Dimethylglycine dehydrogenase	Flavin (ETK)	Dimethylglycine → Sarcosine
	Fe	+ HCHO
Aerobic dehydrogenases		
L-amino acid oxidase	FMN	Amino acid 3 Keto acid + NH_3 + H_2O_2
D-amino acid oxidase	FAD	Amino acid → Keto acid + NH_3 + H_2O_2
Xanthine oxidase	FAD	Xanthine → Hypoxanthine + H_2O_2
		Hypoxanthine → Uric acid + H_2O_2

2) **Role in respiratory chain:** Riboflavin catalyzes numerous oxidation—reduction reactions. Conversion of riboflavin to flavin mononucleotide (FMN) and then to the predominant flavin, flavin adenine dinucleotide (FAD), occurs before these flavins form complexes with numerous flavoprotein dehydrogenases and oxidases. The flavocoenzymes (FMN and FAD) participate in oxidation—reductionreactions in metabolic pathways and in energy production via the respiratory chain.

3) **Drug and lipid metabolism:** Flavoproteins catalyze dehydrogenation reactions, as well as, hydroxylations, oxidative decarobxylations, deoxygenations and reduction of oxygen to hydrogen peroxide.

4) **Antioxidant activity:** Flavoproteins also have powerful antioxidant activity from their role as precursors to FMN and FAD. Among the FAD-requiring enzymes glutathione reductase, is involved in the glutathione redox cycle and provides a major protective role against lipid peroxides.

5) **Protective role:** Riboflavin protects the octodermal tissues and prevents lesions of the skin, eye and nervous system. Riboflavin ameliorates cardiac damage and also has antimalarial effects.

6) **Regulatory functions:** Riboflavin is concerned with the regulatory functions of some hormones involved in carbohydrate metabolism.

7) **Other fimctions:** Riboflavin interrelates with other B vitamins, notably niacin, which requires FAD for its formation from tryptophan, and vitamin B_6 which requires FMN for conversion of the phosphates of pyridoxine and pyridoxamine to the coenzyme pyridoxal 5'-phosphate (PLP). Riboflavin deficiency slows down the uptake of pyridoxine and decreases the conversion of pyridoxine to its metabolites.

Before we move on to the study about the deficiency and toxicity of riboflavin, let us get to know about the bioavailability of riboflavin from the diet.

Rioavailability

Riboflavin availability is sodium-dependent. Prolonged contact of dietary riboflavin with the absorptive surface of the intestinal mucosal cells increases the bioavailability of liboflavin. Intestinal uptake is increased in cellular iiboflavin deficiency and decreased with a high riboflavin status. Diets high in psyllium gum decrease absorption whereas antacids, as well as, the mere presence of food increase absorption.

Metals such as copper, zinc and iron; drugs, caffeine and saccharin and vitamins such as nicotinamide and ascorbic acid, tryptophan and urea form chelates and complexes with iiboflavin and FMN and thus affect bioavailability.

Pregnancy induces the formation of proteins which bind flavins. Bioavailability of riboflavin in foods, mostly as digestible flavocoenzymes, is excellent at nearly 95%, but absorption of the free vitamin is limited to about 27 mg per single meal or dose in an adult.

Deficiency

Riboflavin deficiency results in the condition of hypo- or aribojlavinosis, with sore throat, hyperaemia (condition in which the blood collects in a part of the body), oederna of the pharyngeal and oral mucous membranes, cheilosis (cracking of the corner of the mouth), angular stomatitis (inflammation at the corner of the mouth), glossitis (inflammation or the infection of the tongue), seborrheic deFmatitis and normochromic, normocytic anaemia associated with pure red cell cytoplasia of the bone marrow. As riboflavin deficiency almost invariably occurs in combination with a deficiency of other B-complex vitamins, some of the symptoms (e.g. glossitis and dermatitis) may result from other complicating deficiencies.

The major cause of hyporiboflavinosis is inadequate dietary intake as a result of limited food supply, which is sometimes exacerbated by poor food storage or processing. Children in developing countries like ours will commonly demonstrate clinical signs of riboflavin deficiency during periods of the year when gastrointestinal infections are prevalent. Decreased assimilation of riboflavin also results from abnormal digestion, such as that which occurs with lactose intolerance. This condition is highest in African and Asian populations and can lead to a decreased intake of milk, as well as, an abnormal absorption of the vitamin.

Absorption of riboflavin is also affected in some other conditions, for example, tropical sprue, celiac disease, malignancy and resection of the small bowel and decreased gastrointestinal passage time. In relatively rare cases, the cause of deficiency is inborn errors, in which the genetic defect is in the formation of a flavoprotein (e.g. acyl-coenzyme A [CoA] dehydrogenases). Also, at-risk are infants receiving phototherapy for neonatal jaundice and perhaps those with inadequate thyroid hormone. Some cases of riboflavin deficiency have' been observed in south-east Asian school children infected with hookworm. Next, let us get to know of toxicity of riboflavin.

Toxicity

Riboflavin toxicity is not a problem because of the limited intestinal absorption of this vitamin. So then what are the requirements for riboflavin to maintain optimum health? Read the next sub-section and find out.

Recommended Dietary Allowance (RDA)

Several nutritional and physiological factors govern riboflavin requirements. Negative nitrogen balance reduces riboflavin requirements and excretion. Physical activity reduces urinary riboflavin excretion. Hence, the dietary requirement is increased by exercise and increased physical activity.

Table 8.4: ICMR and FAO/WHO recommended dietary intakesfor riboflavin by groups

Recommended Riboflavin Intake (mg/day)			
Group	**ICMR**	**Group**	**FAO/WHO 2004 RNI**
Man Sedentary work	1.4	*Adults* (19+ years)	
Moderate work	1.6	Males	1.3
Heavy work	1.9		
Woman Sedentary work	1.1	*Adults* (19+ years)	
Moderate work	1.3	Females	1.1
Heavy work	1.5		
Pregnancy	+0.2	Pregnancy	1.4
Luctution		Lactation	1.6
0 - 6 months	+0.3		
7 - 12 months	+0.2		
Infants 0 - 6 months	60 mcg/kg	*Infants* 0 - 6 months	0.3
6 - 12 months	65 mcg/kg	7 - 12 months	0.4
Children 1 - 3 years	0.7	*Children* 1 - 3 years	0.5
4 - 6 years	1.0	4 - 6 years	0.6
7 - 9 years	1.2	7 - 9 years	0.9
Adolescent		*Adolescents*	
Boys 10 - 12 years	1.2	Males (10 - 18 years)	1.3
Girls 10 - 12 years	1.3	Females (10 - 18 years)	1.0
Boys 13 - 15 years	1.5	Boys 16 - 18 years	1.6
Girls 13 - 15 years	1.2	Girls 16 - 18 years	1.2

Therefore, the RDA for individual intake follows the similar pattem as for thiamin. RDI for riboflavin for adults are 0.6 mg / 1000 Kcal, i.e. for adult males, the requirements are 1.4 mg/day while for adult females, it is 1.1 mg/day and increase

up to 1.3-1.4 mg/day during pregnancy and lactation. Compare these Indian requirement with the FAO/WHO 2004 recommendations presented in Table 8.4. How do the requirements compare?

Next, we shall review the criteria used for assessing the riboflavin status.

Criteria for Assessment of Riboflavin Status

Riboflavin status can be assessed by measuring urinary excretion of the vitamin in fasting, random, and 24-hour specimens or by load return tests (amounts measured after a specific amount of riboflavinis given orally); measuring erythrocyte glutathione reductase activity coefficient or erythrocyte flavin concentration

Let us get to know about these methods.

1) **Urinary excretion test:** Urinary excretion of riboflavin is determined at different levels of intake. Under conditions of adequate riboflavin intake (approximately 1.3 mg/day for adults), an estimated 120 mg (320 nmol) total riboflavin or 80 mg of creatinine is excreted daily. The levels indicative of deficiency are given in Table 8.5.

Table 8.5: Urinary excretion of riboflavin levels indicative of deficienc

Condition .	**Urinary** Excretion Levels **mcg/day**
Normal	120-150
Deficiency	50
Sub clinical deficiency	30 - 120

2) **Riboflavin content of RBC:** The erythrocyte glutathione reductase assay, with an activity coe cient (AC) expressing the ratio of activities in the presence and absence of added FAD, continues to be used as a main functional indicator of riboflavin status, but some limitations in the technique have been noted. Addition of FAD to an erythrocyte haemolysate records greater increase in deficient than in repleted subjects.

Interaction with other Nutrients

Riboflavin, as already discussed under the functions, interrelates with other B_6 vitamins, notably niacin, which requires FAD for its formation from tryptophan, and vitamin B_6, which requires for conversion of the phosphates of pyridoxine and pyridoxamine to the coenzyme pyridoxal 5-phosphate (PLP). Riboflavin deficiency slows down uptake of pyridoiine and decreased the conversion of pyridoxine to its metabolites. A lower fat-carbohydrate ratio may decrease the riboflavin requirements of the elderly.

With a discussion on riboflavin, we would like to take a break here and recapitulate what we have learnt so far.

NOTES

8.6 NIACIN

Niacin is chemically synonymous with nicotinic acid although the term is also used for its amide (nicotinamide). Nicotinamide is required for the synthesis of the active forms of niacin i.e. nicotinamide adenine dinucleotide (NAD) and its phosphate nicotinamide adenine dinucleotide phosphate (NADP), which functions as a cofactor for various coenzymes in our body. Nicotinic acid was first isolated from rice polishings and shown to be a component of coenzyme I and II and several transporting enzymes in the tissues. The structure of niacin is given in Figure 8.1 (c). Look up the structure now and then move on to study about the food sources and metabolism of niacin in our body.

Food Sources

Niacin is widely distributed in plant and animal foods mainly as the pyridine nucleotides NAD and NADP. The food sources of niacin are highlighted herewith:

Rich sources: Dried yeast, rice polishings, peanuts, liver.

Good sources: Whole cereals legumes, meat and fish.

Fair sources: Milled cereals, maize, roots and tubers, other vegetables, milk and eggs.

As you may have seen that whole cereals are good sources of niacin, but the removal of the bran in the milling of wheat reduces the niacin content of white wheat flou to a low level. Niacin is readily soluble in water, but it is resistant to heat, oxidation and alkalies. It is, in fact, one of the most stable vitamins.

Figure 8.4 illustrates some important sources of niacin.

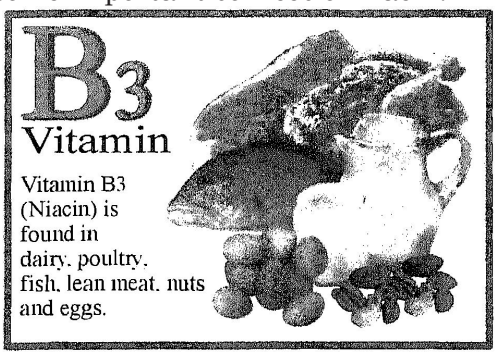


Figure 8.4: Foods rich in niacin

Absorption, Storage and Elimination

Nicotinic acid and nicotinamide are rapidly absorbed from the intestine rather than the stomach. At low concentrations, absorption in the small intestine occurs as Na^+ dependent facilitated diffusion but at higher concentrations, passive diffusion predominates. Nicotinamide is the major form in the blood stream and arises from the enzymatic hydrolysis of NAD in the intestinal mucosa and liver. NAD and NADP, the main dietary forms of niacin are hydrolyzed by enzymes in

the intestinal mucosa to release nicotinamide. The intestinal mucosa is rich in niacin conversion enzymes such as glycohydrolase.

Nicotinamide is released from NAD in the liver and intestines by glycohydrolases and transported into tissues as needed. Tissues take up both forms by simple difussion and erythocytes by facilitated transport. Niacin is methylated in the liver to N 1-methyl nicotinamide (NMN) which is exc eted in the urine along with the oxidation products of NMN. The pattern of niacin products excreted depends on the amount and the form of niacin ingested and the niacin status of the individual. Excess niacin is excreted in the urine primarily as N 1-methylnicotinamide and N 1-methyl- 2-pyridone-5-cuboxanlide.

Having studied the metabolic fate of niacin, next let us get to know about tlze role of niacin in our body.

Functions

The functions of nicotinic acid are as follows:

1) Protective role: Nicotinic acid is vital to the normal functioning of the skin, intestinal tract and nervous system. It protects the tissues from pellagraic lesions.

2) Coenzyme activity: Nicotinamide exists within the redox-active coenzymes, nicotinamide adenine dinucleotide (NAD) and its phosphate (NADP), which åtnction in dehydrogenase—reductase systems requiring transfer of a hydride ion. NAD is also required for non-redox adenosine diphosphate—ribose transfer reactions involved in DNA repair and calcium mobilization. NAD funceions in intracellular respiration and with enzymes involved in the oxidation of fuel substrates such as glyceraldehyde-3-phosphate,lactate, alcohol, 3-hydroxybutyrate and pyruvate. NADP functions in reductive biosynthesis such as fatty acid and steroid synthesis and in the oxidation of glucose-6-phosphate to ribose-5-phosphate in the pentose phosphate pathway.

The role of NAD(P) is summarized in Table 8.6.

Table 8.6 : Functions of NAD(P)

Enzymes	Coenzyme	Reaction
Anaerobic *dehydrogenases*		
Alcohol dehydrogenase	NAD, Zn	Alcohols+ Aldehydes
Aldehyde dehydrogenase	NAD	Aldehydes —— Acids
L-Glycerophosphate dehydrogenase	NAD	Glycerophosphate ⟶ Dihydroxyacetone Phosphate
Hydroxybuyrate dehydrogenase	NAD	Hydroxybutyrate ⟶ Acetoacetate
Lacate dehydrogenase	NAD-NADP	Lactate ⟶ Pyruvate
Malate dehydrogenase	NAD (NADP)	Malate ⟶ Oxaloacetate
Glucose dehydrogenase	NAD (NADP)	Glucose —, Gluconate
L-Glutamate dehydrogenase	NAD (NADP) Zn	Glutamate ⟶ α-Ketoglutarate+NH_3

Isocitrate dehydrogenase	NAD, NADP	Isocitrate ⟶ a-Ketoglutarate
Hydroxysteroid dehydrogenase	NAD, NADP	Hydroxy steroid ⟶ Ketosteroid
Glucose,-P-dehydrogenase	NADP	Glucose-6-P ⟶ Gluconate 6-P
Gluconate–6P-dehydrogenase	NADP	Gluconate-6-P ⟶ Ribulose-5-P + CO_2

3) Metal chelating ability: This explains its biological interactions with essential trace metals. It is a part of the proposed glucose tolerance factor, an organochromium complex that may potentiate insulin response in man. Other than functions, another important aspect related to niacin is its bioavailability in our body. This aspect is covered next.

Bioavailability

We have already learnt earlier that niacin is provided in the diet primarily as the pyridine nucleotides-NAD and NADP. In addition to its synthesis from dietary niacin, NAD may also be synthesized in the liver from the dietary amino acid, tryptophan. The synthesis of niacin from tryptophan also depends on enzymes that require vitamin B6 and riboflavin, as well as, an enzyme containing haeme (iron). On an average, I mg of niacin can be synthesized from the ingestion of 60 mg of tryptophan. Hence, the recommended allowance for niacin is expressed as mg NE (niacin equivalents) where I mg NE lmg niacin or 60 mg tryptophan.

There are several dietary drug and disease factors that reduce the conversion of tryptophan to niacin, such as the use of oral contraceptives.

Next, let us learn about the symptoms of niacin deficiency and toxicity.

Deficiency and Toxicity

Niacin (nicotinic acid) deficiency classically results in pellagra (refer to Figure 8.5), which is a chronic wasting disease associated with a characteristic erythematous dermatitis that is bilateral and symmetrical, a dementia after mental changes including insomnia and apathy preceding an overt encephalopathy, and diarrhoea resulting from inflammation of the intestinal mucous surfaces. The disease is, therefore, characterized by 3 D's- dermatitis, diarrhoea and dementia. The effects of the deficiency on various organs and organ systems are discussed below:

1) Digestive System: The predominant symptoms are glossitis and diarrhpea. Glossitis, cheilosis and stomatitis may vary from mild redness, soreness and smoothness of the tongue and mouth to extreme inflammation with fiery red mucosa and tongue, ulceration and secondary infection'ofthe tongue and buccal mucosa, Nausea and vomiting are seen in most cases. Diarrhoea may range from a few to several loose stools a day with blood and mucous. If untreated, death occurs:

2) Skin: Dermatitis is the characteristic feature of the' disease, It is symmetrical

in distribution. In early stages, a bright red erythema resembling sunburn occurs over the exposed parts of the body. The common sites are the face, neck and on the extremities such as the back of the fingers, hands, wrists and elbows, the forearms, dorsum of the feet, knees and ankles and the neck. In the beginning, the skin is red and slightly swollen, as illustrated in Figure 8.5. The lesion may worsen by the formation of vesicles and bullae with cracking of the skin. Secondary infection is always present. With improvement, the skin becomes dry, less red and the surface desquamates. The dermatitis is precipitated with exposure to sunlight.

3) Nervous System: Delirium is the most common mental disturbance in acute pellagra. Dementia is more frequently seen in the chronic cases. Milder mental disturbances consisting of imitability, peripheral neuritis, paralysis, change in disposition, depression, inability to concentrate and poor memory are more common in the mild cases. The symptoms of postero-lateral tract degeneration, ataxia, spasticity and the involvement of the bladder and rectal sphincters are seen in chronic cases.

At present, pellagra occurs endemically in poorer areas of Africa, China and India. Its cause has been mainly attributed to a deficiency of niacin; however, its biochemical interrelationship with riboflavin and vitamin B6, which are needed for the conversion of L-tryptophan to niacin equivalents (NES), suggests that insuffic encies of these vitamins may also contribute to pellagra. Pellagra-like syndromes occuning in the absence of a dietary niacin deficiency are also attributableto disturbances in tryptophan metabolism (e.g. Hartnup disease with impaired absorption of the amino acid and carcinoid syndrome where the major catabolic pathway routes to 5-hydroxytryptophan are blocked). Pellagra also occurs in people with chronic alcoholism. Cases of niacin deficiency have been found in people suffering from Crohn's disease (inflammatory disease of GI tract)

Figure 8.3: Deficiency Symptoms of niacin

Absorption, Storage and Elimination

Riboflavin is absorbed from the small intestine through tlie portal vein and is passed to all tissues via general circulation. Absorption occurs in the upper part of the gastrointestinal tract by specialized transport involving a phosphorylation-dephosphorylalion mechanism more than by diffusion. This process is sodium-dependent and involves an ATPase active transport system. Delaying intestinal transit time may result in an increase in the total amount of riboflavin absorbed from the intestine. Intestinal uptake is increased in cellular riboflavin deficiency and decreased with a high riboflavin status. Riboflavin is also synthesized by intestinal bacteria and then absorbed by the colon. This riboflavin produced by bacterial synthesis also contributes to overall riboflavin nutrition. Transport of riboflavin involves loose binding to albumin and tight binding to a number of globulins —several classes of immunoglobulins (IgA, IgG and IgM). Riboflavin is not stored in the body. A major part is excreted in urine and the rest is broken down in the tissues.

Next, let us learn what is the role of riboflavin in our body.

Functions

The role of riboflavin in human metabolic processes and in maintaining good health is highlighted herewith.

1) **Precursor of co-enzymes:** The major function of riboflavin is to serve as the precursor of the coenzymes FMN and FAD and of the covalently bound flavins. These coenzymes are widely distributed in metabolism. The role of FMN and FAD as part of enzymes or as coenzymes are shown in

Table 8.3: Role of FMN and FAD

Group		ICMR	Group	FAO/WHO 2004 RNI
Man	Sedentary work	16	*Adults.* (19+ years)	
	Moderate work	18	Males	16
	Heavy work	21		
Women	Sedentary work	12	*Adults* (19+ years)	
	Moderate work	14	Females	14.0
	Heavy work	15		
Pregnancy		+2	*Pregnancy*	18
Lactation			*Lactation*	17
	0 - 6 months	+4		
	7 - 12 months	+3		
Infants	0 - 6 months	710 µg/kg	*Infants* 0 - 6 months	2.0[a]
	6 - 12 months	650 µg/kg	7 - 12 months	4.0

Children 1 - *3* years	8	*Children* 1 - *3* years	6.0
4 - 6 years	11	4 - 6 years	8.0
7 - 9 years	13	7 - 9 years	12.0
Adolescent		*Adolescents*	
Boys 10 - 12 years	15	Males (10 - 18 years)	16.0
Girls 10 - 12 years	13	Females (10 - 18 years)	16.0
Boys 13 - 15 years	16	Boys 16 - 18 years	17
Girls 13 - 15 years	14	Girls 16 - 18 years	14

Having learnt about the requirements, next we shall learn about how to assess the niacin status of individuals.

Criteria for Assessment of Niacin Status

Niacin status can be monitored by daily urinary excretion of methylated metabolites, especially the ratio of the 2-pyridone to N'-methyl-nicotinarnide, etythrocyte pyridine nucleotides, oral dose uptake tests, erythrocyte NAD, and plasma 2-pyridone.

Excretion of N-methyl nicotinamide in urine after an oral niacin load of 20 mg nicotinamide/70 kg body weight over 24 hours is measured and levels of <5.8 mrnol/dl represents deficiency and 5.8-17.5 mmol/dl represents low niacin status. Shibata and Matsuo suggest that the ratio of urinary 2-pyridone to N'-methyl-nicotinarnide .is as much a measure of protein adequacy as it is a measure of niacin status. The ratio of the 2- pyridone to N'-methyl-nicotinamide also appears to be associated 1 the clinical symptoms of pellagra, principally the dermatilic condition. In plasma, 2-pyridone levels change in reasonable proportion to niacin intake. As in the case of the erythrocyte pyridine nucleotides (nicotinamide coenzymes), NAD concentration decreased by 70% whereas NADP remained unchanged in adult males fed diets with only 6 or 10 mg NEs/day.

Interaction with other Nutrients

You may recall reading earlier that trypotophan present in dietary proteins is converted to niacin. There is an interdependence of enzymes within the tryptophan-to-niacin pathway where vitamin B6 (as pyridoxal phosphate) and riboflavin (as FAD) are functional. Besides this interaction, do look up the interaction of niacin with other Unguents presented in section 8.10.

Next, we shall review pyridoxine.

8.6 PYRIDOXINE (VITAMIN)

Pyridoxine or vitamin B_6 is one of the B complex vitamins which prevents and cures dermatitis in rats fed on vitamin B6 deficient diets. Vitamin B_6 comprises a triad of closely related heterocycles that in free form are called pyridoxine

(PN), pyridoxal (PL) and pyridoxamine (PM). Here, for your reference, the basic pyridoxine structure is illustrated in Figure 8.1(d). As you would have noticed, pyridoxine contains a pyridine nucleus, ptimary alcoholic groups and one phenolic hydroxyl group. Pyridoxal contains an aldehyde group in place of one primary alcoholic group and pyridoxamine contains a primary amide side chain in place of a primary alcoholic group. The natural base forms of the three vitamin B_6 vitamins vary in the substituent at position 4 of 2-methyl 3 hydroxy -5 -hydroxy methyl—pyridine.

Let us next review the food sources of pyiidoxine.

Food Sources

Raw foods contain more of this vitamin than cooked foods. The food sources include:

Rich sources: Rice polishings, wheat bran, wheat germ, dried yeast, liver.

Good sources: Whole cereals, legumes, nuts and seeds, milk powder, meat, egg, leafy vegetables.

Fair sources: Milled cereals, vegetables and fruits.

Figure 8.6 illustrates some rich sources of pyridoxine.

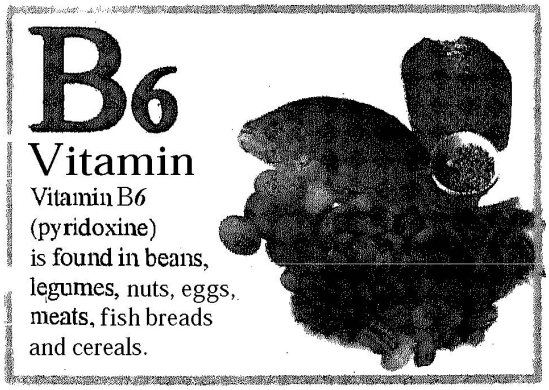


Figure 8.6: Food sources of pyridoxine

Remember, long storage, canning, roasting or stewing of meat, food-processing techniques, use of alcohol are destructive to this vitamin,

Next, let us get to know what happens to this vitamin once it is ingested.

Absorption, Storage and Elimination

Pyridoxine, pyridoxal and pyridoxamine (along with their phosphorylated forms) occur in plant and animal foods. The phospborylated B_6 vitamins are dephosphorylated by membrane bound alkaline phosphatase (found at the intestinal brush border) and absorption occurs primarily in the intestine (jejunum) passive diffusion as illustrated in Figure 8.7.

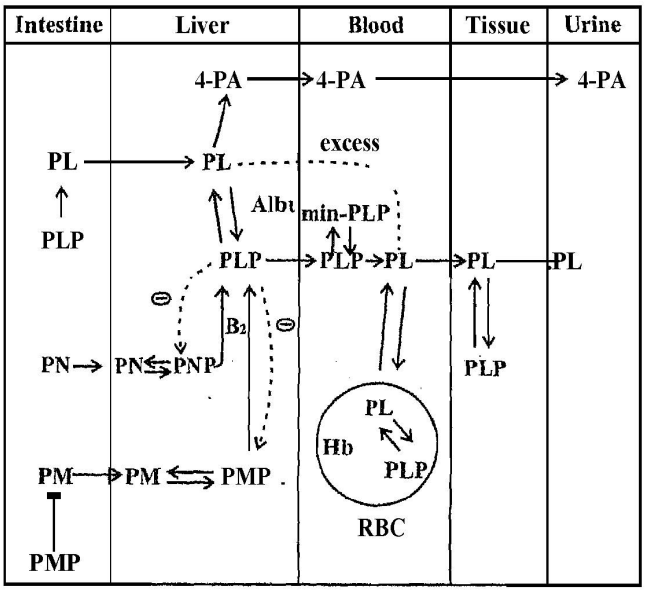


Figure 8.7: Graphical representation of B_6 absorption and transport

After absorption, each form of the vitamin is again phosphorylated (i.e.PLP, PNP, PMP) and retained. This process is called metabolic trapping. Thus, free vitamers enter by passive diffusion, facilitated by metabolic trapping.

The vitamin is transported in blood both in plasma and in red cells, mainly bound to albumin (refer to Figure 8.7) in plasma and haemoglobin in erythrocytes. Eighty percent of vitamin B_6 is present in muscle. Excretion is through the urinary pathway. Once, the pyridoxine is absorbed and utilized by the body, it is used up for the various functions as described next.

Functions

There are three different forms of vitamin B6, namely pyridoxine, pyridoxarnine, and pyridoxal. All three must be phosphorylated and the 5'-phosphates of the first two forms are oxidized to ihe functional pyridoxal phosphate (PLP), which serves as a carbonyl-reactive coenzyme to, a number of enzymes involved in the metabolism of amino acids.
Such enzymes include aminotransferases, decarboxylases, and dehydratases; δ-aminolevulinate synthase in haem biosynthesis, and phosphorylase in glycogen breakdown and sphingoid base biosynthesis.

1) **Formation of amines:** Pyridoxal phosphate (PLP) and pyridoxamine phosphate (PNP) are vital for the fonnation of several amines that are functional in nervous tissues (e.g. epinephrine,nor epinephrine, serotonin

and α-amino butyrate) for the biosynthesis of haem, formation of sphingolipids and phosphorylation of glycogen. A synopsis of the cellular process involving pyridoxine are given in Figure 8.8

NOTES

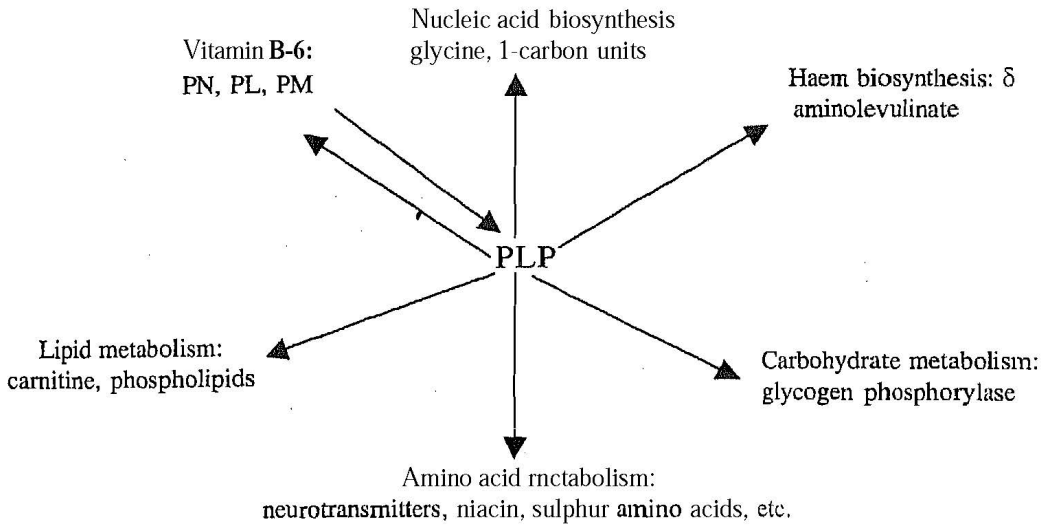


Figure 8.8: Cellular process involving pyridoxine

2) **Growth purposes:** Pyridoxal 5-phosphate (PLP) is essential for growth of infants and prevents degeneration of the nerves.

3) **Coenzyme activity:** Pyridoxal phosphate acts as a coenzyme in the following set of reactions.

   a) Transaminase system: The two imponant transaminase systems are:
   Glutamic acid + Oxaloacetic acid ⟶ α-ketoglutarate + Aspartate
   Alanine + a ketoglutarate ⟶ Glutamic acid + Pyruvic acid

   b) Amino acid decarboxylase system: These enzymes convert the amino acids into the corresponding amines.
   Histidine ⟶ + Histamine + CO_2
   Tyrosine ⟶ + Qramine + CO_2

   c) Conversion of tryptophan to niacin: Tryptophan is converted into niacin, as you may recall studying earlier. Look at Figure 8.9, which illustrates the steps involved in the conversion of tryptophan to niacin.

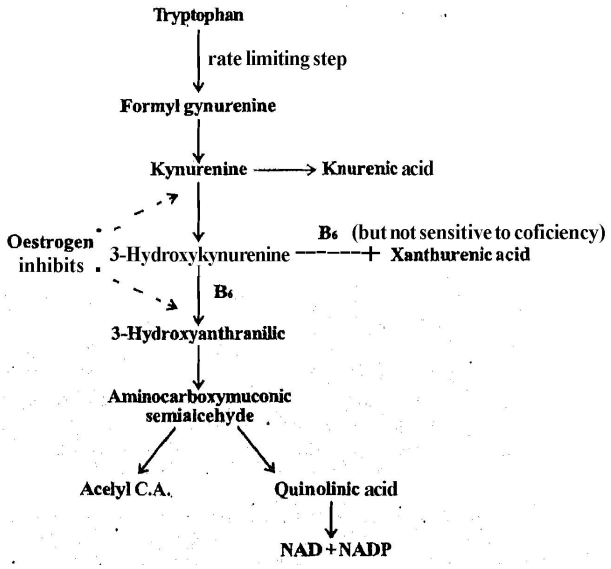


Figure 8.9: Conversion of tryptophan to niacin

Pyridoxine is needed for the conversion of hydroxy kynurenine to hydroxy anthranilic acid. Hence, niacin is not formed in pyridoxine deficiency. Hydroxy kynurenine is converted to xanthurenic acid and excreted in the urine.

d) Muscle phosphorylase: Pyridoxal phosphate is a component of muscle phosphorylase.

e) Dehydrases: These enzymes are vital to the catabolism of threonine, serine and homoserine and contain pyridoxine.

$$\text{Serine} + H_2O \longrightarrow \text{Pyruvic acid} + NH_2C + H_2O$$

f) Racemases: Racernases convert D-amino acids to their L-forms.

$$\text{D-methionine L} \longrightarrow \text{methionine}$$

4) Synthesis of Porphyrin: Pyridoxal phosphate is required for the synthesis of 6-amino levulinic acid, an important intennediate in the synthesis of porphyrin and haem nuclei.

5) Neurohormones: Pyridoxal phosphate is essential for the formation of several neurohormones such as serotonin, a-amino butyric acid and epinephrine.

6) Anti-atherosclerotic effect: Vitamin B6 deficiency precipitales hypercho-lesterolemia and atherosclerosis. However, the exact role of pyridoxine in this process is not clear.

7) Immune bodies: Vitamin B6 deficiency is associated with impairment in both humoral and cell mediated immunity.

8) Coenzyme A synthesis: Pyridoxine is involved in the synthesis of coenzyme A from pantothenic acid. In pyridoxine deficiency, coenzyme A level in the liver is restored.

Having read about the ftmctions, next let us get to know about bioavailability of pyridoxine.

Bioavailability

A recent review by Gregory confirms that bioavailability of vitamin B6 in a mixed diet is about 75%, with approximately 8% of this total contributed by pyridoxine a-d-glucoside, which is about half as effectively utilized as free B6 vitamers or their phosphates. The amine and aldehyde forms of vitamin B6 are probably about 10% less effective than pyridoxine. Despite the involvement of PLP with many enzymes affecting amino acid metabolism, there seems to be only a slight effect of dietary proteins on vitamin B6 status. Several studies have reported decrease in indicators of vitamin B6 status in women receiving oral contraceptives, but this probably reflects hormonal stimulation of tryptophan catabolism rather than any deficiency of vitamin B6 per se.

The deficiency and toxicity symptoms are described next.

Deficiency and Toxicity

A deficiency of vitamin B_6 alone is uncommon because it usually occurs in association with a deficit in other B-complex vitamins. Early biochemical changes include decreased levels of plasma pyridoxal ST-phosphate (PLP) and urinary 4-pyridoxic acid. These are followed by decrease in synthesis of transaminases (aminotransferases) and other enzymes of amino acid metabolism such that there is an increased presence of xanthurenate in the urine and a decreased glutamate conversion to the anti- neurotransmitter a-aminobutyrate. Hypovitaminosis B6 may often occur with riboflavin deficiency, because riboflavin is needed for the formation of the coenzyme PLP. Infants are especially susceptible to insufficient intakes, which can lead to epileptic form convulsions. Skin changes include dermatitis with cheilosis and glossitis.

Moreover, there is usually a decrease in circulating lymphocytes and sometimes a normochromic, microcytic, or sideroblastic anaemia as well. The sensitivity of such systems as sulphur amino acid metabolism to vitamin B6 availability is reflected in homocysteinaernia. A decrease in the metabolism of glutamate in the brain, which is found in vitamin B6 insuffici ncy, reflects a nervous system dysfunction. As is the case with other micronutrient deficiencies, vitamin B6 deficiency results in an impainnent of the immune system. Of current concern is the pandemic-like occurrence of low vitamin B6 intakes in many people who eat poorly (e.g. people with eating disorders). Vitamin B6 deficiency has also been observed in south-east Asian school children (infected with hookworm), elderly Europeans (Dutch), and in some individuals with hyperhomocysteinaemia or who are on chronic haemodialysis. Several medical conditions can also affect vitamin 136 metabolism and thus lead to deficiency symptoms

Toxicity

Though toxicity related to pyridoxine intake are rare, but use of high doses of pyridoxine for the treatment of pre-menstrual syndrome, carpal tunnel syndrome (compression of the median nerve at the wrist resulting in numbness, tingling, weakness in the hand and fingers), and some neurologic diseases has resulted in neurotoxicity. A upper limit (UL) of 100 mg/day as proposed by the United States Food and Nutrition Board has been adopted by the FAO/WHO 2004 Consultation on vitamin and mineral requirements.

So then what are the recommendations for pyridoxine intake'? Let us find out

Recontmended Dietary Allowance (RDA)

Average requirements for pyridoxine vary with age, sex and physiological coilditions such as protein status, pregnancy and lactation.

The ICMR recorninendations for individual hake of pyridoxine for adult nlales and female, is the same – 2.0 mglday, as can be see11 in Table 8.8. During increased demands of the body, i.e. pregnancy and lactation, the recommended level of intake is 2.5 mgtday. These Indian recommeildations are much higher than those recommended by the FAOIWHO 2004.

Table 8.8: ICMR, FAO/WHO recommended nutrient intake of pyridoxine by groups

Recommended Pyridoxine Intake (mg/day)			
Group	ICMR	Group	FAO/WHO 2004 RNI
Man Sedentary work		*Adults* Males	
Moderate work	2.0	(19 50 years)	1.3
Heavy work		(51+ years)	1.7
Woman Sedentary work		*Adults* Females	
Moderate work	2.0	(19 - 50 years)	1.3
Heavy work		(51+ years)	1.5
Pregnancy	2.5	*Pregnancy*	1.9
Lactation	2.5	*Lactation*	2.0
Infants 0 - *6* months	0.1	*Infants* 0 - 6 months	0.1
7 - 12 months	0.4	7-12 months	0.3
Children 1 - 3 years	0.9	*Children* 1 - *3* years	0.5
4 - 6 years	0.9	4 - 6 years	0.6
7 - 9 years	1.6	7 - 9 years	1.0
Adolescent		*Adolescents*	
Boys 10 - 12 years	1.6	Males (10-18 years)	1.2
Girls 10 - 12 years		Females (10-18 years)	1.3
Boys 13 - 15 years	2.0		
Girls 13 - 15 years			
Boys 16 - 18 years	. 2.0		
Girls 16 - 18 years			

Let us next learn about the criteria for assessment of pyridoxine status.

Criteria for Assessment of Pyridoxine Status

Vitamin B_6 status is most appropriately evaluated by using a combination of indicators, namely plasma PLP concentration, urinary excretion, erythrocyte aminotransferases activity coefficients, tryptophan catabolites, erythrocyte and whole blood PLP concentration, and plasma homocysteine concentration, including those considered as direct indicators (e.g. vitamer concentration in cells or fluids) and those considered to be indirect or functional indicators (e.g. erythrocyte aminotransferase saturation by PLP or tryptophan metabolites).

Plasma PLP may be the best single indicator because it appears to reflect tissue stores. A plasma PLP concentration of 20 mmol/l has been proposed as an index of adequacy based on recent findings. Plasma PLP levels have been reported to fall with age. ty.æ.zy 4-pyridoxic acid level responds quickly to changes in vitamin B6 intake and is therefore of questionable value in assessing status. However, a value higher than 3 mmol/day, achieved with an intake of approximately lmg/day, has been suggested to reflect adequate intake. Erythrocyte aminotransferases for aspartate and alanine are commonly measured before and after addition of PLP to ascertain amounts of apoenzymes, the proportion of which increases with vitamin BG depletion. Values of 1.5-1.6 for the aspartate aminotransferase and approximately 1.2 for the alanine aminotransferase have been suggested as being adequate. Catabolites from tryptophan and methionine have also been used to assess vitamin B6 status. In a review of the relevant literature, Leklem suggested that a 24-hour urinary excretion of less than 65 mmol xanthurenate after a 2 g oral dose of tryptophan indicates normal vitamin B_6 status.

Details related to interaction of pyridoxine with other nutrients is presented next.

Interaction with other Nutrients

Pyridoxine is shown to have effects with the macronutrients, as well as, other water- soluble vitamins. What are these? Let us read and find out.

- **Carbohydrates:** Pyridoxine is involved in glyconeogenesis through its action in transaminase reactions. Low levels of pyridoxine impair glucose tolerance. The coenzyme form of vitamin B_6 or pyridoxal phosphate or co-decarboxylase is responsible for non oxidative enzymic amino acid transformations and catalyzes reactions such as decarboxylation transamination, racemization, B_6 urinary elimination, amino acid metabolism. PLP has a key role in lipid metabolism and vitamin B_6 deficiency lowers body fat, liver lipid levels and impairs degradation of lipids. Administration of riboflavin, pantothenic acid and thiamine provide partial protection against seizures in Vitamin B6 deficient experimental animals.
- **Ascorbic acid:** Vitamin B_6 metabolism increases with.higher levels of vitamin C intake. Whole blood ascorbic acid levels fell during vitamin B_6 depletion and returned to normal levels, during repletion phase.
- **Leucine:** Excess of the amino acid, leucine in the diet antagonizes the function of vitamin B6 and impairs the conversion of tryptophan to niacin.

- **Cyanocobalamin:** Vitamin B_6 deficiency is reported to cause impairment in vitamin B_{12} absorption in rats.

With this, we end our study of pyridoxine. Next, let us review folate.

8.8 FOLATE

Folate is a generic term which includes naturally occurring food folate and folic acid in supplements and fortified foods. Pteroyl monoglutamic acid and its derivatives are known as the folic acid group. Common structural features of the folate family include a pteridine bicyclic ring system, para-aminobenzoic acid (PABA) and one or more glutamic moieties (refer to Figure 8. le). The term folic acid relates specifically to the fully oxidized monoglutamate form of the vitamin synthesized for commercial use in supplements and fortified foods.

What are the food sources of folate? Let us have a look.

Food Sources

Folate occurs naturally in foods. Although folate is found in a wide variety of foods, it is present in a relatively low density except in liver. Diets that contain adequate amounts of fresh green vegetables (i.e. in excess of three servings per day) will be good folate sources. Folate losses during harvesting, storage,' distribution and cooking can be considerable. Similarly, folate derived from animal products is subject to loss during cooking. Some staples, such as' white rice are low in folate. Figure 8.10 illustrates some common sources of folate as also highlighted in the classification herewith:

Rich sources: Liver, dried yeast, leafy vegetables, wheat germ and rice polishings,

Good sources: Whole cereals, dried legumes (pulses have twice as much folic acid as cereals), nuts, fresh oranges, green leafy vegetables,

Fair sources: Milled cereals, other vegetables, milk and fruits.

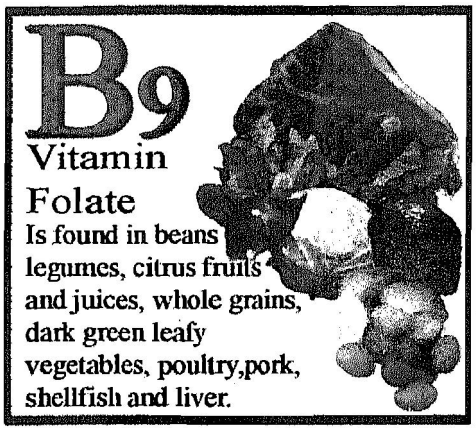


Figure 8.10: Rich food sources of folate

It is important to remember that the natural folates found in foods are in a conjugated form, which reduces their bioavailability by perhaps as much as 50%. In addition, natural folates are much less stable.

NOTES

The metabolic fate of folate in discussed next.

Absorption, Storage and Elimination

Folic acid is readily absorbed from the small intestines througli the portal vein and passed .onto the tissues through general circulation. Naturally occurring food folate is converted into the monoglutamate form by the enzyme p(eroylpolyglutamate hydrolase or folate conjugase or glutamate carboxypeptidase II, located in the jejunal brush border membrane. After deconjugation, the monoglutaniyl folate is transported across the membrane by a pH-dependent carrier-mediated mechanism. Folic acid once absorbed is acted upon by hepatic dihydrofolate reductase to convert to its metabolically active form which is tetrahydrofolic acid (THE). Following absorption, folic acid is largely reduced and methylated in the liver to N-5 methyltetrahydrofolic acid, which is the main transporting and stocage form of folate in the body. Folate transport across membranes into cells in kidney, placenta and choroid plexus, occurs via membrane—associated folate binding proteins that act as folate receptors and facilitate cellular uptake of folate.

Larger doses of folate may escape metabolism by the liver and appear in the blood mainly as folic acid,

Having studied about the metabolic fate of folate, next let us get. to know what role folate plays in our body.

Functions

Folate, also known as folic acid, is essential for good health. Folate requiring reactions include those involved in phases of amino acid metabolism, DNA (purine and pyrimidine) biosynthesis and the formation of the primary methylating agent, S-adenosyl methionine (SAM) as shown in Figure 8.11.

Folate is involved in the de novo synthesis of purines (adenine and guanine), requiring the folate form, 10-formyl tetrahydro folic acid (THF), which is produced from 5, 10-methylene T HF reactions catalyzed by the enzyme T HF synthetase. The 5,10- methylene T I-IF molecule has several fates, one of which is the reconversion to 5- methyl THF, catalyzed by methylene tetra hydrofolate reductase (MTHFR). Thus, folate in its reduced and polyglutamylated forms is essential for the DNA biosynthesis cycle, as shown in Figure 8.11. This conversion (5, 10-methylene THF molecule reconversion to 5-methyl THF) forms methionine from homocysteine. Folate, specially helps in reducing the risk of heart disease and stroke by lowering the level of the amino acid homocysteine in the blood (by forming methionine). At high levels, homocysteine can damage coronary arteries or make it easier for blood clotting cells to clump together and form a clot. This can increase the risk of heart attack or stroke.

This methylation reaction (refer to Figure 8.11) requires the enzyme methionine synthase, cobalamin (vitamin BIJ and 5-methyl THF. A methyl group is removed from 5 methyl T HF and is sequentially transferred first to cobalamin coenzyme and then to homocysteine forming methionine and reconvening 5-methyl THF to tetrahydrofolate (THF). The dependency of methionine synthase on both folate and cobalamin explains why a single deficiency of either vitamin leads to the same megaloblastic changes in the bone marow and other tissues, with rapidly dividing cells.

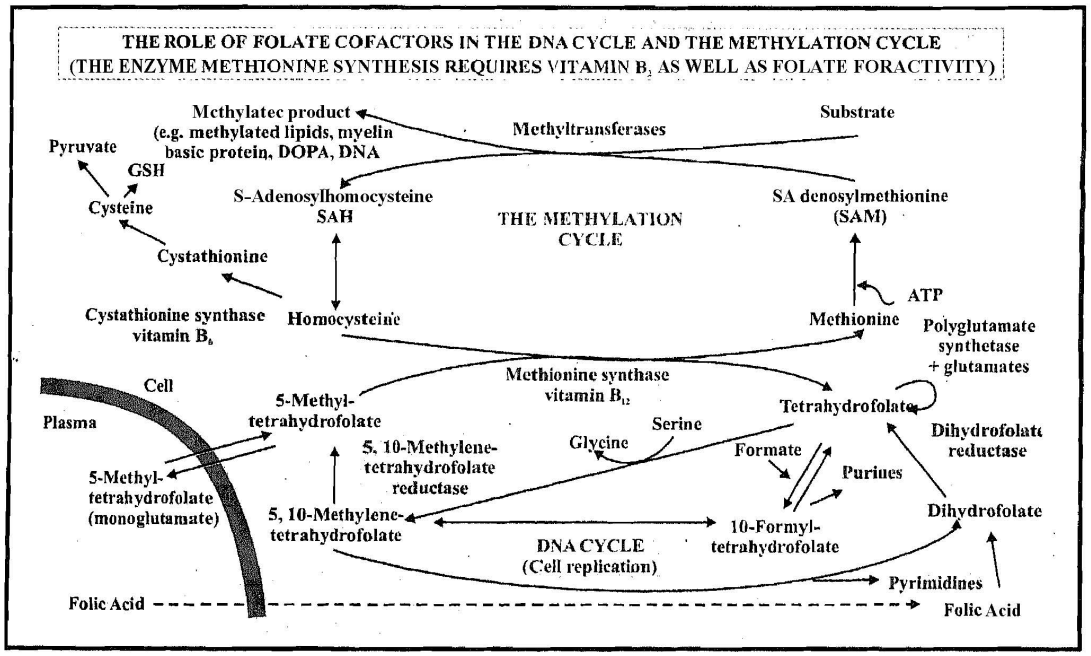


Figure 8.11: The role of folate in the DNA biosynthesis and methylation cycle

Alternatively, 5,10-methylenetetrahydrofolate can be channelled to the methylation cycle (refer to Figure 8.11). This cycle has two functions. It ensures that the cell always has an adequate supply of S-adenosylmethionine (SAM), an activated form of methionine which acts as a methyl donor to a wide range of methyltransferases. The methyltransferases methylate a wide range of substrates including lipids, hormones, DNA and proteins. One particularly important methylation is that of myelin basic protein, which acts as insulation for nerve cells. When the methylation cycle is interrupted, as it is during vitamin B12 deficiency, one of the clinical consequences is the demyelination of nerve cells resulting in a neuropathy which leads to ataxia (lack of coordination), paralysis, and, if untreated, ultimately death.

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Other important methyltransferase enzymes down-regulate DNA and suppress cell division.

Folate is also important for pregnant women. Low blood levels of folate during pregnancy can cause neural tube defects—anencephaly (a defect in the closure of the neural tube) and spina bifida (a congenital defect in which the spinal column is imperfectly closed so that part of the meninges or spinal cord protrudes, often resulting in hydrocephalus and other neurological disorders). And people with anaemia or at risk of anaemia need to be sure they consume enough folate as well.

Having read about the functions of folate, now you should be in a better position to appreciate why it is important to have an adequate intake and availability of folate from our diet. Next, let us learn about the requirements and availability of folate.

Bioavailability

Bioavailability of folate from naturally occurring food sources is variable and frequently incomplete, as mentioned earlier in the food sources section. The bioavailability of natural folates is affected by the removal of the polyglutamate chain by the intestinal conjugase. This process is apparently not complete, thereby reducing the bioavailability of natural folates by as much as 25-50%. Jn contrast, synthetic folic acid appears to be highly bioavailable— 85% or greater. The low bioavailability and, more importantly, the poor chemical stability of the natural folates have a profound influence on the devclopmcnt of nutrient recommendations. This is particularly true if some of the dietary intake is as stable and bioavailable as the synthetic fonn, folic acid. Fortification of foods such as breakfast cereals and flour can add significant amounts of folic acid to the die

Since folic acid (synthetic) taken with food is 85% bioavailable but food folate is only about 50% bioavailable, folic acid taken with food is 85150 (i.e. 1.7) times more available. Thus, if a mixture of synthetic folic acid plus food folate bas been fed, dietary folate equivalents (DFEs) are calculated as follows to determine the EAR: yg of DFE provided = [µg of food folate + (1.7 x mg of synthetic folic acid)]. To be comparable to food folate, only half as much folic acid is needed if taken on an empty stomach, i.e. 1pg of DFE = Iµg of food folate = 0.5 µg of folic acid taken on an empty stomach = 0.6 µg of folic acid with meals.

Alcohol interferes with the absorption of folate and increases excretion of folate by the kidney.

Before we move on to the recommendations for folic acid intake, let us quickly look at the conditions arising when folate is deficient in the diet.

Deficiency

If there is inadequate dietary folate, the activity of both the DNA and the methylation cycles, described above, will be reduced. A decrease in the former will

reduce DNA biosynthesis and thereby reduce cell division. Although this will be seen in all dividing cells, the deficiency will be most obvious in cells that rapidly divide, including for example red blood cells, thereby producing megaloblastic anaemia characterized by large, abnormally nucleated erythrocytes, as can be seen in Figure 8.12, that accumulate in bone marrow.

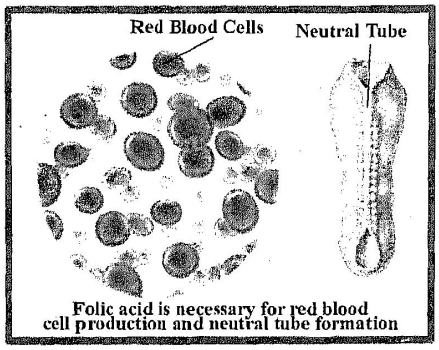

Figure 8.12: Function of folic acid

Taken together, the effects caused by the reduction in the DNA cycle result in an increased susceptibility to infection, a decrease in blood coagulation, and intestinal malabsorption. Folate deficiency will also decrease the flux through the methylation cycle but the DNA cycle may be more sensitive. The most obvious expression of the decrease in the methylation cycle is an elevation in plasma homocysteine. This is due to a decreased availability of new methyl groups provided as 5-methyltetrahydrofolate, necessary for the remethylation of plasma homocysteine. Previously it was believed that a rise in plasma homocysteine was nothing more than a biochemical marker of possible folate deficiency. However, there is an increasing evidence that plasma homocysteine concentration, if only moderately elevated, is an independent risk factor for cardiovascular disease and stroke. Interruption of the methylation cycle resulting from impaired folate status or decreased vitamin B_{12} or vitamin B_6 status may have serious long-term risks.

Pregnant women are at a higher risk of developing folate deficiency because of increased demand for folate. In addition to megaloblastic anaemia, inadequate folate intake is associated with poor pregnancy outcomes. Impaired folate status is associated with increased risk of pre-term delivery, infant low birth weight and foetal growth retardation. An elevated maternal homocysteine concentration leads to increased habitual spontaneous abortion and pregnancy complications (e.g. abruptio placentae or placental infarction with foetal growth retardation and pre eclampsia) which increase the risk of low birth weight and preterm delivery.

Folate deficiency is associated with Neural Tube Defects (NTDs) as highlighted in Figure 8.12. During pregnancy, there is an increased risk of foetal neural tube defects (N T Ds), with risk increasing 10-fold as folate status goes from adequate to poor. Between days 21 and 27 post-conception, the neural plate closes to form what will eventually be the spinal cord and cranium. Spina bifida, anencephaly and other similar conditions are collectively called NTDs. They result from improper closure of the spinal cord and cranium, respectively, and are the most common

congenital abnomalities associated with folate deficiency.

Multivitamin supplements containing folic acid reduce the risk of NTDs. It is now agreed that a supplement of 400 µg of folic acid taken near the time of conception will prevent most NTDs. The recommendation to prevent recurrence in women with a prior NTD bilth remains 4 mg/day.

Folate status is also related to birth defects other than NTDs such as cleft lip and palate, limb deficiencies and conotruncal or the outflow tract defects of the heart. In addition, evidence also suggests a link between colorectal cancer and dietary folate intake and folate status. Low folate status has been associated with an increased risk of colorectal cancer.

Thus, it is evident that folate is very essential for good health. The next question that comes to mind then is their a risk associated with excessive consumption of folate as well. Read the next sub-section on toxicity and find out

Toxicity

There is no evidence to suggest that it is possible to consuine sufficient natural folate to pose a risk of toxicity. However, this clearly does not apply to folic acid given in supplements or fortified foods. The main concern with fortification of high levels of folic acid is the masking of the diagnosis of pernicious anaemia, because high levels of folic acid correct the anaemia, allowing the neuropathy to progress undiagnosed to a point where it may become irreversible, even upon treatment with vitamin B„. Consumption of large amounts of folic acid might also pose other less well-defined risks. The United States National Academy of Sciences (NAS), after reviewing the literature, has suggested an upper level of 1000 yg. There is probably no great risk of toxicity at a range of intakes between 400 and 1000 gg of folic acid per day, with the exception of some increased difficulty in diagnosing pernicious anaemia.

So then what are the requirements for folate? Let us find out,

Recommended Dietary Allowance (RDA)

Folate requirements are the intake levels necessary to prevent deficiency with clinical symptoms. The requirements are expressed as differences in bioavailability between dietary folate equivalents (DFE) and food folate. One DFE is equal to I mcg of food folate. Table 8.9 presents the ICMR and the FAO[WHO recommended nutrient intake for folic acid by groups. The individual requirements of folate for both the sexes lecommended by ICMR is 100 pg/day, which increases in conditions of pregnancy and lactation to 400 and 150, respectively.

In 1998, the United States National Academy of Sciences (NAS) exhaustively reviewed the evidence regarding folate intake, status, and health for all age groups, including pregnant and lactating women. On the basis of their review, the NAS calculated estimated average requirements (EARs) and recommended

dietary allowances (RDAs), taken to be the EAR plus 2 standard deviations, for folate. The 2004 FAO/ WHO Expert Consultation has adopted the RDAs of the NAS as the basis for their RN1s (Table 8.9).

Table 8.9: ICMR and FAO/WHO recommended dietary intakes for folic

Group	ICMR µg/day	Group	FAO/WHO 2004 EAR (µg/day)	FAO/WHO 2004 RNI (µg/day)
Man Sedentary work Moderate work Heavy work	100	*Adults* Mnles (L9 - 65 years) (65+ years)	320	400
Worzen Sedentary work Moderate work Heavy work	100	*Adults* Females (19 - 65 years) (65+ years)	320	400
Pregnancy Lactation	400 150	Pregnancy Lactation	520 450	600 500
Infants 0 -6 months 6-12 months	25	*Infants* 0-6 months[a] 7-12 months	65 65	80 80
Children 1-3 years 4-6 years 7-9 years	30 40 60	*Children* 1-3 years 4-6 years 7-9 years	120 160 250	150 200 300
Adolescents Boys 10-12 years Girls10-12 years Boys 13-15 years Girls 13-15 years Boys 16-18 years Girls 16-18 years	70 100 100	*Adolescents* (10-18 years)	330	400

The RNIs suggested for various groups by FAO/WHO in Table 8.9 assume that food folate is the sole source of dietary folate because most societies in developing countries consume folate from naturally-occurring sources. As discussed earlier, natural folates are found in a conjugated form in food, which reduces their bioavailability by perhaps as much as 5090.1n addition, natural folates are much less stable. If chemically pure folic acid (pteroylmonoglutamate) is used to provide part of the RNI, by way of fortification or supplementation, the total dietary folate, which contains conjugated forms (pteroylpolyglutamates), could be reduced by an appropriate amount.

Finally, let us find out how can we assess the folate status in the body

Criteria for Assessment of Folate Status

Red cell folate, continues to be used as an important index of folate status. It is suggested that adequate folate status is reflected in a red cell folate level of greater than 150 gg/L. Indicators of haematologic status such as raised mean comuscular volume, hypersegmentation of neutrophils, and, eventually, the first stages of anaemia also remain important indicators of reduced folate status.

More recently, the biomarker plasma homocysteine has been identified as a very sensitive indicator of folate status and is added to the list of possible indicators of folate adequacy. Any elevation in plasma homocysteine, even at levels where overt folate deficiency is not an issue, may be undesirable because it is a risk factor for chronic disease. This new information requires the consideration of a folate intake that would reduce plasma homocysteine to a minimum level of less than 7.0 mmol/L.

Before we end our study on folate, let us quickly review the interaction of folate with other nutrients.

Interactions with other Nutrients

The interaction of folate with few nutrients is highlighted herewith:

Vitamin C : Anaemia is observed in vitamin C deficient patients. Normochromic, normocytic or macrocytic or megaloblastic anaemia has been reported. These conditions responded to ascorbic acid therapy alone or along with folic acid.

Vitamin B_{12} : For the conversion of folic acid to folinic acid, vitamin B_{12} is required. Vitamin B_{12} deficiency causes a rise in unconjugated folates and a marked depletion of intracellular conjugated folates. One of the vitamin B_{12} dependent enzymes, methionine synthase, functions in one of the two folate cycles, namely, the methylation cycle, as you may recall reading earlier. Interruption of the cycle reduces the level of S-adenosylmethionine. Disruption of the methylation cycle also causes lack of DNA biosynthesis and anaemia.

8.9 CYANOCOBALAMIN (VITAMIN BE)

Vitamin B_{12} (cobalamin, cbl) is a unique vitamin in human nutrition, since its malabsorption leads to the fatal syndrome of pernicious and megaloblastic anaemias with dernyelinating lesions of the central nervous system. The structure of vitamin B_{12} is shown in Figure 8.1. As you may have noticed, vitamin B_{12} is the largest of the B complex vitamins. It consists of a corrin ring made up of four pyroles with cobalt at the centre of the ring. There are several vitamin B_{12}-dependent enzymes in bacteria and algae, but no species of plants have the enzymes necessary for vitamin B_{12} synthesis. This fact has significant implications for the dietary sources and availability of vitamin B_{12} as highlighted next.

Food Sources

Vitamin B_{12} is unique among vitamins in the sense that it is mostly found in foods of animal origin but is not generally present in plant products as also is evident from the food sources highlighted herewith and in Figure 8.13.

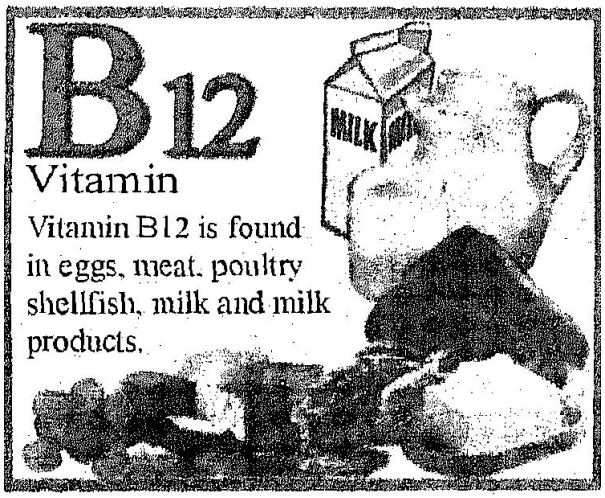

Figure 8.13: Food sources of vitamin B_{12}

Most microorganisms, including bacteria and algae, synthesize vitamin B_{12}, and they constitute the only source of the vitamin. The vitamin B_{12} synthesized in microorganisms enters the human food chain through incorporation into food of animal origin. In many animals, gastrointestinal fermentation supports the growth of these vitamin Bli synthesizing micloorganisms, and subsequently the vitamin is absorbed and incolporated into the animal tissues. This is particularly true for the liver, where vitamin B_{12} is stored in large concentrations. Products from herbivorous animals, such as milk, meat and eggs, thus constitute important dietary sources of the vitamin.

Humans, therefore, derive dietary vitamin B_{12} almost exclusively from animal tissues or products (i.e. milk, butter, cheese, eggs, meat, poultry). Considering the fact that this vitamin intake can only be assured through animal food sources, vegetarians, therefore, have to be very cautious about meeting their vitamin B_{12} requirements and are hence often advised to increase their milk intake or take vitamin Bn as a supplement. Next, let us learn about the metabolic fate of vitamin B_{12}.

Absorption, Storage and Elimination

Vitarnin B_{12} in food is bound to proteins and is only released by the action of a high 'concentration of hydrochloric acid present in the stomach. Once released from foods, vitamin B_{12} absorption involves contact with two proteins, intrinsic factor (IF) and R binder. The glycoprotein, called R-binders (or haptoconins), protect vitamin B from chemical denaturation in the stomach, IF is a glycoprotein synthesized by the gastric parietal cells and function in the small intestine.

Although the formation of the vitamin B_{12}— intrinsic factor complex was initially thought to happen in the stomach, it is now clear that this is not the case. At an acidic pH, (in the stomach) the affinity of the intrinsic factor for vitamin B_{12} is low whereas its affinity for the R-binders is high. When the contents of the stomach enter the duodenum, the R-binders become partly digested by the

pancreatic proteases, which in turn causes them to release their vitamin B_{12}. Because the pH in the duodenum is more neutral than that in the stomach, the intrinsic factor has a high binding affinity to vitamin B_{12}, and it quickly binds the vitamin as it is released from the R-binders. The vitamin BIF intrinsic factor complex then proceeds to the lower end of the small intestine, where it is absorbed by phagocytosis by specific ileal receptor. The absorbed cbl is processed into a complex transcobalamin—ll—cbl (TCII-cbl), secreted into portal blood and delivered to the liver and ultimately all tissues.

Vitamin B_{12} is the only B vitamin our body can store. The average adult body contains 2 to 5 mg of vitamin with 80 percent of this stored in the liver.

What is the role of vitamin B12 in our body? Next, let us find out.

Functions

The manufacture and normal functioning of blood cells requires vitamin B_{12} as highlighted in Figure 8.14. Vitamin Bn is also essential for metabolism of fats and carbohydrates ancl the synthesis of proteins. You may also recall studying under the folate vitamin that vitamin B_{12} is essential for the transport and storage of folate in cells and for conversion to its active form. Rapidly dividing cells, such as those in Ille epithelium and bone manow, have the greatest need for vitamin B_{12}.

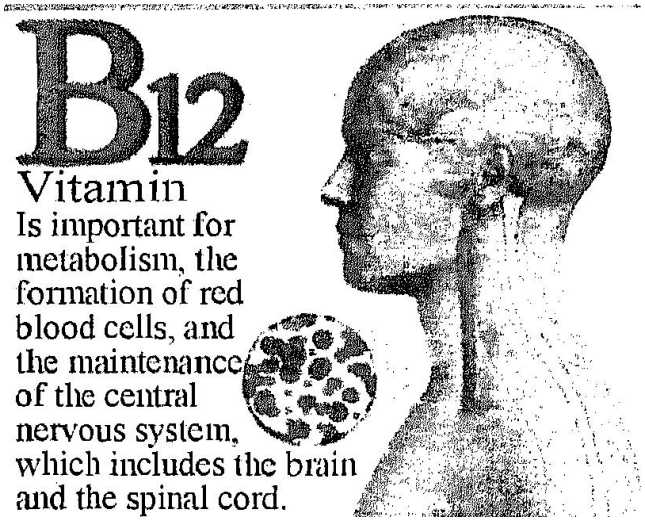

Figure 8.14: Some important functions of vitamin B_{12}

The functions of cyanocobalamin can thus be summarized as follows. It:

- promotes the maturation of erythroid cells,
- acts on other bone marrow elements and increases WBC and platelet count,
- stimulates the appetite and general health of the subject,
- cures neurological symptoms of pernicious anaemia. It is involved in the manufacture of the myelin sheath, a fatty layer which insulates nerves,
- is necessary for the production of nucleic acids, which make up DNA, the genetic material of the cell,

- functions as a coenzyme for the following reactions.:

  5^1-deoxyadenosyl cyanocobalamin isomerizes glutamic acid to threo-α-methyl aspartate,

  converts methyl malonyl CoA to succinyl CoA,

  dehydrates ethylene glycol to acetaldehyde, and

  converts homocysteine to methionine.

In mammalian cells, there are only two vitamin B_{12}— dependent enzymes. One of these enzymes, methionine synthase, uses the chemical form of the vitamin which has a methyl group attached to the cobalt and is called methylcobalamin. The other enzyme, methybnalonyl coenzyme (CoA) mutase, uses a form of vitarnin B_{12} that has a 5' -adeoxyadenosyl moiety attached 10 the cobalt and is called 5' -deoxyadeno- sylcobalamin, or coenzyme B_{12} (as mentioned in the reaction above).

In nature, there are two other forms of vitamin B_{12}. hydroxycobalamin and aquacobalamin, where hydroxyl and water groups, respectively, are attached to the cobalt. The synthetic form of vitamin B_{12} found in supplements and fortified foods is cyanocobalamin, which has cyanide attached to the cobalt. These three forms of vitamin B_{12} are enzymatically activated to the methyl-or deoxyadenosylcobalamin in all mammalian cells.

Bioavailability

Vitamin B_{12} is widely available. Availability is more from non-vegetarian foods as described earlier under the food sources section. Atrophic gastritis, loss of intiinsic factor (IF), surgical manipulations of the gastrointestinal tract including total and partial gastrectomy, gastric bypass operations, ileal resections, parasitic infection with fish tapeworm and jejunal bacterial overgrowth cause malabsorption of vitamin B_{12}.

Bioavailability decreases with age. A common problem is that of hypochlorhydria associated with atrophic gastritis, where there is a progressive reduction with age of the ability of the parietal cells to secrete hydrochloric acid. The absence of acid in the stomach is postulated to prevent the release of protein bound vitamin B_{12} contained in food but not to interfere with the absorption of the free vitamin B_{12} found in fortified foods or supplements.

Drugs like nitrous oxide, metforrnin and stomach acid blockers decrease availability.

Other factors that destroy this vitamin are sunlight, alcohol, oestrogen—the female hormone. Calcium and protein-rich foods greatly help the absorption of this vitamin in the intestine. Hence, remember these practical tips discussed above to ensure good vitamin status.

What would be the outcome of lack of this vitamin in our diet. Read the next sub- section and find out.

Deficiency

Malabsomtion of vitamin B_{12} can occur at several points during digestion. By far, the most important condition resulting in vitamin B_{12} malabsorption is the autoimmune disease called pernicious anaemia (PA). In most cases of PA, antibodies are produced against the parietal cells causing them to atrophy, and loose their ability to produce intrinsic factor and secrete hydrochloric acid. In some forms of PA, the parietal cells remain intact but autoantibodies are produced against the intrinsic factor itself and attach to it, thus preventing it from binding vitamin BE. In another less common form of PA, the antibodies allow vitarnin B_{12} to bind to the intrinsic factor but prevent the absorption of the intrinsic factor—vitamin B_{12} complex by the ileal receptors. The principal signs and symptoms of pernicious anaemia are as follows:

1) **Blood:** The RBC count is low— 1.5-2.5 million per mm^3 (normal range is 4.5- 5.5 million per mm^3). The avelage diameter of the cells is well above normal, about 8.2µ as compared to a normal diameter of 7.3µ. Abnormal circulating red cells undergo excessive destruction with a consequent increase in the serum bilirubin content. The haemoglobin content is low (8-9 percent).

2) **Bone marrow:** The nucleated red cells of the marrow are greatly increased. The successive nucleated cell stages in erythropoiesis are called stages I, II, Ill and IV and in pernicious anaemia, cells of stages I and II constitute 70 percent and of stages 111 and IV, 30 percent while in normal persons, the case is reverse. The cells of stage I are peculiar and differ from the normal cells and are called megaloblastic. The overacting bone marrow in pernicious anaemia shows megaloblastic hyperplasia.

3) **Stomach:** The cells which secrete acid and enzymes are atrophied. The gastric secretions are devoid of acid, pepsin and intrinsic factor (IF).

4) **Mouth:** Soreness and inflammation of the tongue are commonly observed.

5) **Nervous system:** Parasthesia (numbness and tingling) occurs in fingers and toes. Occassionally, there are objective signs of involvement of the spinal cord B_{12} neuropathy). In advanced cases, demyelination of the white fibres of the spinal cord occurs, affecting first the dorsal column and later, the lateral column.

Historically, PA was considered to be the major cause of vitamin B_{12} deficiency, more recently, it has been suggested that a far more common problem is that of hypochlorhydria associated with atrophic gastritis, where there is a progressive reduction, with age, of the ability of the parietal cells to secrete hydrochloric acid.

Vitamin B_{12} Deficiency in Vegans

Because plants do not synthesize vitamin B_{12}, individuals who consume diets

completely free of animal products (vegan diets) ale at risk of vitamin BE deficiency. This is not true of lacto-ovo vegetarians, who consume the vitamin through eggs, milk and other dairy products.

Persons living exclusively on vegetarian diets (vegans) have low serum levels of vitamin Bli and develop specific symptoms such as sore tongue, paraesthesia and signs of degeneration of the long tracts of the spinal cord as a result of low intakes of vitamin B_{12}. Megaloblastic anaemia is not so common when folic acid intake is adequate. The anaemia results from decreased DNA synthesis and failure of the cells to divide properly, coupled with the continued formation of RNA.

So now you would appreciate how important this vitamin is for all of us. What then is the recommended dietary allowance for this vitamin? Let us find out. But before that, we will also review the toxicity aspect of vitamin B_{12}, if any.

Toxicity

Intake of 1000 gg vitamin B_{12} has never been reported to have any side-effects. Similar large amounts have been used in some preparations of nutritional supplements without apparent ill effects. However, there are no established benefits for such amounts. Such high intakes thus represent no benefit in those without malabsorption and should probably be avoided.

Recommended Dietary Allowance (RDA)

Vitamin B12 deficiency is common in true vegans who can be treated with small doses since the daily requirement is only 1.0 gg/day, as you inay have noticed in Table 8.10 which presents the TCMR recommendations for vitamin B12 for all age groups. However, the requirements do increase in lactation by 0.5 gg/day.

Table 8.10: ICMK and FAO/WHQ recommended dietary intakes for vitamin B_{12} by group

Group	ICMR µg/day	Group	FAO/WHO 2004	
			EAR (µg/day)	RNI (µg/da
Man Sedentary work Moderate work Heavy work	1	*Adults* Males (19 - 65 years) (65+ yews)	2.0	2.4
Woman Sedentary work Moderate work Heavy work	1	*Adults* Females (19 - *65* years) (65+ years)	2.0	2.2
Pregnancy Lactation	1 1.5	Pregnancy Lactation	2.2 2.4	2.6 2.8

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Infants 0 -6 months	0.2	*Infants* 0-6 months	0.3	0.4
6-12 months		7-12 months	0.6	0.7
Children 1-3 years	0.2-1.0	*Children 1-3* years	0.7	0.9
4-6 years		4-6 years	0.1	1.2
7-9 years		7-9 years	1.5	1.8
Adolescent		*Adolescents*	2.0	2.4
Boys 10-12 years	0.2-1.0	(10-18years)		
Girls10-12 years				
Boys 13-15 years	0.2-1.0			
Girls 13-15 years				
Boys 16-18 years	0.2-1.0			
Girls 16-18 years				

The FAD/WHO) 2004 recommendations also given in Table 8.10 include both the estimated average requirement (EAR) and the recommendaed nutrient intake (RNI) calculated as the EAR plus 2 SD. FAO/WHO suggests a requirement of 0.7- 1.0 gg/day for those without pernicious anaemia. Since vitamin B12 is not coinpletely absorbed from food, an adjustment of 50% has to be added, giving a range of 1.4-2.0 gg/day.

Finally then how do we assess the vitamin status in our body? The next sub-section: focuses 'on this aspect.

Criteria for Assessment of B_{12} Status

Low serum or plasma levéls of vitamin B_{12} should be the first indication of poor status and this could be confirmed by an elevated methylmalonic acid (MMA) which is excreted in urine. Let us get to know more about these measures.

1) Serum vitamin B_{12} assay: The vitamin B_{12} content of serum can be determined. A serum level of < 140 ug/ml indicates vitamin B_{12} deficiency.

Status	Serum level (µg/mL)
Normal	200 - 960
Subnormal	140 - 190

2) E.vcretion of Methyl malonic acid. in urine (Methyl malonil aciduria): Methyl malonic acid is found only in traces in normal urine (1-2 mg/day). In vitamin B_{12} deficiency (pernicious anaemia), the excretion of methyl malonic acid in urine increases to about 100 to 200 mg/day due to the absence of

vitamin B_{12} co-enzyme (methyl malonyl CoA isomerase) involved in the conversion methyl malonyl CoA to succinyl

Before we end our discussion on vitamin B_{12}, we would like to highlight that vitamin B_{12} interaction with folate or folic acid is very important from the human nutrition point of view. We have already emphasized earlier under the folate section that the vitamin B_{12} dependent enzymes, methionine synthase, functions in one of the two folate cycles, namely, the methylation cycle. Interruption of the cycle reduces the level of S-adenosylmethionine.

This occurs in pernicious anaemia and other causes of vitamin B_{12} deficiency, producing as a result demyelination of the peripheral nerves and the spinal column, giving rise to the clinical condition called subacute combined degeneration. This neuropathy is one of the main presenting conditions in peinicious anaemia. The other principal presenting condition in PA is a megaloblastic anaemia molphologically identical to that seen in folate deficiency. Disruption of the methylation cycle also causes a lack of DNA biosynthesis and anaenua.

With this, we end our study of vitamin B_{12} and also our study of the B- complex vitamins. Finally let us review the other water soluble vitamin i.e. ascorbic acid.

8.10 ASCORBIC ACID (VITAMIN C)

Ascorbic acid was discovered as the anti-scurvy vitamin. Vitamin C (chemical names ascorbic acid and ascorbate) is the six-carbon lactone of a-keto-L-gulonic acid. It is, infact, a derivative of carbohydrate. It is closely related to monosaccharide sugars in its structure.

Vitamin C is synthesized in the liver in some mammals and in the kidney in birds and reptiles. However, humans are unable to synthesize vitamin C. Hence, when there is insufficient vitamin C in the diet, humans suffer froin the potentially lethal deficiency disease-scurvy.

Having learnt about some basic facts about vitamin C, we move on to the food sources.

Food Sources

Food sources of vitamin C include:

Rich sources: Amla and guava.

Good sources: Drumstick leaves, other leafy vegetables and fruits such as cashew fruit melons, berries, pine apple and tomatoes.

Fair sources: Apples, banana, grapes.

Vitamin C is found in many fruits and vegetables as highlighted in Figure 8.14. Citrus fruits and juices are particularly rich sources of vitamin C but other fruits

including honeydew melons, cherries, kiwi fruits, mangoes, papaya, strawberries, tangelo, tomatoes, and water melon also contain variable amounts of vitamin C. Vegetables such as cabbage, broccoli, brussels sprouts, bean sprouts, cauliflower, mustard greens, red and green peppers, peas, and potatoes may be more important soutces of vitamin C than fruits, given that the vegetable supply often extends for longer periods during the year than does the fruit supply. Figure 8.15 highlights the foods in the food pyramid which provide you vitamin C.

The vitamin C content of food is strongly influenced by season, transport to market, length of time on the shelf and in storage, coolcing practices, and the chlorination of the water used in cooking. Cutting or bruising of produce releases ascorbate oxidase. Blanching techniques inactivate the oxidase enzyme and help to preserve ascorbate, lowering the pH of a food will similarly achieve this, as in the preparation of sauerkraut (pickled cabbage). In contrast, heating and exposure to copper or iron or to mildly alkaline conditions destroys the vitamin, and too much water can leach it from the tissues during cooking.

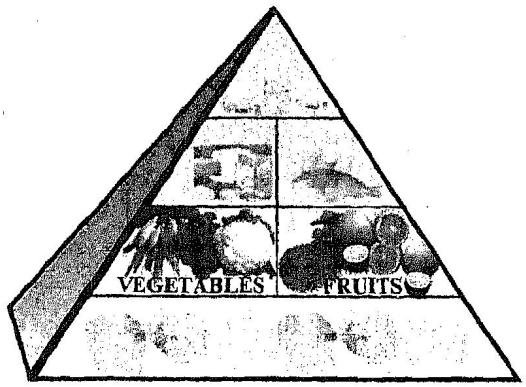

Figure 8.15: Vegetable and fruits— the rich sources of vitamin C

From food sources, we move on to facts about the absorption, storage and elimination of this vitamin from our body.

Absorption, Storage and Elimination

Ascorbic acid is rapidly absorbed from the intestines primarily by active transport. Simple diffusion or carrier-mediated transport may also contribute to a small extent of uptake of the vitamin from the mouth and stomach. Prior to absorption, ascorbate may be oxidized to form dehydroascorbatewhich is absorbed by passive diffusion or by use of glucose transporters.

It passes through the portal vein to the general circulation and to all tissues. Each organ or tissue has an optimal saturation level of ascorbic acid. It is not stored to any appreciable extent in the body. The degree of absorption decreases with increased vitamin intake and varies from 16% to 98%, the average overall absorption being about 80% to 95%. Unabsorbed vitamin C may be metabolized by the intestinal flora. Pectin and zinc are a few substances that impair its absorption. Excess is excreted in urine.

Next, the role of vitamin C is described.

Functions

The vitamin C is involved in several physiological and biochemical ftmctions in the body. Ascorbate is the biochemically active form of the vitamin, which has several functions. It is essential for the following:

1) **Enzyme function:** Vitamin C acts as an electron donor for 11 enzymes. Three of those enzymes are found in fungi but not in humans. Of the eight remaining human enzymes, three participate in collagen hydroxylation and two in carnitine biosynthesis; of the three enzymes which participate in collagen hydroxylation, one is necessary for biosynthesis of the catecholamine norepinephrine, one is necessary for amidation of peptide hormones, and one is involved in tyrosine metabolism.

2) **Protective role as an antioxidant:** Vitamin C is a powerful antioxidant because it can donate a hydrogen atom and form a relatively stable ascorbyl free radical (i.e. L-ascorbate anion). As a scavenger, ascorbate has been shown to be effective against the superoxide radical anion, hydrogen peroxide, the hydroxyl radical, and singlet oxygen which could damage DNA, proteins or membrane structures. Vitamin C also scavenges reactive nitrogen oxide species to prevent nitrosation of target molecules. The ascorbyl free radical can be converted back to reduced ascorbate by accepting another hydrogen atom or it can undergo further oxidation to dehydroascorbate. Dehydroascorbate is unstable but is more fat-soluble than ascorbate and is taken up 10-20 times more rapidly by erythrocytes, where it will be reduced back to ascorbate from the hexose monophosphate shunt.

3) **Synthesis of hormones:** Ascorbate is involved in the amidation, thereby conferring stability to hormones such as thyrotropin releasing hormone, adrenocoflicotropic hormone, vasopressin, oxytocin and cholesystokinin.

4) **Formation of collagen and inter cellular cement substance:** The vitamin is required in the formation of collagen and in the formation of intercellular cement substances for capillaries, teeth, bones etc. When the vitamin is deficient, these tissues are not formed fully.

5) **Absorption of iron and incorporation of plasma iron in ferritin:** A common feature of vitamin C deficiency is anaemia. The antioxidant properties of vitamin C may stabilize folate in food and in plasma. Vitamin C promotes absorption of soluble non-haem iron possibly by chelation or simply by maintaining the iron in the reduced (ferrous, Fe2+)form. The effect can be achieved with the amounts of vitamin C obtained in foods. However, the amount of dietary vitamin C required to increase iron absorption exceeds 25 mg and depends largely cn the amount of ilffibitors, such as phytates and polyphenols, present in the meal.

6) **Reduced cancel- risk:** Concentrations Of vitamin C appear to be high in gastric juice. Vitamin C present in gastric juice may prevent the formation of N-nitroso compounds, which are potentially mutagenic. High intakes of vitamin C correlate with reduced gastric cancer risk, but a cause-and-effect relationship has not been established. Epidemiological studies indicate that diets with a high vitamin C content have been associated with lower cancer risk, especially for cancers of the oral cavity, oesophagus, stomach, colon and lung.

7) **Hydroxylation of aromatic nuclei:** Ascorbic acid plays a central role in the hydroxylation of deoxycorlicosterone, hydroxylation of tryptophan to 5-hydroxytlyptophan and phenylalanine 10 tyrosine etc.

8) **Bone fonnation:** Ascorbale is vital for bone formation. In deficiency, though calcification is unaffected, formation of bone inatrix and ground substance is defective. Osteoblasts invading the area of calcification change histologically into fibroblasts. The bone matrix is abnormal, as it lacks ossification.

9) **Wound healing:** Ascorbic acid deficiency delays healing of wounds, as collagen formation is affected. The rapid healing of wounds require the formation of strong connective tissue on the scar.

10) **Cholesterol metabolism:** Vitamin C plays a protective or curative role in diseases resulting from atherosclerosis through its effect on cholesterol metabolism. It protects low density lipoproteins against oxidation.

From our discussion above, it must be evident what important role vitamin C has in maintaing good health. Next, let us study about its bioavailability and the consequences of lack of vitamin C in our body.

Bioavailability

Ascorbic acid is a crucial constituent of plants which brings about efficient photosynthesis. In humans, its availability is inversely related to the vitamin C status (f the individual. More absorption and retention occur to compensate tissue depletion. Humans maintain a body pool of vitamin C 114 gmol/kg (20 mg/kg) and a plasma vitamin C concentrates of 28-40 gmolfL (0.5-0, 7 mg/dl). Hence, humans though incapable of manufacturing the vitamin, are adept at conserving it.

Next, let us get to know about the consequences of ascorbic acid deficiency

Deficiency

Severe ascorbic acid deficiency results in the development of the disease known as scurvy, as highlighted in Figure 8.16, Three important manifestations of scurvy — gingival changes, pain in the extremities and haemorrhagic manifestations — precede oedema, ulcerations, and ultimately death. The disease occurs in adults and infants. In infantile scurvy, the changes are mainly at the sites of most active

bone growth, characteristic signs are a pseudoparalysis of the limbs caused by extreme pain on movement and hemorrhages under the periosteum, as well as, swelling and haemorrhages of the gums confounding erupting teeth.

Vitamin C deficiency can be detected from early signs of clinical deficiency, such as the follicular hypeskeratosis, petechial haemolThages, swollen or bleeding gums, and joint pain, or from the very low concentrations of ascorbate in plasma, blood, or leukocytes. In adults, one of the early principle adverse effects of the collagen- related pathology may be impaired wound healing.

Figure 8.16: Scurvy

Symptoms of scurvy in adults include:

1) **General weakness:** The first symptoms are weakness, easy fatigue and listlessness. These are followed quickly by shortness of breath, pain in bones, joints and muscles of the extremities.

2) **Swollen and tender joints and haemorrhage in various tissues:** HaemolThages occur deep in muscle, particularly in calf, thigh, buttocks and forearm, causing pain in surrounding tissues. The most specific sign includes the hyperkeratotic hair follicle with a haemotrhagic halo. Haemorrhages may also occur in joints, causing swelling and pain.

3) **Bleeding gums and loose teeth:** As ascorbic acid deficiency advances, the gums become swollen, blue-red, spongy and very friable. They may become infected by bacteria. The teeth loosen in the alveolar bone. So that was a morbid picture. The populations at risk of vitamin C deficiency are those for whom the fruit and vegetable supply is minimal. Epidemics of scurvy are associated with famine and war, when people are forced to become refugees and food supply is small and irregular.

But, is there a danger also linked with excessive consumption of vitamin C? Let us find out next.

Toxicity

The potential toxicity of excessive doses of supplemental vitamin C relates to

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intraintestinal events and to the effects of metabolites in the urinary system. Intakes of 2-3 g/day of vitamin C produce unpleasant diarrhoea from the osmotic effects of the unabsorbed vitamin in the intestinal lumen in most people.

Further, oxalate is an end-product cf ascorbate catabolism and plays an important role in kidney stone formation. Excessive daily amounts of vitamin C produce hyperoxaluria.

Vitamin C may also precipitate haemolysis in some people, including those with glucose-6-phosphatedehydrogenase deficiency, paroxysmal nocturnal haemaglobinuria (a disorder characterized haemolytic anaemia, haemoglobinuria, pallor, bronzing of skin, splenomegaly and hepatoinegaly), or other conditions where increased risk of red cell haelnolysis may occur or where protection against the lemoval of the products of iron metabolism may be impaired. On the basis of the above, the FAO/WHO 2004 Consultation agreed that Ig of vitamin C appears to be the advisable upper limit of dietary intake per day.

Let us then learn about the recommended dietary allowances for this important vitamin, next.

Recommended Dietary Allowance (RDA)

Table 8.11 presents the recommendations for vitamin C, as lecommended by ICMR and FAO/WHO 2004. As you may have noticed, the ICMR recommendation is 40 mg/day for both adult males and females. The requirements go up by another 40 mg (total 80 mg) in case or lactation.

Table 8.11: ICMR and FAO/WHO recommendeddietary intakes for vitamin C by groups

Recommended Vitamin C Intake			
Group	**ICMR (mg/day)**	**Group**	**FAO/WHO 2004 RNI (mg/day)[a]**
Man Sedentary work Moderate work Heavy work	40	*Adults* Males (19 - 65+years) (65+ years)	45
Woman Sedentary work Moderate work Heavy work	40	*Adults* Females (19 - 65+ years) (65+ years)	45
Pregnancy Lactation	40 80	Pregnancy Lactation	55 70
Infants 0 -6 months 6-12 months	25	*Infants* 0-6 months 7-12 months	25 30[b]
Children 1-3 years 4-6 years 7-9 years	40	*Children* 1-3 years 4-6 years 7-9 years	30[b] 30[b] 35[b]
Adolescent Boys 10-12 years Girls 10-12 years Boys 13-15 years Girls 13-15 years Boys 16-18 years Girls 16-18 years	40 40 40	*Adolescents* Males (10-18 years) Females (10-18 years)	 40[b] 40

To ensure that we are in a goad vitamin C status, various assessment parameters are available. Let us learn about them.

Criteria for Assessment of Vitamin C Status

The different measures which can be used for assessment include:

1) **Ascorbic acid content of white blood cells:** The ascorbic acid content of white blood cells and platelets is a good index of the tissue levels of ascorbic acid. The levels of ascorbic acid in normal persons range from 24-38 mg/100g. After feeding individuals on vitamin C defcient diet for 121 days, the valu becomes zero. Determination of ascorbic acid content of white blood cells thus offers a highly sensitive index of the ascorbic acid nutrition of the individuals

2) **Plasma or serum ascorbic acid levels:** The serum or plasma ascorbic acid levels are used as an index of ascorbic acid nutriton of humans. The normal serum values vary over a wide range from 0.5 to 2.2 mg percent.

3) **Urinary excretion:** The urinary excretion of ascorbic acid falls when the dietary intake is low. Since the tissues are not saturated, a greater part of the test dose of ascorbic acid will be retained by the tissues and only a small part will be excreted in urine. In contrast, when the daily intakes are high, a greater part of the test dose will be excreted. A normal saturated person excretes 50 percent of the test dose while a person on a deficient diet excretes only about 35 percent.

4) **Intradermal dye test:** The rate of decolouration of a small quantity of the dye, 2,6- dichlorophenol injected intradermaly is an index of the ascorbic acid nutrition. In persons saturated with ascorbic acid, the dye is decolourised in 5 minutes. In deficient persons the time taken is 10 minutes or more.

5) **Skin capillary fragility test**: One of the earliest signs of ascorbic acid deficiency is the fragility of the capillaries. Capillary fragility is measured by applying negative pressure on a particular area and the number of petechiae (haemolThagic spots) that have appeared in that area counted. It is low in normal persons (<10 petechiae) and high in deficient persons (10-20 petechiae).

With this, we end our study on ascorbic acid. Now read section 8.10 which covers the important aspect related to the interaction of these water soluble vitamins with other nutrients, This is an important issue hence we have taken this up separately in this unit.

8.11 INTERACTION WITH OTHER NUTRIENTS

Having gone through the discussion above it must be evident to you that nutrients are interdependent and are related to one another. The excess or deficiency of

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certain vitamins affects the requirements of certain other nutrients. The interaction of the B complex vitamin and vitamin C with other nutrients can be traced under the following headings:

1) Interaction with carbohydrate, fats and proteins

Dietary carbohydrates, fats and proteins require water-soluble vitamins for their metabolism and in turn influence the requiremnts of these vitamins. Let us review these interactions one by one.

a) **Thiamin:** Carbohydrates require thiamin for their metabolism since thiamin pyrophosphate (TPP) is a coenzyme of decarboxylases and aldehyde transferases. Thiamin plays a key role in the oxidative decarboxylation of pyruvic acid (in the breakdown of carbohydrate and proteins and a-keto glutarate (in the citric acid cycle). TPP is a coenzyme for transketolase in lipid metabolism.

b) **Riboflavin** The two coenzyme foms of riboflavin are FMN and FAD. They are found in a large number of systems which function in the metaboslim of carbohydrates, fats and protein. The role of riboflavin is central to energy production. In its role as a precursor to FAD, riboflavin exhibits significant antioxidant activity and protects against lipid peroxides.

c) **Nicotinic acid:** NAD, NADP and NMN act as constituents of the hydrogen transfen-ing coenzymes in glycolysis, Kreb's cycle and in the oxidation and biosynthesis of lipids. Also, trypotophan present in dietary proteins in converted to niacin. Thus, tryptophan serves as a source of nicotinic acid meets the niacin requirements.

d) **Pyridoxine:** Pyridoxine is involved in glyconeogenesis through its action in transaminase reactions. Low levels of pyridoxine impair glucose tolerance. The coenzyme form of vitamin B_6 or pyridoxal phosphate is responsible for all non-oxidative enzymic anlino acid transformations and catalyzes reactions such as decarboxylation, transamination, racemization. PLP has a key role in lipid metabolism and vitamin B_6 deficiency lowers body fat, liver lipid levels and impairs degradation of lipids.

e) **Ascorbic acid:** The biologically active form, ascorbate, is a cofactor or co- substrate for eight isolated enzymes involved in hydroxylation of amino acids, metabolism of tyrosine etc. It protects lipids, protein and membrane structures from oxidative damage. It also regulates protein translation and gene transcription. Since ascorbic acid closely resembles glucose, most mammals can synthesize ascorbate from glucose. However, man lacks the terminal enzyme in the biosynthetic pathway and hence must ingest ascorbic acid to survive.

f) **Leucine:** Excess of the amino acid, leucine in the diet antagonizes the function of vitamin B_6, and impairs the conversion of tryptophan to niacin.

2) Interacton with other vitamins

a) **Ascorbic acid and other vitanlins:** Ascorbic acid synthesis is diminished in thiamin and riboflavin deficiency. Vitamin A also plays an important role in the biosynthesis of ascorbic acid.

b) **Thiamin and riboflavin** Thiamin deficiency is accompanied by disturbances in riboflavin metabolism and excretion of riboflavin in urine.

c) **Vitamin B_6 an other vitamins:** Administration of riboflavin, pantothenic acid ancl thiamin provide partial protection against seizures in vitamin B6 deficient experimental animals.

d) **Niacin and other vitamins:** Livers of rats fed thiamin or riboflavin deficient diets contained smaller amounts of niacin than normal controls. Treatment of pellagra with niacin precipitates symptoms of thiamin and riboflavin deficiencies indicating that niacin deficiency is accompanied by secondary deficiencies of thiamin and riboflavin.

e) **Vitamin B_6 and C:** Vitamin B_6 metabolism increases with higher levels of vitamin C intake. Whole blood ascorbic acid levels fall duling vitamin Bo depletion ancl returned to normal levels, during repletion phase.

f) **Vitamin B_6 and vitamin B_{12}:** Vitamin Bo deficiency is reported to cause impairment in vitamin B_{12} absorption in rats.

g) **Folic acid and vitamin C:** Anaemia is observed in vitamin C deficient patients. Normochromic, normocytic or macrocytic or megaloblastic anaemia has been reported. These conditions responded to ascorbic acid therapy alone or along with folic acid.

h) **Vitamin E and C:** Both vitamin E and vitamin C are powerful anti oxidants. They protect biological systems against oxidative damage due to free radicals. Their functions are synergistic to each other. Vitamin C synthesis is reduced in the livers of vitamin E deficient rats and several vitamin E deficiency symptoms resemble those of scurvy

i) **Riboflavin and pyridoxine:** Riboflavin deficiency slows down the uptake of pyridoxine and decrease the conversion of pyridoxine to its metabolites.

j) **Folic acid am vitamin B_{12}:** For the conversion of folic acid to folinic acid vitamin B_{12} is required. Vitamin B_{12} deficiency causes a rise in unconjugated folates and a marked depletion of intracellular conjugated folates.

3) Interaction with minerals

a) **Vitamin C and iron:** Ascorbic acid powerfully enhances absorption of non- haem iron and reverses the inhibiting effect of tea and calcium phosphate. Iron absorption is directly proportional to the quantity of ascorbic acid present. Ascorbic acid forms a chelate with ferric iron at acid pH and renders it soluble for absolption.

b) **Vitamin C, iron and cadmium:** Toxic levels of dietary cadmium (5-200 ppm) interfere with iron absorption and produces iron deficiency. Supplements of iron and ascorbic acid protect against cadmium toxicity. With low levels of dietary cadmium, supplements of iron and ascorbic acid decreased cadmium uptake in the liver, kidney and small intestines.

c) **Vitamin C, lead and mercury:** Iron alleviates lead toxicity but ascorbic acid is ineffective. Ascorbic acid alleviates mercury toxicity but iron exhilarates the condition.

d) **Riboflavin and iron:** Riboflavin' deficiency is reported to decrease mobilization of hepatic iron and impair absorption of dietary iron.

8.12 LET US SUM UP

Vitamins are vital to the body functions though needed in very small amounts. Water- soluble vitamins comprise of vitamin C and vitamins of the B complex group. In this unit, we learnt about the important functions and food sources of water-soluble vitamins which are summarized herewith. We also learnt about the recommended nutrient intake for each of these vitamins.:

Vitamin	Food Sources	Function
Vitamin of the B-complex group		
Thiamin or B_1	Whole grain cereals, pulses, nuts, egg yolk, meat	Role in carbohydrate meabolism in particular.
Riboflavin or B_2	Green leafy vegetables, milk, eggs, organ meats like liver, kidney	Role in the metabolism of carbohydrates, fats and proteins.
Niacin	Cereals, pulses, milk, nuts & oil seeds, organ meats Fish	Role in the metabolism of carbohydrates, fats and proteins.
Folic acid	Whole grain cereals, leafy vegetables, milk and eggs, organs meats like liver and kidney	Role in the formation of normal red blood cells in the bone marrow.
Vitamin B_{12}	Animal foods like milk, egg, organ meats	Role in the formation of normal red blood cells in the bone marrow and proper functioning of the digestive tract and nervous system.
Ktamin C	Citrus fruits, amla, guava, capsicum, green leafy vegetables, green chillies	Role in collagen formation and hence in wound healing. Role in absorption of iron and prevention of destruction of other substances.

8.13 GLOSSARY

Angular stomatitis : inflammation of the mucous membrane of the mouth.

Antacids : medicines used to reduce or prevent acid collecting in the stomach.

Apoenzyme : a protein that combines with a coenzyme to fonn an active enzyme.

Cheilosis : a disorder of the lips marked by scaling and fis-sures at the corners of the mouth; caused by ribo-flavin deficiency

Coenzymes : a small molecule associated with an enzyme that participates in enzymatic catalysis.

Cyanosis : bluish colour of the skin due to the insufficient oxygen in the blood.

Delirium : a state in which the thoughts, expressions, and ac- tions are wild, irregular.

Dysnpoea : difficult respiration.

Dyspepsia : a kind of indigestion or a state of the stomach in which its functions are distributed.

Enzyme : proteins produced by living organisms and functioning as biochemical catalysts.

Erythema : a disease of the skin, in which a diffused inflam- mation forms rose-coloured patches of variable size.

Erythroid : red coloured tissue.

Glossitis : inflammation of the tongue.

Haptocorrin : a cobalamin- binding protein.

Hyperaesthesia : an abnormal increase in sensitivity to sensory stimuli, as of the skin to touch or the ear to sound.

Immunoglobulins : group of large glycoproteins that are secreted by plasma cells which function as antibodies in the immune response by binding with

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antigens incoherent as a consequence of fever or some other disease.

Lesions : inflammations.

Ligand : a molecule that binds to a receptor protein to form a larger complex.

Megaloblastic anaemia : deficiency of RBCs characterized by many large immature and dysfunctional RBCs in the bone marrow associated with pernicious anaemia.

Metabolic trapping : phosphorylation and retention of each form of vitamin after the process of absorption.

Neural "hibe Defect : malformations of the neural tube, during embryo- genesis (i.e., formation of embryo).

Neural tube : a tube of extradermal tissue in the embryo from which the brain and spinal cord develop.

Niacin equivalents : 1 mg of niacin or 60 mg of tryptophan.

Opriguria : a lower than normal volume of urine.

Ossificatio : the process of forming new bone by which inorganic material is deposited in cartilage or membrane, forming bony tissue.

Oxaluria : abnormal excretion of oxalates or oxalic acid in the urine, especially calcium oxalate.

Pernicious anaemia : condition caused by vitamin B_{12} deficiency and characterized by deficiency of RBCs and spinal cord abnormalities.

Polishings : bran layers of a cereal (rice).

Redox system : a group of compounds having oxidizing and reducing properties.

Sideroblastic anaemia : a form of refractory anaemia caused by small ba- sophilic granules containing ferric iron in the bone marrow.

Tachycardia : a very rapid heart beat.

Vitamers : different forms of vitamin occurring in free form.

8.14 CHECK YOUR PROGRESS

1) What are the salient features in the processes of absorption, storage and Elimination of thiamin?

2) List any five factors that affect the bioavailability of riboflavi

3) Write notes on thiamin deficiency

4) Bring out the significance of determination of ETK activity

5) Trace the interaction of macronutrients with thiamin.

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UNIT

9

MACRO MINERALS

STRUCTURE

9.1 LEARNING OBJECTIVE

After studying this unit you will be able to:

discuss the importance of minerals,

describe the metabolism, functions,

importance of food sources of all the essential macro minerals,

identify the various deficiency and toxicity symptoms of selected macro minerals,

explain the significance of interactions among the minerals, and

identify the dietary requirements of various macro minerals for different age groups.

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9.2 INTRODUCTION

In the previous units we learnt about the structure, properties, deficiencies/toxicity and recommended dietary intakes of several vitamins. In this unit, we shall brief ourselves about several minerals. As we all know, humans require several mineral elements for optimal functioning. These mineral elements are broadly divided into two classes i.e. macro and micro minerals. Macro minerals, also referred to as major minerals are distinguished from micro minerals by their occurrence in the body. Thus, macro minerals constitute at least 0.01 % of the total body weight or occur in minimum quantity of 5 g in a 60 kg body. They are required in amounts greater than 100 mg per day. On the other hand, requirement of micro minerals varies from a few milligrams to micrograms per day.

This unit will focus on macro minerals while the next unit (Unit 10) will deal with micro minerals. Before studying individual minerals, you will learn about some common features of minerals. Thereafter, we will briefly go through the salient and important aspects of calcium, phosphorus, magnesium, sodium, potassium and chloride.

9.3 GENERAL NUTRITIONAL FUNCTIONS OF MINERALS

We hear and talk about minerals almost everyday with regards to maintaining good health. But what are minerals and what functions do they usually pelform? Well, a mineral is a solid homogeneous crystalline chemical element or compound that results from the inorganic processes of nature. Different minerals perform their own respective specialized functions and have a variety of roles to perform. Before we deal with the function of each of these, let us brief ourselves with their overall functions. The varied functions of minerals can be grouped under four general physiologic roles viz.:

Structural: They form an integral part of structures such as the bones/ skeleton, blood etc.

Catalytic: Certain minerals are required as constituents of enzymes, co-enzymes in various metabolic pathways.

Cellular: Some are necessary for membrane stability, as well as, inter and intra cellular transport mechanisms.

Others: They play an impottant role in muscle contraction, nerve transmission etc.

In the previous section wc read about the difference in the requirements of various macro and micro minerals. Well, the functions of macro and micro minerals may also be different. For instance, macro minerals largely perform structural functions e.g. 99% of body calcium, 85% of phosphorous and 50-60% of magnesium

is in the bone and is calcified tissue. Besides this, phosphorus is an important component of phospholipids and phosphoproteins that form important structural component of the cell membranes. Some macro minerals, in addition to their structural role, are involved in catalytic function e.g. magnesium exerts catalytic and regulatory role in number of biochemical reactions. Calcium functions as a messenger in signal transduction in nerve and muscle cells, as you may recall studying earlier in the Applied Physiology Course in Unit 9. Phosph01us, by way of phosphorylation-dephosphorylation cycle, is involved in the regulation of enzymes.

Micro minerals are found in small quantities (parts per million or parts per billion) in tissues and cells function primarily as a part of enzymes. They are present at the active site or are regulators of enzymatic activity. As component of enzymes, they often participate in redox reactions (i.e. oxidation/reduction reactions) and function as the electron carrier. Metalloproteins and metalloenzymes containing iron (Fe), selenium (Se), copper (Cu), manganese (Mn) function in a variety of redox and respiratoiy chain enzymes and proteins. Certain micro minerals provide binding sites for the enzyme-substrate combination e.g. zinc.

A major portion of the iron in the body is present in haeinoglobin, and a smaller proportion as component of several enzymes. Similarly, zinc, besides its catalytic role, exerts a structural role in protein synthesis, particularly as zinc finger protein which is involved in gene transcription. Gene transcription, as you may be aware, is the synthesis of mRNA from the complementary strand (f DNA. We will learn about this aspect in unit 19 later in this course.

Although macro minerals are mainly involved in structural role while micro elements are involved in catalytic role, there seems to be some overlap, for some minerals, Specific functions of each will be dealt with in the following sections.

Next, we shall quickly brief upon the overall absorption and metabolism of minerals.

9.4 ABSORPTION AND METABOLISM OF MINERALS

All minerals in the diet are not equally absorbed. Also different compounds and complexes of same mineral are absorbed with different degree of efficiency. The fraction of the dietary intake of minerals absorbed and utilized for specific functions is defined as the bioavailability of the minerals. In addition to the chemical form in which minerals are present in the diet, factors such as age, sex, general health, and other constituents of the diet affect bioavailability of minerals.

Upon absorption across the intestinal mucosa, minerals enter their metabolic pool. They are transported in the blood by specific transport protein(s) to their storage site or to the active physiologic/biochemical site.

The physiologic effects of minerals depend on the level of intake. There is

a range of intake, known as safe and adequate range which provides optimal function. If the intake is p ogressively below this range there is a gradual decrease in the respective function of minerals until overt signs of deficiency appear. On the other hand when the intake exceeds the upper limit safety (i.e. upper tolerable limit) signs of toxicity begin to appear. In fact, all the essential minerals are toxic if consumed in excess; however the concentration at which toxicity occurs varies widely. It must be emphasized here that as long as a mixed diet is the only source of minerals, toxicity is most unlikely to occur.

In our subsequent sections we will learn in detail about the metabolism, functions, requirements, food sources etc of calcium, phosphorus, magnesium, iron, sodium, potassium and chloride. Let us begin with one of the most crucial element for maintaining bones and our skeletal system i.e., calcium and learn why is this mineral so important for us?

9.5 CALCIUM

Among minerals, calcium (Ca) is the most abundantly present in humans, representing 52% of the body's mineral content and amounting to 1.2% of body weight.

In the elementary composition of the human body, calcium ranks fifth after oxygen, carbon, hydrogen and nitrogen, and it makes up I .9% of the body by weight. Nearly all (99%)of total body calcium is located in the skeleton. The remaining I % is equally distributed between the teeth and soft tissues, with only 0.1% in the extracellular fluid (ECF).

You all must be aware of the food sources of calcium. However, we will quickly review them.

Food Sources

Dairy products are of course the primary source of calcium followed by grains and pulses. Among the millets, ragi contains substantial amount of calcium. The bio- availability of calcium from different dietary sources is variable. For instance, phytates in whole grain cereals inhibit calcium absorption. Fermentation, on the other hand, reduces phytate content and improves calcium absorption. We will learn more on calcium bioavailability later in this section. The calcium content of some important foods is given in Table 9.1.

Table 9.1: Calcium content of some calcium-rich foods (mg/100 g edible portion)

Food	Calcium Content	Food	Calcium Content
Cereals/Millets		*Green Leafy Vegetables*	
Ragi	344	Agathi	1130

Amaranth seeds	510	Amaranth	397
Pulses		Fenugreek	395
Bengal gram whole	202	Rape leaves	370
Horse gram whole	287	***Milk & Milk products***	
Rajmah	260	Cow's milk	120
Nuts and Oilseeds		Buffalo milk	210
Gingelly seeds	1450	Cheese	790
Mustard seeds	490	Khoa	956
Cumin seeds	1080	***Fish & Sea foods***	
Poppy seeds	1584	Hilsa	180
		Rohu	650

Source: Nutritive Value of Indian Foods by C. Gopalan, B.V. Ramasastri, S.C. Balasubramanium, revised and updated by B.S. Narasinga Rao, Y. G. Deosthala and K.C. Pant, NIN, 1989.

Next, let learn about the metabolic fate of calcium in our body.

Absorption, Transport and Excretion

Calcium (Ca) in food occurs as calcium salts e.g. calcium phosphate or is associated with other dietary constituents e.g. calcium caseinate in milk. Before absorption, Ca must be released from foods and solubilized. This is achieved by the combined actions of gastric acid, intestinal enzymes, intestinal contractions and peristalsis. When calcium intake is low, calcium is mainly absorbed by active (transcellular) transport, but at higher intakes, an increasing proportion of calcium is absorbed by simple (paracellular) diffusion. Thus, calcium is absorbed from the intestine by transcellular route and paracellular route. What are these routes? Let discuss each one of these in detail.

Transcellular Route: It operates primarily in the duodenum and proximal jejunum, It is stimulated when Ca ingestion is lower relative to requirement. It is a metabolically active process, which means energy in the form of AIP is required to absorb and transport the calcium across the intestinal mucosal cells,

Transcellular Route: It operates primarily in the duodenum and proximal jejunum, It is stimulated when Ca ingestion is lower relative to requirement. It is a metabolically active process, which means energy in the form of AIP is required to absorb and transport the calcium across the intestinal mucosal cells,

Transcellular movement involves 3 sequential steps, The first from the intestinal lumen to the intestinal mucosal cells across the brush border, the second within the cell from the lumen to the serosal side and finally the third, extrusion from the cell into the blood circulation. All three steps are regulated by calcitriol (1 ,25 di- hydroxy cholecalciferol), the biologically active hormone form of vitamin D3 about which you may recall studying earlier in Unit 7.

Paracellular Route: It involves passive Ca transport through the tight

junctions between mucosal cells. The salient features include:

It is independent of nutritional and physiological regulation.

It is concentration-dependent and occurs when there is an increased intake or a person is taking supplements.

It occurs throughout the small intestine, ileum being the important site.

Thus, we can say that most Ca absorption takes place in the small intestine. There is some evidence, which suggests that not more than 4% (8 mg) of dietary Ca is absorbed the colon per day. The unabsorbed component which appears in the faeces together with the unabsorbed component of digestive juice calcium is known as endogenous faecal calcium. The faeces, therefore, contain unabsorbed dietary calcium and digestive juice calcium that was not reabsorbed. True absorbed calcium is the total amount of calcium absorbed from the calcium pool in the intestines and therefore contains both dietary and digestive juice components. Net absorbed calcium is the difference between dietary calcium and faecal calcium and is numerically the same as tme absorbed calcium minus endogenous faecal calcium. At zero calcium intake, all the faecal calcium is endogenous and represents the digestive juice calcium which has not been reabsorbed; net absorbed calcium at this intake is therefore negative to the extent of about 200 mg (5 mmol).

When the intake reaches about 200 mg (5 mmol), dietary and faecal calcium becomes equal and net absorbed calcium is zero. As calcium intake increases, net absorbed calcium also increases, steeply at first but then, as the active transpon becomes saturated, more slowly until the slope of absorbed or ingested calcium approaches linearity with an ultimate gradient of about 5-10%. True absorption is an inverse function of calcium intake, falling from some 70% at very low intakes to about 35% at high intakes.

There are several factors which influence the amount of calcium absorbed through the intestine. These factors can thus be related to the bioavailability of calcium. The subsequent discussion will look at these factors in detail. But first we shall look at the excretion of unabsorbed calcium.

Excretion: Calcium is excreted approximately in equal amounts in urine and through intestinal secretions. Bile and other secretions into the intestine account for 150 mg calcium per day of which 30% is reabsorbed. The minimum endogenous (from the body as distinguished from exogenous which is from the diet) excretion of calcium is thus 100 mglday (2.5 inillimoles). Ulinary calcium excretion varies greatly among individuals and varies from 2.5-6.0 millimoles/day (100-240 mglday). Urinary and endogenous faecal calcium are not the only forms of excreted calcium; losses through skin, hair md nails also need to be taken into account (insensible losses). Sweat losses are minimal, about 15 mglday. Total calcium loss may thus amount to 350 mglday.

Moderate to high intakes of sodium increases renal excretion of calcium. An intake of 500 mg of sodium as sodium chloride was found to draw out 10 mg of

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calcium in the urine. One study in post menopausal women found a correlation between high urinary sodium excretion and increased bone loss from the hip.

Another factor that increases urinary calcium losses is high intake of protein. In typically vulnerable groups like post menopausal women, in whom decreased oestrogen production is associated with accelerated bone loss, 3% of the skeletal mass per year, it is advisable to regulate sodium intake and avoid high protein intakes. However, the data are very insufficient to make any adjustments in requirements of the general population based on sodium intake. Reduced sodium intake can have other advantages such as control of high blood pressure.

Now that we have studied about the excretion of calcium, let us get back to the factors, which influence calcium absorption.

Factors Affecting Calcium Absorption

It is a well known fact that the amount of calcium that eat need not be the amount of calcium that gets absorbed. The difference between the two is primarily due to certain factors which may hinder/enhance the absorption or bioavailability of calcium. Thus, the bioavailability of calcium can be defined as the fraction of dietary calcium that is potentially absorbable by the intestine and can be used for physiological functions, particularly bone mineralization or to limit bone loss. Several factors affect the proportion of dietary calcium absorbed by humans, also known as fractional absorption of dietary calcium. The fractional absorption varies inversely with the quantity of calcium ingested. Lower the intake, higher the percentage of calcium absorbed.

A study on healthy adult women, in which intakes were lowered from 2000 mg calcium per day to 300 mg per day (i.e. from 50 to 7.5 millimoles/day), the fractional whole body retention of ingested calcium, an index of absorption increased from 27% to 37%. It should be noted that this adaptation does not fully make up for the increased losses on higher intake. In absolute amounts, the women would have absorbed much more calcium on 2000 mg intake versus 300 mg. This adaptation was reported to take 2-3 weeks, and was accompanied by increase In 1,25 di OH D3, which as already seen, increases intestinal absorption of calcium. Age is another factor which infl ences the absorption of calcium. Fractional absorption Of calcium is highest in infancy i.e., 60%, followed by the early pubertal period.

One study found 28% calcium absorption in pre pubertal children that increased to 34% in early puberty returning to the adult value of 25% two years later. Absorption of calcium is also increased in pregnancy to levels higher than 25% reported for adults. Available data suggests that in post menopausal women, absorption declines by 0.21% every year. Thus, from 50 years 10 7() years, absorption may decline by 4%. Ageing also reduces renal losses of calcium, due to reduced absorption and decrease in filtered calcium load.

Several dietary constituents have an effect on calcium absolption. The differences in fractional absorption from different foods can be partly explained

by their constituents. Calcium is poorly absorbed from foods that are rich in oxalic acid or phytic acid. Phytates, mesent in the husk of many cereals, as well as, in nuts, seeds, and legumes, can form insoluble calcium phytate salts in the gastrointestinal tract. Excess oxalates can precipitate calcium in the bowel. In comparison to calcium absorption from milk, calcium absolption from phytic acid rich grains is one half and from spinach it is only one tenth. This is so because spinach is high in oxalic acid. Among the dietary factors, which increase calcium absorption, lactose is prominent. In fact all metabolizable sugars have been shown to increase calcium absorption.

Table 9.2 The factors known to affect calcium absorption.

Factors	Effect on Absorption	Possible Mechanism (s)
A Physiological Factors		
1) Ca Deficiency	Increases	Stimulates PTH, which in turn increases calcitriol, that in turn increases intestinal absorption.
2) Pregnancy & Lactation	Increases	Increased requirement & stimulates. trans-cellular route.
3) Ageing	Decreases	With age, efficiency of renal calcitriol production in response to PTH reduces, thereby reducing intestinal absorption.
4) Menopause	Decreases	Oestrogen deficiency reduces vitamin D mediated Ca absorption.
5) Malabsorption syndrome	Decreases	In steatorrhoea, unabsorbed Patty acids form insoluble Ca soaps, and inhibit calcium absorption.
B *Dietary Factors*		
1) Lactose	Increases	Possibly improves Ca solubility in the intestine.
2) Sugar, sugar alcohols, protein, xylitol	Increase	
3) Phytates	Decreases	Binds Ca molar ratios of more than 0.2. Phytate:Ca increase risk of deficiency, by forming insoluble calcium-phytate complexes.
4) Oxalates	Decreases	Chelates and increase faecal excretion
5) Non fermentable Fibers	Decreases	Results in reduction in transit time and less time for absorption.

The presence of substances which fonn insoluble complexes with calcium, such as the phosphate ion also influences calcium absorption. High calcium-phosphorus ratio increases calcium absorption. The relatively high calcium-phosphate ratio of 2.2 in human milk compared with 0.77 in cow milk may be a factor in the higher absorption of calcium from human milk than cow milk.

Intestinal calcium absorption is mainly controlled by the serum concentration of 1,25- (OH)2D as discussed above. The activity of the I-a-hydroxylase, which catalyzes I production from 25-hydroxyvitanlin D (25-OH-D) in the kidneys, is negatively related to plasma calcium and phosphate concentrations and positively related to plasma parathyroid hormone concentrations. Thus, the inverse relationship between calcium intake and fractional absorption described above is enhanced by the inverse relationship between dietary calcium and serum.We will learn about this aspect later in this section under the heading regulation Ca concentration.

Absorption from dietary calcium supplements is important to know, since they are almost universally recommended for post menopausal women. As far as supplement tablets are concerned, tablet disintegration is an important consideration. In one study, absolption from different supplements were studied under similar test conditions and compared with absorption from milk. When 250 mg of calcium was given along with breakfast meal, the absorption was from calcium-citrate-inalate (35%), calcium carbonate (27%) and tri calcium phosphate (25%) which was similar to the calciuin absorption from milk (29%). Another finding of importance is that calcium from calcium carbonate in achlorhydric patients is reduced only when taken on an empty stomach. When taken with a meal, the absorption is greatest when calciuin is taken in doses of 500 mg or less and with foods.

We have so far learnt about the absorption of calcium and the factors which influence calcium absorption. It would be interesting to note here that majority of the calcium absorbed is stored in the bones/skeletal tissues. You may also have observed altered blood and bone calciuin levels during clinical conditions involving a low intake. We shall now learn about calcium homeostasis and the inter-relationship of blood calcium with bone calcium and other tissues of the body.

Tissue Distribution and Regulation of Calcium Concentration

As already discussed, development and preservation of bone mass is quantitatively an important function of calcium. It should also be noted here that the calcium content of the body at birth is only 30 mg which increases to 1000-1200 g by adulthood through deposition of mineral in the skeleton. It is not surprising, then, that of 1200 g calcium found in an adult human, 99% is present in bones and teeth. The remaining 10% found in blood, extracellular fluid (ECF), muscles and other tissues, nevertheless plays an important role in vascular contraction, vasodilation, muscle contraction, nerve transmission and glandular secretions. The concentration of ionized calcium in blood plasma is very critical for their functions and therefore the plasma calcium is controlled within very narrow limits, the skeletal calciuin providing a large reserve for doing this. Thus, calcium in plasma is present in three major fractions:

Ionized calcium

Protein bound calcium

Complexed calcium

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The ionized calcium that constitutes 50% of the total plasma calcium is the only biologically active fraction. Of the remaining half 40% of the plasma calcium is protein bound, 80%being bound to albumin and 20% to globulin. Although the protein bound calcium, does not participate in the biological actions, it serves as a ready reservoir of ionized calcium. When plasma calcium levels fall, the first line of defense against hypocalcemia is the dissociation of the calcium from the protein complexes to make the cation Ca^{++} available. About 8% of plasma calcium is present as complexes with organic phosphate. This has little importance as a reservoir of ionized calcium.

The regulation of plasma calcium is finely controlled by three sets of hormones and these are crucial for maintaining plasma level constant in the long term. The normal range for total serum calcium is velY narrow i.e. 2.0-2.5 millimoles per litre (9-10 mg/dl) when plasma protein concentrate are normal, total plasma calcium less than 2.2 millimoles/litre reflects hypercalcemia. Let us read a little further about the regulation of extra and intracellular levels of calcium. We will first talk about plasma calcium concentration.

a) Regulation of Plasma Ca^{+2} Concentration: The concentration of ionized Ca in plasma is maintained within range by regulating processes such as absorption, excretion, secretion and storage in the bone. This tight regulation is achieved through the following three hormones:

parathyroid hormone (PTH),

calcitriol (1,25 $(OH)_2$ D_3), and

calcitonin.

When the plasma Ca concentration is low, parathyroid gland is stimulated to secrete PTH. To some extent, high plasma phosphoms level stimulates secretion of PTH. PTH increases plasma Ca concentration by following interactions:

In bones, PTH promotes resorption (dissolution of bone calcium) that is added to the blood.

kidney tubules, PTH also increases reabsorption of Ca, thus conserving calcium plasma.

In kidney, PTH also increases the synthesis of calcitriol. Calcitriol acts on the small intestine to promote calcium absorption, thus adding calcium to the blood.

Calcitonin, in contrast to PTH, serves to lower serum Ca^{+2} by preventing dissolution and mobilization of Ca^{+2} from bone.

The serum calcium concentration varies despite large changes in dietary calcium because of endocrine control of this mineral.

Next, we shall discuss about the maintenance of intracellular levels of calcium.

b) Regulation of intracellular Ca concentration: The cytoplasmic calcium concentration is regulated by a series of calcium pumps, which either concentrate calcium ions within the intracellular storage sites or extrude them from the cells (where they flow in by diffusion). The physiology of calcium metabolism is primarily directed towards the maintenance of the concentration of ionized calcium in the ECF. This concentration is protected and maintained by a feedback loop through calcium receptors in the parathyroid glands, which control the secretion of parathyroid hormone . This hormone increases the renal tubular reabsorption of calcium, promotes intestinal calcium absorption by stimulating the renal production of 1,25-dihydroxyvitamin D or calcitriol [1,25- $(OH)_2D$], and, if necessary, resorbs bone. However, the integrity of the system depends critically on vitamin D status; if there is a deficiency of vitamin D, lhe loss of its calcaemic action leads to a decrease in the ionized calcium and secondary hyperparathyroidism and hypophosphataemia. This is why experimental vitamin D deficiency results in rickets and osteomalacia whereas calcium deficiency gives rise to osteoporosis.

Thus, intracellular cytoplasmic calcium concentration is maintained by the following mechanisms:

a) Limited entry rate, governed by limited number of calcium channels.

b) Efficient extrusion where by ATP — dependent Ca transport system pumps Ca^+ out of the cell. In addition, a calcium pump can drive calcium into mitochondria matrix for storage as calcium phosphate until needed.

c) Sequestration of Ca+2 in the endoplasmic reticulum or in the case of muscle ir the sarcoplasmic reticulum. It must be evident from the discussion above that calcium levels in bones, blood anc other tissues is maintained by a complex interaction of several mechanisms. Thi: it self is suggestive of the fact that calcium forms an integral and important part 01 these tissues. In our subsequent discussions, we will be able to identify the reason! be hind the significa ce of maintaining adequate levels of calcium in our body. Let then brief ourselves regarding the functions of calcium.

Functions

Calcium salts provide rigidity to the skeleton and calcium ions play a role in many if not most, metabolic processes. In the vertebrate skeleton, rigidity is provided by form of calcium phosphate which approximates hydroxyapatite and is embedded in collagen fibrils.

Let us get to know the role of calcium in mineralization of bones.

Mineralization of Bones

An understanding of the role of calcium in skeletal structures requires that the

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process of bone formation and mineralization be clearly comprehendecl. Bone is unique living tissue as it is rigid and strong and at the same time light enough to b€ moved by coordinated muscle contractions. There are two types of bones: the cortica bone, densely packed mineralized collagen laid down in layers and the trabecullcu bone (cancellous bones), which is spongy and provides strength and elasticity. Cortica bone is the main component of long bones of the extremities while cancellous bont is a component of the axial (central part of the body such as the spine) skeleton Defective cortical bones lead to long bone fractures while defective trabecullar bones leads to vertebral fractures.

Two-thirds of the weight of bones is due to minerals and the remaining one-third is due to water and collagens. Bone is continuously resorbed (dissolved) and formed throughout life and there are three major types of bone cells that play an important role in this process. The osteoblnstszue actively involved in the synthesis of matrix components of bones (i.e. collagen) and in the transport of calcium and phosphate involved in the mineralization of collagen, crucial to bone formation. Once the protein matrix is laid down, and mineralization begins, the osteoblasts are transformed into osteocytes, the second type of bone cells. Protein synthesis reduces at this stage and the osteocytes develop multiple processes that connect the osteocytes with each other. The main function of the osteocytes is to translocate the minerals from surface to in and out of the bone until the bone formation is complete. Osteocyte is multinucleated giant cell that resorbs bone. The osteoclasts have all the enzylnatic components which when secreted will solubilize the matrix and release the calcium and phosphorous, that are added to the blood, travelling via the ECF.

In children and adolescents, skeletal turnover occurs such that formation of bone exceeds resorption. Ca accumulates in the skeleton at an average rate of 150 mg/day. In adulthood, skeleton turn over continues such that activities of osteoblasts and osteoclasts are in equilibrium. From 50 years in men and from menopause in women, bone balance becomes negative.

As discussed earlier, in addition to the structural role in bones, Ca also performs many other functions in the body. These functions include:

- Clotting of blood
- Nerve conduction
- Muscle contraction
- Enzyme regulation
- Membrane permeability

Ionized Ca is chiefly involved in these functions. As the levels of serum total and ionic calcium are tightly controlled, these functions are well regulated. Bone mineral serves as the ultimate reservoir for the calcium circulating in the ECE Many neuromuscular and other cellular functions depend on the maintenance of the ionized calcium concentration in the ECF. Calcium fluxes are also important mediators of hormonal effects on target organs through several intracellular

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signalling pathways, such as the phosphoinositide and cyclic adenosine monophosphate systems.

It can be concluded from the discussions above that our body requires considerable quantities of calcium in order to create and maintain its skeletal structures and perform other important functions such as clotting of blood. Adequate intake of calcium is thus important to maintain a good physiological status. In our subsequent discussions, we will learn about the relevance of calcium levels in different tissues and what should be the ideal intake of calcium to maintain calcium homeostasis in the body.

Assessment of Calcium Status and Calcium Requirements

There is no biochemical indicator, which can clearly reflect calcium status. It has also been seen that in case of dietary calcium deficiency; plasma levels are maintained at the cost of bone calcium. Thus, prolonged calcium deficiency will affect the skeletal calcium rese ves. Therefore measures of bone mass may be used as indicators of calcium status. These include: Bone Mineral Content (BMC) and Bone Mineral Density (BMD).

BMC is the amount of mineral at a particular skeletal site such as femoral neck, lumbar spine or total body. BMD is BMC divided by the area of the scanned region. Besides their relationship to bone mass and strength, BND and BMC are strong predictors of fracture risk and thus functional indicators of Ca status,

So how much amount of calcium should we consume to ensure that adequate levels are maintained in the bones, blood and other essential tissues? Let us find out.

Dietary Calcium Requirements

There are variations in the amount of calcium recommended by different advisory groups. This is mainly due to the different criteria used as the basis for estimating requirements. The factorial approach is the most common one for determining the calcium needs. In this approach, estimates of how much calcium is deposited in the body on a daily basis are made for infants, children and adolescents and for each group and this is added to the endogenous' calcium losses through different routes.

The total of this is converted to dietary calcium by using the fractional absorption rates observed at different life stages. A recent refinement involves the use of mathematical modeling of experimental data from balance studies to estimate the optimal calcium intakes at or above which calcium retention is maximal or desirable.

Another approach is to estimate the optimal calcium intake for bone health, in terms of reduced risk of osteoporosis in later life. Lack of quantitative data in support of this approach is a constraint in using it widely, Calcium requirements have been measured by long-term balance studies. With respect to the desirable

intake of phosphorus, it is suggested that an elemental Ca:P ratio of 1:1 may be maintained in most age groups except in infancy where the ratio suggested is 1:1.5. We shall learn about phosphorus in the next section.

Requirements for calcium depend upon the rate at which calcium is incorporated into bone; they are therefore highest during periods of growth, especially during infancy and adolescence and fall after peak bone mass is achieved at about 25 years of age. The RDA for Indian adult male is based on replacing the losses of calcium in urine, stools, bile and sweat, which is estimated to be 700 mg calcium per day. The fractional absorption in adults is taken to be 20-30% in the presence of adequate vitamin D. Additional calcium for growth, pregnancy and lactation are calculated separately. The ICMR recommended dietary intake per day for calcium has been given in Table 9.3.

Table 9.3: Daily requirements of calcium and phosphorus for Indians

Group	Calcium mg/day	Phosphorus mg/day
Adult man	400	400
Adult woman	400	400
Pregnant woman	1000	1000
Lactating woman		
Infants (0 - 6m)	500	750
(6 - 12m)		
Children		
1 - 3 yrs	400	400
4 - 6 yrs		
7 - 9 yrs		
Adolescents 10 - 12 yrs		
Boys	600	600
Girls	600	600
13 - 15 yrs		
Boys	600	600
Girls	600	600
16 - 18 yrs		
Boys	500	500
Girls	500	500

Source: Recommended Dietary Allowances for Vitamins, Dietary Guidelines for Indians, NIN, ICMR, Hyderabad, India (1998).

How do these requirements compare with Other recommendations, particularly the FAO/WHO 2004 recommendations for calcium? Look at Table 9.4, which presents the current recommendations of the FAO/WHO, Canada/United States and the United Kingdom. You may have noticed that our recommendations are different then these, particulariy for ethnic or dietary reasons. The FAO/WHO

2004 recommendations for adults are very close to those of Canada and the United States but higher than those of the United Kingdom, which do not take into account insensible losses. It is important to remember that if the intake of calcium is not adequate, normal levels of calcium cannot be maintained in the blood and other tissues. So, would happen when the calcium equilibrium gets disturbed? What clinical signs may develop due to a deficient or low intake? The subsequent discussion deals with these issues.

Deficiency and Toxicity

Dietary calcium intake above or below the requirements can result in the elicitation of several signs of deficiencies and excess. Let us first talk about the deficiency of calcium.

Deficiency

If there is a continued inadequate intake or poor intestinal absorption of calcium, plasma calcium concentrations will be maintained from increased bone resorption. The cumulative effect of calcium depletion on the skeleton over many years contributes to the increasing frequency of fractures with age. Prolonged inadequate calcium intake in young growing children will reduce the rate of accretion of the skeleton and may prevent the attainment of the genetically determined maximal bone mass. In extreme cases, Ca deficiency can give rise to rickets in children. Let us discuss the effects of calcium deficiency one by one.

Table 9.4: Current calcium intake recommendations (mg/day)

Group		FAO/WHO 2004[b]	Canada and United States 1997[a]	United Kingdom 1991[a]
Infants	0-6 months			
	Human Milk	300		
	Cow Milk	400	210 - 270	525
	7 - 12 months	400		
Children	1 - 3 years	500		
	4 - 6 years	600	500 - 800	350-550
	7 - 9 years	700		
Adolescent				
	Boys 10 - 18 years	1300*	1300	1000
	Girls 10 - 18 years		1300	800
Adults	Females			
	19 years to menopause	1000	1000	*700*
	Post menopause	1300	1200	*700*
	Males			
	19 - 65 years	1000	1000	*700*
	65+ years	1300	1200	*700*
Pregnant Women				
	(last trimester)	120	1000- 1300	*700*
Lactating Women		1000	1000 - 1300	1250

[a] Adequate intake; [b] Reference nutrient intake; * particularly during the growth spurt

Calcium and Osteoporosis: Gain in bone mass occurs throughout childhood; however, during adolescent growth spurt, the gain in bone mass, as well as, calcium retention is accelerated two to three times more than at younger ages in both boys and girls, The bone mineral content continues to increase beyond the growth spurt into the middle of.the third decade. Progressive increase in total body calcium have been shown in one study upto 30 years in female subjects of 19-30 years on an average calcium intake of 700 mg per day. Thus, peak bone mass may be achieved 5-10 years after longitudinal bone growth has been completed. Achievement of adult height is an indication of completion of longitudinal growth.

There is some data to show that increased calcium intakes in children beyond their habitual intakes could increase bone mineral density. What needs to be established is whether such increase in bone density could contribute to increased peak bone mass (i.e. maximum bone mass attained by the middle third decade). The other factor of importance contributing to increased bone mineral density and peak bone mass is weight bearing exercise. The current recommendations in fact focus on adequate dietary calcium intakes and exercise to promote acquisition of peak bone mass and density fracture risks due to osteoporosis at later ages can be reduced.

Accelerated bone loss with age is a consistent finding in both women and men. It occurs earlier in women than in men as decreased oestrogen production in menopause is associated with accelerated bone loss in women, estimated at 3% per year in the first five years after menopause. The effectiveness of calcium supplements in retarding bone loss in post menopausal women is not entirely settled. However, clinical trials in this area seem to indicate that supplements of calcium can have beneficial effect in slowing the rate of bone loss in post menopausal women.

The amounts recommended by different advisory groups differ considerably. It seems prudent to recommend that women with calcium intakes below 400 mg per day may benefit by increasing their dietary intakes or by taking supplements of calcium. This is supported by a study on two groups of post menopausal women, one with usual intakes less than 400 mg per day and the other with usual intakes between 400-650 mg per day. Calcium supplementation benefited the group with intakes less than 400 mg per day by slowing the rate of bone loss at several sites while supplements were not effective for the group with intakes between 400-650 mg per day.

The role of appropriate exercise, in addition to adequate calcium intake, must receive proper attention. The other nutrient in relation to calcium absorption and bone mineral density is vitamin D, about which we have already discussed earlier. It must however, be emphasized here that vitamin D nutrition is as important as that of calcium in relation to prevention of osteoporosis and fractures.

An important aspect that we shall discuss now is the relationship of calcium with blood pressure and what is the significance of calcium deficiency with respect

to hypertension.

Calcium and Hypertension: Chronic inadequate intake of calcium may play some role in etiologies of hypertension. Calcium deficiency has been linked to hypertension.

Numbers of epidemiological studies, animal experiments and human clinical studies have reported an inverse relationship between Ca intake and blood pressure. Meta- analysis of studies reveal that Ca supplementation (median intake lg of Ca) resulted in reduction in systolic blood pressure in selected hypertensive patients. People who appear to benefit from calcium therapy are those who have low calcium intakes, low ionized calcium concentration or elevated PTH and those who have low renin activity and are salt-sensitive.

The precise nature of the anti-hypertensive action of dietary calcium is not clear. Calcium has a membrane stabilizing vasorelaxing effect on smooth muscle cells. Calcium can exert its effect through other mechanisms also. Salt sensitive, low renin individuals exhibit low plasma ionized calcium concentration, increased urinary calcium excretion and elevated PTH and calcitriol. Further work is still waiTanted in this aspect.

It is, therefore, clear from our discussion above, that a positive calcium balance (i.e. net calcium retention) is required throughout life. A positive calcium balance is required throughout growth, particularly during the first 2 years of life and during puberty and adolescence. These age groups therefore constitute populations at-risk for calcium deficiency, as do pregnant women (especially in the last trimester), lactating women, post menopausal women and possibly, elderly men.

We had mentioned about calcium toxicity a little while ago. Hypocalcaemia, though rare, can result in the development of serious metabolic complications. A few of these are being discussed below.

Calcium Toxicity

Elevated blood calcium can occur in association with high parathyroid hormone, hyper- or hypothyroid conditions, bone metastasis, vitamin D toxicity, excess intake or absorption of calcium, Addison's disease and with thiazide diuretics. High blood calcium may be asymptomatic or can cause constipation, nausea and vomiting, increased urination, thirst, muscle weakness, kidney failure, irritability, confusion, psychosis and coma.

The role of calcium supplements in eliciting hypercalcemia has always been under scrutiny. Since the efficiency of absorption from large doses is poor, no adverse effects have been found with calcium supplements providing up to 2400 mg/day. However, at such high levels, iron absorption is reduced and risk of iron deficiency increases. A practical suggestion would be not to consume high dose of calcium with meals that provide most of the iron. Supplements of calcium do

not carry the risk for renal stones in normal individuals but can increase the risk in patients with renal hypercaliuria. In fact, it has been suggested that dietary calcium may protect against renal calculi because it binds dietary oxalate and reduces oxalate excretion.

In 1997, the Tolerable Upper Intake Level (UL) for Ca for adults was set at 2.5 g daily as a part of Dietmy Reference Intakes. Toxic effects of a high calcium intake have only been described when the calcium is given as the carbonate form in very high doses; this toxicity is caused as much by the alkali as by the calcium and is due to precipitation of calcium salts in renal tissue (milk-alkali syndrome). However, in practice, an upper limit on calcium intake of 3 g (75 rnmol) is recommended by the FAO/WHO 2004.

So far we have read about the properties, food sources, metabolism, requirements and the effects of deficient/excess intake for calcium in this section. We also read that the requirements and absorption of calcium and phosphorus are interlinked with each other. We shall now proceed our discussions with phosphorus, which we know is closely related to calcium.

9.6 PHOSPHORUS

Phosphorus is the second most abundant element in the human body, comprising 30% of the total mineral content. An adult human body contains approximately 600 g of phosphorus. Most phosphorus like Ca is stored in the bone and teeth in an inorganic metal state, the hydroxyapatite. The remaining 15% is distributed in soft tissues in both organic and inorganic form.

Before we proceed with the metabolism of phosphorus, let us quickly brief ourselves on the dietary sources.

Food Source

Phosphorus is widely distributed in food. Food phosphorus is a mixture of both organic and inorganic forms although the relative amounts vary with the type of food. Both animal and plant foods are important sources and include meat, fishpoultry, egg, milk and its products, nuts, legumes and cereals. 80% of phosphorus in grains is bound with phytic acid. In milk, 33% is in the inorganic form.

Let us now proceed to the absorption, transport and excretion of phosphorus.

Absorption, fransport and Excretion

As you have seen that food contains both organic and inorganic phosphorus, but most of it is absorbed in its inorganic form. Therefore, organically bound phosphorous is hydrolyzed in the lumen by intestinal phosphatases. However, organic phosphate of phytic acid may not be available. Phosphoms absorption occurs throughout the

small intestine, although duodenum and jejunum are important sites. Phosphorus absorption is efficient—60-70%. Ingestion of antacids containing magnesium or aluminium hydroxide can interfere with phosphorus absorption.

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It is important to note that unlike calcium, absorption efficiency of phosphorus does not increase on low intake nor any adaptive mechanism is available for the same. Most phosphoms is absorbed by passive concentration dependent process. However, a portion of phosphorus is absorbed by active transport, facilitated by calcitriol. Unabsorbed phosphoms is excreted in faeces. In plasma, phosphorus is distributed in different forms, as illustrated in Figure 9.1,

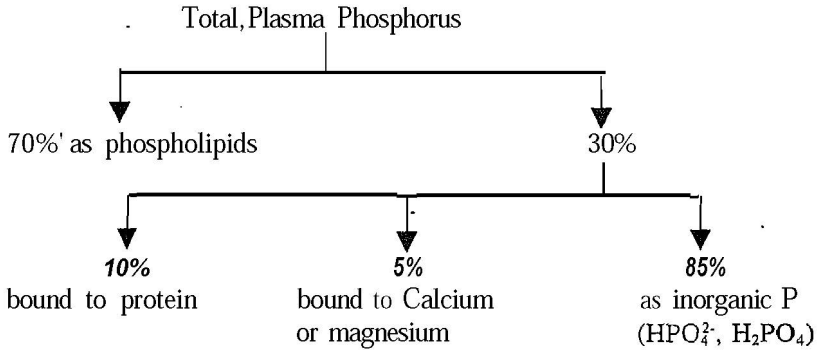

Figure 9.1: Phosphorous distribution in plasma

Inorganic phosphorus is also referred to as ultra-filterable phosphate and ranges between 2.5 and 4.4 mg/dl in adults. Excretion of endogenous phosphorus is mainly through kidney.

So far we have read' about the properties, food sources, absorption, transport and excretion of phosphorus. It would be important to note here that phosphorus shares similar homeostatic mechanisms with calcium and that the phosphate balance is largely maintained by the renal tubules. Keeping this in mind, read the subsequent discussions pertaining to Öe functions of phosphorus.

Functions

Distribution of phosphorus in body clearly explains that it functions as a structural component, as well as, has a role in metabolic reactions. Also both organic and inorganic forms are important. Important ftlnctions of both these forms are explained below:

Inorganic Phosphorus: The major functions of inorganic phosphorus include:

a) **Structural component of bones and teeth:** Phosphorus is a part of calcium phosphate in various crystalline. Ca forms required for ossification. (See section on functions of Calcium)

b) **Acid-base balance:** Within cells, phosphate is the main intracellular buffer.

$H_2PO_4 \rightleftharpoons H^+ + HPO^{2-}_4$

Organic Phosphorus: It is inyolved in the following reactions/components:

a) Structural component (f nucleic acids: It is important component of DNA and RNA.

b) Components of cell membrane: Phospholipids with their polar and non polar regions are important for the bilayer structure of cell membranes.

c) Component of coenzymes like NADP, TPP, PLP, coenzyme A, FAD, NAD.

d) Phosphorus is of vital importance in intermediary metabolism of the energy nutrients contributing to temporary storage and transfer of energy in the form of MP.

e) Many enzymatic activities are controlled by alternating phosphoiylation or dephosphorylation. Thus, it is required in regulating metabolism.

For all these functions, it is important to maintain normal level of inorganic phosphate in plasma. However, plasma levels of phosphate are not so closely controlled as those of calcium.

It would be important to note here that like calcium, phosphate metabolism is also regulated three hormones. These include:

Parathyroid hormone (PTH),

1,25-dihydroxyvitamin D (1,25-$(OH)_2D_3$), and

Calcitonin.

The PTH exerts its regulation primarily by way of the kidney, exerting a phosphaturic effect. When resorption of bones occurs under the influence of increased PTH, thecalcium is added to the blood while the phosphates are excreted in the urine.

Vitamin D stimulates intestinal absorption and enhances bone resorption. Its effect on renal handling of phosphate is thought to be indirect. The increase in calcium mediated by 1,25-$(OH)_2$ D_3 suppresses PTH secretion and enhances phosphate reabsorption in the tubules, as you may recall studying earlier under the calcium section.

Finally, let us get to know about the phosphorus requirements.

Dietary Requirements

We read in the previous section that the requirements of phosphorus are closely linked with those of calcium. The phosphorus requirements for different age groups

have been mentioned in Table 9.3 earlier. Phosphate requirements are fully met usually when diets provide adequate calcium as these two minerals generally occur together in foods.

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However, situations' may develop when the phosphate levels in blood and other tissues may increase or decrease beyond normal levels. Such disturbances in the phosphonts levels may develop with or without any effects in the calcium metabolism. We shall now brief upon the clinical conditions of hypo and hyper phosphaternia.

Deficiency and Toxicity

We shall firstdiscuss about low phosphorus levels in the blood. Inadequate phosphorus intake results in abnormally low serum phosphate levels (hypophosphatemia). The effects of hypophosphatemia may include loss of appetite, anaemia, -muscle weakness, bone pain, rickets (in children), osteomalacia (in adults), increased susceptibility to infection, numbness and tingling of the extremities, and difficulty in walking. Severe hypophosphatemia may result in death.

Because phosphorus is so widespread in food, dietary phosphorus deficiency is usually seen only in cases of near total starvation. Other individuals at-risk of hypophosphate!nia include alcoholics, diabetics recovering from an episode of diabetic ketoacidosis, and Starving or anorexic patients on refeeding regimens that are high in calories but too low in phosphorus.

High levels of phosphoms are rarely observed, but when they develop it results in the development of several complications. Let us review these in brief.

The most serious adverse effect of abnormally elevated blood levels of phosphate (hyperphosphatemia) is the calcification of non-skeletal tissues, most commonly the kidneys. Such calcium phosphate deposition can lead to organ damage, especially kidney damage. Because the kidneys are very efficient at eliminating excess phosphate frorn the circulation, hyperphosphaternia from dietary causes is a problem mainly in people with kidney failure (end-stage renal disease) or hypoparathyroidism.

When kidney function is only 20% of normal, even typical levels of dietary phosphorus may lead to hyperphosphaternia. Pronounced hyperphosphatemia has also occurred due to increased intestinal absorption of phosphate salts taken by mouth, as well as, due to colonic absorption of the phosphate salts in enemas.

In the section(s) above, we learnt about the properties, food sources, functions, absorption, transport, excretion, as well as, the deficiency and excess of calcium and phosphorus—the most significant macro minerals required by our body. In the next section we shall learn about magnesium, sodium, potassium and chloride.

9.7 MAGNESIUM

Magnesium (Mg) ranks fourth in overall abundance in body among the cations. It is also the least abundant among macro minerals, the total amount in the body being 25 g. Like Ca and P, this mineral is also present in the bones but unlike them which constitute 99% and 85% of the bones, respectively only 55-60% of total magnesium is located in the skeleton. Another 20-25% is found in muscles with remaining in other soft tissues. Only I % of total body magnesium is extracellular. Magnesium is closely associated with cells and is the 2nd most abundant mineral in cells after potassium. Let us brief ourselves regarding the food sources of magnesium.

Food Sources

Magnesium is widely distributed in variety of foods and beverages. In plants it is associated with chlorophyll. Thus, green leafy vegetables are excellent sources of magnesium. Most green vegetables, legume seeds, beans, tea, coffee, cocoa and nuts are rich in magnesium, as are some shellfis , spices, and soya flour, all of which usually contain more than 500 mg/kg fresh weight. Although most unrefined cereal grains are reasonable Sources, many highly-refined flours, tubers, fillits and most oils and fats contribute little dietary magnesium (<100 mykg fresh weight). Corn flour, cassava and sago flour, and polished rice flour have extremely low magnesium contents. Refining of whole cereals can reduce the magnesium content considerably (upto 80%).

We shall now learn about the absorption; transport and excretion of this nutrient.

Absorption, Transport and Excretion

Magnesium absorption to some extent is similar to that of Ca. Absorption of Mg occurs throughout the small intestine, although jejunum and ileum are important sites. It crosses the intestinal membrane by both active transport and passive diffusion. Colon may also play a role in its absorption. About 30-65% of dietary Mg is absorbed in healthy adults. Like Ca, absolption of Mg is also more efficient when its status is marginal or intake is low. Regulation of intestinal absorption is generally thought to occur only for active component of absorption, although mechanism is unclear. Because of chemical similarity of Mg to Ca, it is postulated that vitamin D could regulate its absorption. However, it appears that only large changes in vitamin D intakes could lead to alternations in Mg absorption.

As observed for calcium, some dietary factors influ nce absorption of Mg, although data supporting this is limited. High intakes of dietary fibre (40-50 g/day) lower magnesium absorption. This is probably attributable to the magnesium-binding action of phytate phosphorus associated with the fibre. However, consumption of phytate- and cellulose-rich products increases magnesium intake (as they usually contain high concentrations of magnesium) which often compensates for the decrease in absorption. The effects of dietary components such as phytate on

magnesium absolption are probably critically important only when magnesium intake is low. There is no consistent evidence that modest increases in the intake of calcium, iron, or manganese affect magnesium balance. In contrast, high intakes of zinc (142 mg/day) decrease magnesium absorption and contribute to a shift towards negative balance in adult males. Unabsorbed fatty acids present in 'high quantities (Steatorrhoea) may bind to Mg to form soaps, Lactose, fructose and protein appear to increase its absorption.

In the plasma, most magnesium is found free (55%), some is bound to protein (32%) while small amounts (13%) is cornplexed with citrate, phosphate or other ions. Magnesium homeostasis is maintained chiefly by controlling its excretion through urine. The kidney has a very significant role in magnesium homeostasis. Active reabsorption of magnesium takes place in the loop of Henle in the proximal convoluted tubule and is influenced by both the urinary concentration of sodium and probably by acid—base balance.

Contrary to calcium homeostasis which is under tight hormonal control, regulation of Mg homeostasis occurs chiefly through renal excretion. About 70% of serum Mg is filtered by kidney, but 95% of this is reabsorbed by a healthy kidney. When the dietary Mg intake is low, renal output of Mg is further reduced. When Mg intake is severely restricted in humans with normal renal functions, Mg output reaches lowest levels of 6 mg/ day (< 0.25 millimoles/day) within 5-7 days. Intake of diuretics increases Mg excretion. Similarly thyroid and aldosterone stimulate excretion while P TH inhibits excretion.

Magnesium plays some very important functions in our body. Let us understand the salient ones.

Functions

Like Ca, Mg too has a role in bone formation. Soft tissue magnesium functions as a cofactor of many enzymes involved in energy metabolism, protein synthesis, RNA and DNA synthesis, and maintenance of the electrical potential of nervous tissues and cell membranes. Of particular importance with respect to the pathological effects of magnesium depletion, is the role of this element in regulating potassium fluxes and its involvement in the metabolism of calcium. Some of the important functions of Mg are listed below:

1) Between 50% and 60% of body magnesium is located within bone, where it is thought to form a surface constituent of the hydroxyapatite (calcium phosphate) mineral component. Initially, much of this magnesium is readily exchangeable with serum and therefore represents a moderately accessible magnesium store which can be drawn on in times of deficiency.

2) Within cells, Mg is bound to phospholipids of the cell membrane (plasma, mitochondria, endoplasmic reticulum). It helps in membrane stabilization.

3) Mg is responsible for the structural integrity of the subunits forming

ribosomes. It also maintains double helical structure of DNA.

4) Intracellular free Mg^{+2} regulates ion movements. It modulates ion transport systems such as Ca pumps and Na-K-ATPase. These are most sensitive to depletion of body Mg* levels. The impaired activity of these ion pumps is likely to be responsible for the neuromuscular problems that are present during Mg deficiency. The defects would involve difficulty in maintaining the normal movements of Ca, sodium, potassium ions required for nerve conductions.

5) Mg is vital for energy production as it is required by ATP synthesizing protein in the mitochondria.

6) As intracellular component, it is essential for different enzyme reactions, as structural cofactor or an allosteric activator of enzyme activity.

   All ATP requiring kinases use ATP in the form of Mg-ATP complex. ATP chelates the Mg ion. Thus, phosphate donating substrate is not ATP but Mg-ATP complex e.g. enzymes in glycolysis.

Some enzymes require Mg-ATP as well as free Mg^{+2}. e.g. carbomyl phosphate synthase of urea cycle.

Mg* is required by various enzymes participating in the synthesis of carbohydrates, lipids. Mg ions are also required by enzymes that are used in transmitting signals within cells. These enzymes include adenylate cyclase which catalyzes phosphorylation of number of proteins / enzymes, thus regulating metabolic pathways. Because of its function in the formation of cAMP, Mg is involved in mediating the effects of . numerous hormones.

Having looked at the functions of magnesium, next let us review the dietary requirements and the asqessment of magnesium status in the body.

Assessment of Magnesiunt Status and Dietary Requirements

In order to estimate Mg requirements and establish relationship between magnesium intake and deficiency, it is important to have reliable marker/s for diagnosing Mg depletion and its severity. Several indicators of Mg status have been described. These include

1) Total Serum Mg: Serum Mg concentration are routinely measured to assess its status. However, extracellular Mg represents only 1% of. the total Mg and appears to be homeostatically regulated. Normal serum levels may occur despite intracellular deficit, But when serum Mg is below normal, the intracellular Mg is definitely lower. Thus, low serum levels can help to detect advanced Mg deficiency. It is suggested that level of ionized Mg may. be more reliable and relevant determinant of deficiency than the total serum Mg, as protein bound Mg is subjected to more variations.

2) Magnesium levels in erythrocytes and lymphocytes: These measures appear to provide a more accurate assessment of body Mg status than serum Mg levels. Peripheral lymphocyte Mg concentration conelate with skeletal and cardiac muscle Mg concentration. Erythrocyte Mg concentration may reflect long term Mg status due to longer span of RBC.

3) Level of Magnesium in urine: Urinary Mg excretion decreases with Mg deficiency. The refore, Mg excretion before and after administration of an intravenous Mg load could be used to assess status.

As is evident from the above discussion, most methods are expensive, time consuming and not applicable to large populations.

Next, let us learn about the magnesium requirements. Since plant foods are particularly high in magnesium, on a vegetarian diet with plenty of green vegetables, it is unlikely that Mg deficiency will occur. No specific recommendations are made by ICMR for Mg intakes in Indians. However, the FAO/WHO 2004 recommended nutrient intake for magnesium is given in Table 9.5. FAO/WHO recommend 220 and 260 mg magnesium per day for adult females and males, respectively.

Table 9.5: Recommended nutrient intake (RNIs) for magnesium, by group

Group[a]		Assumed Body Weight (kg)	RNI (mg/day)
Infants	0 -6 months		
	Human Milk-fed	6	26
	Formula-fed	6	36
	7 - 12 months	9	54
Children	*1* - 3 years	12	60
	4 - 6 years	19	76
	7 - 9 years	25	100
Adolescent			
	Females 10 - 18 years	49	220
	Males 10 - 18 years	51	230
Adults	Females		
	19 - 65 years	55	220
	65+ years	54	190
	Males		
	19 - *65* years	65	260
	65+ years	64	224

[a] No increment for pregnancy: 50 mg/day increment for lactation.

Although rare, magnesium homeostasis may get disturbed due to alterations in the metabolism of other nutrients or due to an underlying disease condition. Let us find out more about magnesium deficiency and toxicity

Magnesium Deficiency and Toxicity

Deficiency of magnesium is rare for two reasons: firstly, the mineral is widely distributed in the foods, secondly, kidney is able to adjust re-absorption of filtered magnesium to body needs. However, Mg depletion occurs in 'various conditions,

which either impair its intestinal absorption or increase its urinary excretion.

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Studies have shown that a decline in urinary magnesium excretion during protein— energy malnutrition (PEM) is accompanied by a reduced intestinal absorption of magnesium. The catch-up growth associated with recovery from PEM is achieved only if magnesium supply is increased substantially. Most of the early pathological consequences of depletion are neurologic or neuromuscular defects, some of which probably reflect the influe ce of magnesium on potassium flux within tissues. Thus, a decline in magnesium status produces anorexia, nausea, muscular weakness, lethargy, staggering and if deficiency is prolonged, weight loss. Progressively increasing with the severity and duration of depletion are manifestations of hyperirritability, hyperexcitability, muscular spasms, and tetany, leading ultimately to convulsions. An increased susceptibility to audiogenic shock is common in experimental animals. Cardiac arrhythmia and pulmonary oedema frequently have fatal consequences. It has been suggested that a suboptimal magnesium status may be a factor in the etiology of coronary heart disease and hypertension but additional evidence is needed.

Hypomagnesernia associated with deficiency represents a plasma Mg levels of less than 1.5 mg/dl. It leads to impairment in Ca and K homeostatsis. Hypocalcernia and hypokalemia have been observed in both experimentally produced and disease-related Mg deficiency. These disturbances are partially caused by hypomagnesemia induced changes in the production and function of P TH. Reduced serum Mg initially stimulates parathyroid gland to produce more PTH, but as deficiency becomes more severe, the sensitivity of parathyroid gland to a low serum Ca concentration is impaired and level of PTH is low in relation to degree of hypocalcernia.

Decreased Mg status has been suggested as a factor contributing to the pathogenesis of several chronic diseases. Both dysrhythmias and myocardial ischemia have been attributed to low Mg intakes. Hypomagnesemia in diabetes may be one of the risk factors in the development of diabetic retinopathy.

Studies of Mg use in patients with acute myocardial infarction suggest a reduced mortality with rapid post myocardial infarct Mg treatment. Oral supplements in middle aged and elderly women with mild to moderate hypertension has been found to reduce systolic and diastolic blood pressure. However, further research is warranted with respect to the use of Mg supplements.

Let us now brief upon toxicity of magnesium.

It is clear from the dbove discussion that exdessive intake of Mg is not likely to cause toxicity except in people with impaired renal function. Excessive intakes of Mg salts such as $MgSO_4$ can lead to diarrhoea.

In this unit we have read about some important minerals required by our body. In continuation with the same we shall discuss in detail the various aspects of a few other minerals i.e., sodium, potassium and chloride which are often also referred

to as electrolytes. The significance of these electrolytes lies in their contribution towards maintaining the fluid shift mechanism inter and extracellular. Let us read about these minerals in detail.

NOTES

9.8 SODIUM, POTASSIUM AND CHLORIDE

Claude Bernard was the first to draw attention to the internal environment (milieu interior), referring to the extracellular fluid (ECF)—a medium in which all cells are bathed. Homer presented a convincing argument that "the extracellular compartment contains constituents and concentrations similar to the precambrian seas, which presumably bathed the earliest piimordial unicellular organisms". As we know that the total body water (TBW) in a 70 kg man is 60% of the body's weight i.e. about 40 litres. Two-thirds of this resides inside the cells, i.e. the intracellular fluid (ICF), while one-third is in the extracellular compartment (ECF) that bathes the cells. A minor portion about 1 litre is present in the intestines and anterior chambers of the eyes. The most important electrolytes in the ECF are sodium (135-145 millimoles/L and chloride (98-108 millimoles/ L). The concentration of potassium in the ECF is very low, 3.5-4.5 milli moles/L, however, potassium is the predominant cation (K+) in the ICF, whereas sodium and chloride in the ICF are negligible. Muscle cells have much higher water content than the others and therefore ICF and TBW are closely related to lean body mass.

The three macro minerals, Na, K and Cl are related to each other and hence will be discussed together, which makes it easier to appreciate their roles in metabolism. You know that Na and K are monovalent cations (ions that carry a positive charge) while Cl is a monovalent anion (ions that can-y a net negative charge). All three are known as electrolytes as their ions are used for generating electric charge differences across the plasma membrane of most cells.

Na constitutes 2%; K 5% and Cl 3% of the total mineral content of the body. These minerals exist as ions in the body fluids and are principal electrolytes in the body. K is a major intracellular electrolyte while Na and Cl are present in the extracellular fluids. Let us learn about their principal food sources.

Food Sources

The major source of sodium and chloride is common salt added to our food in the form of sodium chloride. Naturally occurring sources of sodium are milk, meats, eggs and most vegetables. In addition, food additives used in processed foods such as baking powder, preservatives etc. contribute towards dietary sodium intake. Therefore, it is important to take note of all these while calculating the sodium content of diets, On the other hand, potassium is abundant in unprocessed foods, fruits, many vegetables and fresh meats. Also many salt substitutes contain potassium instead of sodium. Absorption of these electrolytes is governed by several factors including body fluids, honnones and presence of other nutrients, to name a few. We shall now highlight the salient features of absorption, transport

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Absorption, Transport and Excretion

All these three elements are readily absorbed from the small intestine with almost 90- 100% efficiency. They are excreted primarily via urine, although faeces and sweat are other routes of elimination. It is important to note that profuse sweating can result in substantial losses of these elements. Both sodium and chloride are absorbed by the following mechanisms:

a) Sodium glucose and sodium amino acid co-transporters exist in the apical membranes of enterocytes and mediate sodium uptake coupled with glucose or amino acid uptake. Look at Figure 9.2, which illustrates this mechanism.

As seen in Figure 9.2, sodium and glucose/amino acid both bind to the carrier which shuttles them from the outer surface to the inner surface. Here, both sodium and glucoselamino acid are released from the carrier and carrier returns back to the outer membrane. The absorbed Nac is then pumped out across basolateral membrane by Na+/K+-ATPase pump while glucose diffuses across by facilitated transport. Thus, glucose and Nac are co-transported. Recollect that the oral formula used to correct diarrhoeal fluid losses always contain glucose and sodium chloride in a single combination. This is the reason why.

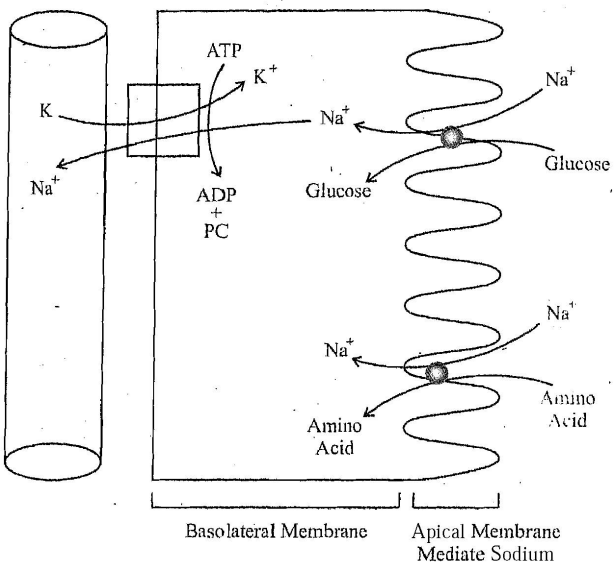

Figure 9.2: Intestinal absorptioh of sodium

b) Another mechanism proposed is electroneutral Na^+ and Cl- co-transport. This is based on the observation that significant proportion of sodium uptake requires presence of chloride and vice-versa. Na+ and Cl- enter the enterocytes and are exchanged for H^+ and HCO_3 respectively. Figure 9.3 illustrates the sequence of events.

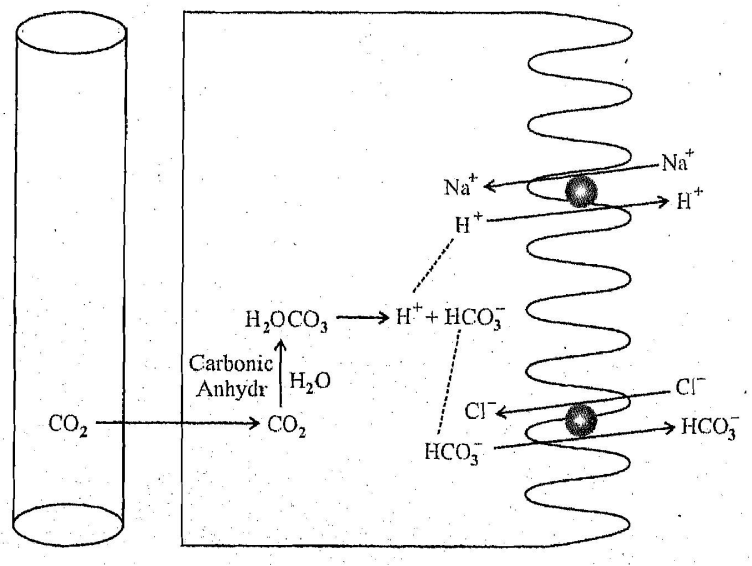

Figure 9.3: Absorption of sodium and chloride

So far we have read about the absorption of sodium and chloride. What about potassium? How is it absorbed? Let us read further to brief ourselves on the mechanism linked to its absorption.

Potassium is absorbed in thesmall intestine as a consequence of bulk fluid absorption. Both sodium and potassiuin are also absorbed in the distal colon. Sodium enters the luminal membrane of colonic mucosal cells through Na+ channels and pumped out across the basolateral membrane by Na+ / K+-ATPase pump. On the other 'hand, absorption of potassium in the colonic cells is mediated by K+/H+-ATPase pump. This exchanges intracellular H+ for Ki. Potassium then diffuses across the basolateral membrane via the K + channel.

We will now discuss about the regulation of normal levels of sodium and potassiuin in the body and a few details about their excretion.

Regulation and Excretion

Renal excretion and retention of these elements is closely regulated. The total content of body sodium especially the concentralion in the extracellular fluid (ECF) is under homeostatic control. Let us see how body regulates Na content in ECF.

Of the total Na filtered through the glomemli, over 99% is reabsorbed by the kidney tubules. A large proportion of this reabsorption takes place in the proximal tubule, but the final adjustment is achieved by the cells of distal tubules and collecting ducts. When the need for sodiuin by the body increases, several mechanisms such as decreased arterial volume, low blood pressure, decreased sodium at distal tubular exchange site, low plasma levels of sodium alert kidney. In response, specialized tissue of renal cortex release renin in the blood. Renin converts pro-hornlolie angiotensinogen secreted by liver to angiotensin Tl This, in turn, stimulates the adrenal cortex to produce aldosterone, which increases sodium re-absorption. The

accompanying water retention helps, 10 normalize the arterial volume thereby suppressing further renin production.

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You must remember here that the regulation of chloride is achieved indirectly through sodium regulation. We need to read further to understand the details of potassium.

As observed for sodium, the maintenance of K balance also depends on the kidney. Unlike sodium, the transport of K is bi-directional during the passage of the filtrate through nephron. In the proximal tubule and loop of Henle, major portion of filtered K is reabsorbed. In the distal tubule, it can be reabsorbed from the filtrate or can be secreted into it depending on the body's need. Aldosterone acts reciprocally on Na and K You have just seen that this hormone stimulates Na reabsorption, but it accelerates the secretion of K and thus increases its excretion. Other factors that increase K excretion are increased serum K + concentration and alkaline PH.

It is important to note that body's ability to conserve Na by restricting loss in the urine is more efficient than its ability to conserve K. Also, sodium is absorbed more efficiently from the gastrointestinal than K, Therefore, K deficiency will appear before sodium deficiency, However, dietary deficiency of these minerals does not normally occur. Deficiency is more commonly caused by vomiting and diarrhoea, which results in excessive loss of these electrolytes.

You may have come across the messages that convey the significance of promptly replenishing the electrolyte losses such as those associated with acute dirrhoea, vomiting, profuse sweating etc. Why is it important to replenish the lost reserves? This is perhaps in view of the fact that these electrolytes perform some very critical functions in the body. Our subsequent discussion highlights some of the salient functions.

Functions

So far you have learnt that most minerals participate in important functions of body as they support the activity of specific enzymes. In striking contrast to these, Na+ and K* mostly function by changing their location i.e. by passing from one side of the plasma membrane to other. These electrolytes are involved in number of functions as enumerated herewith.

These electrolytes are required for maintenance of total body water and water balance.

- They are major determinants of osmotic pressure and electrolyte balance.
- They are involved in the maintenance of acid—base balance.

- They are major determinants of membrane potential. As you know that sodium is present in higher concentration out side the cell while K within the cell. This intracellular/extracellular difference in their concentration is responsible for the electrical potential gradient across membranes of all cells with nerve and muscle cells having highest gradients. This is critical in signal transmission across the nerve cells, muscle contraction and relaxation, synaptic transmission.
- They are required for the transport of glucose, amino acids within enterocyte.

The plasma membrane enzyme Na+/K+-ATPase is important for many functions such as water balance, membrane potentials and transpon of nutrients.

In addition to the above functions, potassium is required for normal growth. Early experiments in intact cells have demonstrated a linear relation between intracellular potassium concentration and cell growth and incorporation of amino acids into protein. Sodium is involved in the formation of mineral apatite of bone while chloride is a constituent of gastric juice.

Next, we shall proceed over to the states of deficiencies and excess for these electrolytes.

Deficiency and Excess of Electrolytes

The symptoms associated with deficiency and excess intake of each of the three electrolytes is described in this section. We will begin with the hypo and hypernatremic states associated with sodium levels in the body.

Hyponatremia and Hypernatremia: Serum concentration of sodium is normally regulated within the range of 135 to 145 milimole per litre (mM/L). Hyponatremia is defined as a Na level under 130 mM/L. When plasma Na level falls below 120 mWL, symptoms such as headache, confusion, seizures and coma can occur. Hyponatremia can arise from shift of water from cells to extracellular compartment, which is induced by an increase in solutes in plasma for example increased plasma glucose in diabetes can result in the shift of water from ICF to ECF, diluting the Na concentration. Hyponatremia is also induced by renal failure when kidney's impaired ability to excrete waste products results in build up of solutes in plasma. It can also occur from an overall decrease in body, Na, as occurs during diarrhoea and vomiting. Rare instances of hyponatremic dehydration have been reported in sports persons rehydrated only with water.

Hvpernatremia occurs less commonly and is defined as serum sodium level above 145 mM/L. The initial symptoms include irritability, lethargy and restlessness. Seizures and death may occur when plasma levels rise above 160 mM/L.

Hypernatremia occurs with loss of water that is dispropofiionately greater than sodium and is associated with excessive sweating and hyperventilation. It can also occur when thirst mechanism is impaired because of damage to hypothalamus.

Next is discussed the states of potassium deficiency and excess.

Hypokalemia and Hyperkalemia: Normal serum K ranges from 3.5-5 mM/L. Hypokalemia or low plasma K levels can occur with a net shift of K from the plasma to the cells. This shift can occur in alkalosis. Overall depletion of body's K, which occurs in vomiting, prolonged fasting can also result in this shift. Mild hypokalemia results in weakness and muscle cramps and can cause arrhythmias in patients with heart diseases. Serve hypokalemia (<2.5 mM/L of K) can result in paralysis.

Hyperkalemia occurs when serum K levels are greater than 5 m M/L. High plasma K results in cardiac arrhythmias. A K level of 8.0 m WL can cause cardiac arrest and death. Hyperkalemia can occur in severe acidosis when the activity of Na+/ K+- ATPase is inhibited resulting in redistribution of K. It can also occur in severe kidney diseases where ability to excrete K is impaired especially if K consumption is not restricted and patient is experiencing tissue or RBC breakdown.

So then we have reviewed the deficiency symptoms and those linked with excess intake of these electrolytes. As for the recommendations for these electrolytes, no specific recommendations are made.

With this, we end our study of sodium, potassium and chloride.

So far we have learnt about the general and specific properties of several minerals. It is clear from the discussions above that several factors influence the metabolism of these minerals. Let us learn about this aspect in little more detail.

9.9 INTERACTIONS OF MACROMINERALS WITH OTHER NUTRIENTS

Various nutrients interact with minerals thereby affecting their bioavailability. These interactions occur at different sites in the body including gastrointestinal tract, during transport, at the level of storage or in the kidneys.

Most of the minerals interact with other nutrients in the intestine which either increase or reduce their absorption. These interactions which occur in the gastrointestinal tract have been covered for Ca, P, and Mg earlier under the section on absorption. The interactions which occur at other sites are briefly enumerated herewith.

- Calcium excretion through kidneys has been shown to be influenced by the levels of other minerals. Increased potassium (K) reduces urinary loss o? Ca, thereby conserving the mineral. On the other hand, sodium load (mmol/ or 2.3 g/day) increase urinary Ca excretion. In post menopausal women urinary sodium excretion was negatively correlated which changes in hip bone density.
- Although increased phosphorous level reduces urinaly losses of Ca, animal

studies have indicated that low Ca : P ratios lead to progressive bone loss due to phosphoms induced stimulation of PTH release.

Ca and Mg interact at the level of. kidneys. Both minerals use overlapping transport systems in the kidney and thus complete with each other for reabsorption.

- Nig may mimic Ca by binding to calcium binding sites. The ratio of calcium and magnesium has been shown to affect muscle contraction. Magnesium may compete with Ca for non-specific sites on troponin C and myosin

  Normally Ca binding initiates acetyl choline release and smooth muscle contraction. However, binding of Mg prevents Ca binding and inhibits its contraction.

- In blood coagulation, Ca and Mg are antagonistic, with Ca promoting the process and magnesium inhibiting it.

  A close relationship also exists between Mg and K. Mg appears to be necessary for the function of Na+/K+ -ATPase. Therefore, deficiency of Mg would lead to impaired pumping of sodium out of the cell and the movement of potassium into the cell.

Thus, above discussion emphasizes the need of consuming diets containing appropriate amounts oi all the nutrients. Prolonged use of a nutrient supplement or fortification with a single nutrient can offset the balance thereby affecting the bioavailability and physiological functions of nutrients.

In this unit, detailed discussions have been carried out for various macro minerals. We shall continue with further discussions on other nutrients such as iron, zinc, copper and selenium in the next unit. Now try to attempt the check your progress exercise 2 to make your concepts clear.

9.10 LET US SUM UP

In this unit, we learnt about calcium, phosphorous, magnesium sodium, potassium and chloride which are the major macro minerals required by our body. All these macro minerals constitute an important part of our daily diet and perform both structural and metabolic functions in the body. Most minerals support the activity of specific enzymes and are thus involved in catalytic function. However, Na and K majorly function by changing their location i.e. from one side of plasma membrane to other.

Concentrations of most minerals especially in the plasma are maintained within a narrow range. Regulation occurs either at the level of absolption or excretion or storage. Also, these minerals interact with each other and other nutrients thereby influencing their bioavailability. Therefore, there is a need to consume diets containing appropriate amounts of all the nutrients.

9.11 GLOSSARY

Achlorhydric patients : patient with a lack of hydrochloric acid in thestomach.

Enterocytes : is a type of epithelial cell of the superficial layer of the small and large intestine tissue.

Wydroxyapatite : it is the major component, and an essential ingredient,of normal bone and teeth. It is hy droxyapatite that makes up bone mineral and the matrix of teeth.

Resorption : dissolution of bone calcium.

Vasodilation : is the process where blood vessels in the bocly become wider following the relaxation of the smooth muscle ill the vesscl wall.

NOTES

9.12 CHECK YOUR PROGRESS

1) Mention important differences between macro and micro minerals.

2) Explain the following

   a) Elderly people are more vulnerable to fractures.

   b) Plasma Ca levels cannot be used to assess calcium status.

3) Enumerate the key functions of electrolytes.

NOTES

UNIT

10
MICRO MINERALS

STRUCTURE

10.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

differentiate between macro and micro minerals,

list important food sources of micro minerals,

describe the absorption and metabolic fate of each mineral,

explain the nutritional and biochemical role of various micro minerals and relate them to physiological functions and symptoms of inadequate intakes, and

select appropriate methods for assessing status.

NOTES

10.2 INTRODUCTION

The last unit focused on the macro minerals. Now in this unit we will study about the micro minerals, namely, iron, zinc, copper, selenium, chromium, manganese, iodine and fluorine. We will study the food sources, functions, metabolism and methods of assessing status of these important micro minerals.

10.3 MICRO MINERALS-AN OVERVIEW

Micro minerals are those minerals, which comprise less than 0.01% of the total body weight and are required in concentrations of one part per million or less. Initially, these minerals were also referred to as 'trace minerals' or 'trace elements' as their concentrationin tissues were not easily quantified by early analytical methods. A trace element/mineral, as you may be aware, can be defined as a chemical element present in minute quantities; especially one used by organisms and held essential to their physiology. A micro mineral or a micro nutrient, on the other hand, is an organic compound essential in minute amounts for the growth and health of an animal.

Like macro minerals, micro minerals must also be present in the body in optimal range for normal functioning. Whenever, the concentration is too low or too high, the body functions are impaired. The functions and routes of metabolism for some micro elements are well established both in animals and humans while for others, the data are available only from animal studies. They normally function as a cation (ion with a positive charge) complexed with organic ligands or chelators. Proteins are the most important chelators. Besides these, porphyrin (the ring structure present in haemoglobin) and corrins (the ring structure in vitamin B12) are other important chelators. As components of enzymes and proteins, these minerals frequently participate in redox reactions (reactions which involve the transfer of electrons) with the metal often functioning as the electron can-ier. However, minerals such as zinc and manganese along with macro elements calcium and magnesium, perform non-redox functions in proteins and enzymes. Since many of the micro minerals share common mechanism for absorption, they compete with each other for absorption in the small intestine.

Thus, excess of one micro element can aggravate the deficiency of another. Iron and zinc are the best known examples.

With this basic overview, we shall get to know about micro minerals in greater detail in the subsequent section(s). We begin our study with iron.

10.4 IRON

Iron was a familiar metal even in the ancient civilization. In India, iron implements

made their appearance in between 1300-1000 BC and in due course, iron was used in a variety of cookery utensils. The presence of leached iron, especially when acidic foods were cooked in such utensils, was considered to be a significant contributor to dietary iron. The most important clinical application of iron was described in the 17th century, for treating "chlorosis"—a condition that resulted from severe iron deficie cy in adolescent females in whom the dietary iron intake was only 4-3 mg/day as against the average iron content of 8-11 mg/day in normal persons. Major aspects of iron metabolism were elucidated by 1960 and today iron is one of the most investigated minerals in nutrition. Let us read further to understand the importance of iron in maintaining good health.

We all associate iron with its presence in blood and that its deficiency results in low haemoglobin levels and hence anaemia. But is iron present only in blood? Of course not. In our subsequent discussion, we will learn about the iron stores in the human body.

Total Body Iron

In humans, the total quantity of iron in the body varies with haemoglobin concentration, body weight, gender and the amount of iron stored in various tissues. Approximate distribution of body iron is shown in Table 10.1.

Table 10.1: Distribution of body iron in different compartments

Compartment	Iron Content (mg)	Total Body Iron %
Haemoglobin Iron	2000	67
Storage Iron	Varies from 200 - 1000	627
Tissue Iron: Myoglobin	130	3.5
Enzyme Iron	8	0.2
Other-transport Iron & labile pool	83	2.28

Source: Modem Nutrition in Health and Disease 8th Ed., 1994.

You may have observed in Table 10.1 that maximum amount of iron is incorporated in haemoglobin. The amount of storage iron shall depend upon the dietary iron consumed and its bioavailability. It would be interesting to note here that iron can exist in a number of oxidation states ranging from Fe_2^- to Fe_6^+ .You inust also remember that in the human body and food, occurs generally as fenic (Fe^{3+}) and ferrous (Fe_2+) iron. We have so far discussed aboul the presence of iron in the body. Let us now quickly find out about the presence of iron in food i.e. learn about the food sources of iron.

Food Sources

Iron is found in foods in one of the two forms i.e. haem or non-haem. In the human diet, the primary sources of haem iron are the haemoglobin and myoglobin from consumption of meat, poultry and fish whereas non-haem iron is obtained from cereals, pulses, legumes, fruits and vegetables. Dietary non-haem iron accounts for about 85% of the total iron intake even among non-vegetarians. The good plant and animal food sources of iron are shown in the Table 10.2 (a) and (b).

Table 10.2 (a): Sources of haem iron and their content (mg)

Haem Iron Sources	Fe Content
Chicken liver	7.5
Chicken	1.1
Eggs	1.1
Salmon	1.0

Source: Nutritive value of Indian foods by C. Gopalan, B.V. Ramasastri, S.C. Balasubramanium, revised and updated by B.S. Narasinga Rao, Y.. G. Deosthala and K.C. Pant, NIN, 1989.

Table 10.2(b): Sources of non-haem iron and their content (mg/100)

Non-haem Iron Sources	Fe Content
Dried apricots	5.5
Almonds	1.3
Raisins	3.5
Soybeans, Tofu	1.9
Spinach	3.1
Wheat germ	0.9
Kidney beans	2.5
Baked beans	1.5
Broccoli	0.5
Lentils	6.0

Source: Nutritive value of Indian foods by C. Gopalan, B.V. Ramasastri, S.C. Balasubramanium, revised and updated by B.S. Narasinga Rao, Y. G. Deosthala and K.C. Pant, NIN, 1989.

Let us read further to find out as to how dietary iron is digested, absorbed, transported, utilized and excreted from the human system or in other words, how are. adequate levels of iron maintained in different body compartments.

Metabolism Iron

In this sub-section, we will study how body gets its iron supply, how iron is transported and utilized by the various tissues and how iron balance is maintained.

Like other minerals, we obtain iron from the diet, which is absorbed from the gastrointestinal tract. A unique feature of iron metabolism is that the body re-utilizes quantitatively the iron released from the degradation of erythrocytes, with

very little being excreted. Hence, it is very frequently mentioned that once iron enters the body, the body holds on to it tenaciously. We will first learn how dietary iron is absorbed and then review how the iron is re-utilized.

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Absorption of Iron

Before it can be absorbed, iron whether it is in the form of haem or non-haem. must be released from the foo& matrices where it is bond with other constituents. Proteases (the enzyme) in the stomach and small intestine hydrolyze haem iron from the globin portion of haemoglobin or myoglobin. In the case of non-haem iron, gastric secretion including HCI and pepsin aid its release from food components. Most non-haem iron is present in the ferric form which is reduced to ferrous form in the acidic environment of the stomach. However, as the ferrous iron passes into the small intestine (alkaline pH), some Fe^{2+} may be oxidized to become ferric iron. Following its liberation from food components, absorption' takes place. Like other minerals, iron is also absorbed in duodenum and upper jejunum. The process of absorption is divided into three phases:

i) Iron uptake by enterocytes (epithelial cell of the superficial layer of the small and large intestine tissue)

ii) Intra enterocyte transport

iii) Storage and extra enterocyte transport.

The mechanism of absorption differs for non-haem and haem iron and therefore they will be dealt separately. Let us have a look at the non-haem iron absorption first.

a) Mechanism of Non-haem Iron Absorption

We will discuss all the three phases one by one.

i) **Uptake of iron by enterocytes:** Ferrous iron traverses the brush border of the intestine better than the ferric iron. The mechanism of absorption of the latter is not clear but it is postulated that it binds to lurninal binding proteins. Mucin, a small protein made in the intestinal cells and released into the gastrointestinal tract, is thought to facilitate iron absorption. It binds multiple Fe3+ions at an acidic pH and maintains its solubility even in alkaline pH and thus aids in its absorption. After traversing the brush border, iron binds to the receptor on the luminal surface of enterocyte and is transported inside the cell.

ii) **Intra enterocyte transport:** In the enterocyte, the absorbed iron can have one of the following metabolic fates:

transported through the enterocyte into the blood, and

stored in the enterocyte for future use or elimination.

Iron is transported through the enterocyte to the baso-lateral membrane by iron

binding protein— mobilferrin. Mobilferrin can also bind to Ca, Cu and Zn. The multiple metal ion-binding properties of mobilferrin may be partially responsible for interactions. between these minerals at absorptive surface.

The iron which is not transported across the cell for release is stored as ferritin in mucosal cells. If required for the body, it is released for transport. If not needed, the iron remains as ferritin and is excreted when mucosal cells are sloughed off in the lumen, Thus, ferritin in the enterocyte acts as an 'iron sink', trapping excess iron and removing it via intestinal excretion.

iii) **Extra enterocyte transfer:** Little is known about iron transport across the baso- lateral membrane. After crossing the baso-lateral membrane, it binds to plasma transport protein transferrin. Iron is oxidized before it can bind to transfemn. This is brought about by ceruloplasmin, a Cu-containing protein. The process has been depicted in Figure 10.1.

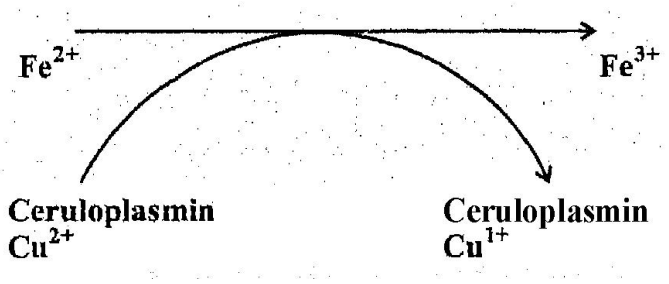

Figure 10.1: Oxidation of iron

Next, we shall review the mechanism of absorption of haem iron.

b) Mechanism of Absorption of Haem Iron

Haem iron is soluble in the alkaline environment of the intestine. It binds to the receptor on the enterocytes and is internalized. After entering the mucosal cell, haem is degraded to iron, carbon monoxide and bilirubin IXa by the enzyme haemeoxygenase. The liberated iron is then treated in the same manner as is the non-haem iron.

We have read in the previous units that whatever may be the quantity of a particular nutrient that we may consume, the entire amount may not get digested and absorbed (bioavailable) due to varied reasons. Let us see what factors affect the bioavailability of dietary iron.

Factors affecting Absorption & Dietary Iron

Haem iron is more bioavailable than non-haem iron because it is absorbed intact as a soluble complex by endocytosis (process whereby cells absorb material, molecules such as proteins, from outside by engulfing it with their cell membrane). Non-haem iron, on the other hand, forms insoluble complexes with many components concurrently present in the diet, rendering the iron unavailablefor mucosal uptake.

The absorption of iron also depends on the iron status of the individual and on the availability of an iron-binding mucosal transport protein (transferrin) to facilitate the uptake from the intestines.

NOTES

There are mainly four factors that determine iron bioavailability/ absorption from the diet. These include:

i) Form of iron; whether haem or non-haem

ii) Solubility; specially of the non-haem iron compounds

iii) Other dietary factors; inhibitors and enhancers

iv) Iron status of the individual

Our subsequent discussions will elaborate upon each of these aspects.

i) **Form of Iron:** We have read earlier that iron in foods occurs either as haem or non-haem iron. Haem iron comprises of iron in combination with porphyrins and is found only in the flesh foods in the form of haemoglobin and rnyoglobin. Muscle meats are therefore good sources of haem iron. Haem iron is absorbed to a much greater extent than non-haem. Haem iron absorption is generally 2- 3-fold higher than non-haem iron absorption. The average absorption of haem iron from meat-containing meals is about 25%. The absorption of haem iron can vary from about 40% during iron deficiency to about 10%during iron repletion. Haem iron can be degraded and converted to non-haem iron if foods are cooked at a high temperature for too long. Iron absorption is not affected by other dietary factors except calcium which has been shown to depress haem iron absorption. In addition to providinghigher bioavailableiron, haem iron compounds also enhance non-haem iron absorption. Further, non-haem iron absorption in healthy adults may vary from less than 1% to about (P/o depending on the composition of the diet,

The next factor that is being discussed is the solubility of the iron/its complex with other substances.

ii) **Solubility:** Solubility is crucial for non-haem iron absorption as the inorganic iron salts have to be solubilized in the intestine for the iron to be taken up by the muscosal cells. The acidic pH of the stomach makes iron soluble. However, as the chyme passes into the small intestine, the rising pH tends to precipitate iron as femc hydroxide complexes, The presence of ascorbic acid and other organic acids in the small intestine solubilize to chelate the iron so that it can be absorbed. Ferrous salts are more soluble than ferric salts and are therefore better absorbed.

iii) **Inhibitors and Enhancers:** Phytates and fibre from whole grain cereals, tannins and polyphenols in tea, oxalates in green leafy vegetables like spinach and excess calcium taken as supplements can all depress non-haetn iron absorption significantly, by forming insoluble components. The Indian

vegetarian diet consisting predominantly of cereals and pulses, high in phytates, has a low iron bioavailability. This is further compromised when tea is drunk with a meal, as polyphenols in tea depress iron absorption. Iron absorption from wheat has been reported to be 5%. However, when tea is taken with a breakfast meal comprising of wheat chapattis and potato vegetable, the reponed absorption has been only 1.8%. Ragi balls or sorghum breakfast with potato vegetable and tea resulted in only 0.8-0.9% absorption of iron.

On the contrary, ascorbic acid is a potent enhancer of iron absorption. Addition of orange juice containing 40-50 mg ascorbic acid to a breakfast meal consisting of bread, eggs and tea was found to increase iron absorption from 3.7% to 10%. Thus, ascorbic acid can counter the inhibitory effect of tannins or phytates, producing a 2-3 fold increase in iron absorption.

Thus, ascorbic acid can enhance iron absorption in a number of ways. Firstly, it reduces insoluble ferric iron to soluble ferrous iron; secondly, ascorbic acid forms low molecular weight chelates with iron that remain soluble in the intestine; thirdly, ascorbic acid-iron chelates preferentially release the iron for absorption to the brush border. Together, these mechanisms ensure that dietary iron is well absorbed in the presence of ascorbic acid.

Other factors known to enhance iron absorption are meat and flesh foods and some amino acids such as cysteine.

The best way to increase bioavailability of iron in Indian vegetarian diet is to consume adequate amounts of ascorbic acid rich fruits and vegetables with the meals, reduce phytate content by appropriate home levels processes such as gemination and fermentation and avoid dlinking tea with the meals.

Another factor which may determine the absorption of iron is the existing iron status of the individual. This is particularly relevant with respect to iron deficiency anaemia.

iv) Iron Status (f the Individual: Lastly, iron status of the individual is a floury determinant of how much iron is absorbed. On a mixed diet with some haem iron, the overall absorption may approximate to 10% in normal subjects while it is about 20% in iron deficient subjects.

Table 10.3 lists the currently known dietary factors affecting iron absorption.

Table 10.3: Dietary factors affecting iron absorption

Increase Absorption	Decrease Absorption
• Gastric Acidity	• Increased intestinal motility
• Ascorbic Acid	• Phytates and oralates
• Certain organic acids like citric, lactic and tartaric acid	• Iron-binding phenolic compounds such as ferrous pyrophosphate, ferrous citrate

• Animal proteins such as meat, fish, poultry	• Calcium, Phosphorus and Magnesium
• Sugars – Fructose, sorbitol	• Zinc, Manganese and Copper
• Physiological factors–pregnancy and growth	• Tannic acid in coffee and tea
• Depleted iron status	• High Iron status
	• Antacids
	• Achlorhydria, Hypochlorhydria
	• Poor fat digestion

So far we have discussed about the various aspects of iron absorption. H owever, it was also mentioned that once iron gets absorbed, it is utilized judiciously again and again by our body. What is the mechanism that regulates iron balance and absorption? Let us understand about 'it in detail.

Iron Balance and Regulation of Iron Absorption

The body has three unique mechanisms for maintaining iron balance.

The first is the continuous reutilization of iron from catabolized erythrocytes in the body. When an erythrocyte dies after about 120 days, it is usually degraded by the macrophages of the reticular endothelium. The iron is released and delivered to transfe1Tin in the plasma, which blings the iron back to red blood cell precursors in the bone marrow or to other cells in different tissues. Uptake and distribution of iron in the body is regulated by the synthesis of transfe1Tin receptors on the cell surface.

This system for internal iron transpon not only controls the rate of flow of iron to different tissües according to their needs, but also effectively prevents the appearance of free iron and the formation of free radicals in the circulation.

The re-utilization of iron is a highly significant process. As mentioned earlier, the red blood cells (erythrocytes) contain two thirds of the total body iron. If 1/120111 of this is to be degraded daily, (note: life span of erythrocytes is 120 days) it results in the release of about 20 mg of iron daily within the body. Almost all of this is re-utilized for the synthesis of new haelnoglobin and erythrocytes. Only an extremely small proportion i.e., about I mg is lost from the body to be replaced by dietary iron. The amount of iron released from erythrocytes and re-utilized for new haemoglobin is termed as iron turnover in the body.

The second mechanism involves access to the specific storage protein, ferritin.. This protein stores iron in periods of relatively low need and releases it to meet excessive iron demands. This iron reservoir is especially important in the third trimester of pregnancy.

The third mechanism involves the regulation of absorption of iron from the intestines; decreasing body iron stores trigger increased iron absorption and increasing iron stores trigger decreased iron abscnption. Iron absorption decreases until equilibrium is established between absøtption and requirement,

Now we shall discuss the transport and storage of absorbed dietary iron in our body.

Transport and Storage

You have seen that transferrin binds both newly absorbed iron and iron released after degradation of haemoglobin. Transferrin is a glycoprotein and has two binding sites for Fe^{3+}. It acts as an iron transport protein. Normally, in plasma it is one-third saturated with ferric ions. It distributes iron throughout the body to wherever it is needed, mostly to erythrocyte precursors in the bone marrow. In iron deficiency, transfenin saturation is reduced while in iron overload, tansfenin saturation gets increased.

Any absorbed iron in excess of body needs is stored in the liver, in two forms, as ferritin and haemosiderin. Ferritin and haemosiderin are the two major iron storage proteins. The ratio of these two proteins in the liver varies according to the level of iron stored, with ferritin predominating at lower iron concentrations and haemosiderin at higher concentrations. Iron is released from these stores in times of need more readily from felTitin than haemosiderin.

Binding ofiron by protein during storage and transport serve as a defense mechanism.

How? If iron ions are left unbound, the redox activity of iron can lead to the generation of harmful free radicals that can cause damage to the cells and their membranes.

We have been reading that once iron is absorbed, our body tries to use it conservatively and re-utilizes it again and again. What would happen then, if iron is consumed in excess of our requirements? Further, the iron absorption need not always be complete.Unabsorbed iron would get excreted. Let us read how iron gets excreted from the body.

Excretion

Our body has a limited capacity to excrete iron once it has been absorbed. Daily losses in adult man are between 0.9 to 1.05 mg. About 0.08 mg is lost via Illine, 0.2 mg via skin,and remaining in the faeces. Women in the reproductive age lose more iron owing to menstrual cycles.

Iron is unique among the minerals, that once absorbed the body holds onto it, and therefore, major regulation of iron balance is through absorption of iron rather than through excretion. The percentage of iron absorbed can vary from less than 1% to more than 50%, depending on the food eaten and the response of the

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regulatory mechanisms that reflects body's physiological need for iron. However, this regulatory mechanism is not perfect across the entire range of intakes.

Next, we shall discuss how iron is taken up by different tissues to perform various frtnctions in the body.

Iron Uptake by Cells and its Functions

Iron participates in a large number of biochemical reactions. However, for iron to perform any function, it first needs to be taken up by the cells. Let us then first review iron uptake by cells.

Cell membranes contain a protein specific for binding transfer in called 'transferring receptor'. Transfer-in containing two ferric ions, binds to this receptor. Thereafter, iron-transgenic-transferring receptor complex is internalized by endoyctosis. Within the cell, iron is released from transferring.

It has been shown that intracellular iron concentration more or less remains constant. This intracellular iron homeostasis is maintained by regulating the synthesis and action of proteins involved in the iron acquisition, utilization and storage. When intracellular iron is scarce, cell needs to increase its iron concentration. This is achieved acquisition of plasma iron and mobilization of storage iron. Also, there is a need to prioritize utilization of iron so that iron is preferentially available for the synthesis of life sustaining iron-containing proteins. Therefore, whenever the intracellular iron concentration is low, the number of transferrin receptors on the cell increase.

Further, it is postulated that iron concentration also regulates the synthesis of apoferritin and δ-aminolevulinic acid synthase. The latter is the key enzyme for haem synthesis. Now that we have been acquainted to the mechanism involved in iron uptake by cells, let us focus on the functions of iron.

Iron has several vital functions in the body. It serves as a carrier of oxygen to the tissues from the lungs by red blood cell haemoglobin, as a transport medium for electrons within cells, and as an integrated part of imponant enzyme systems in various tissues. The general classification of the reactions in which iron is involved includes:

Oxygen transport and storage

Electron transfer

Substrate oxidation- reduction

Four major classes of iron containing proteins carry out these reactions in the mammalian system. These are illustrated in Figure 10.2.

As a component of cytochromes and other enzymes of electron transport chain, it is critical for conversion of food into ATP. Iron-containing molecules ensure that macromolecules like carbohydrates and fats are oxidized to provide the energy necessary for all physiological processes and movements.

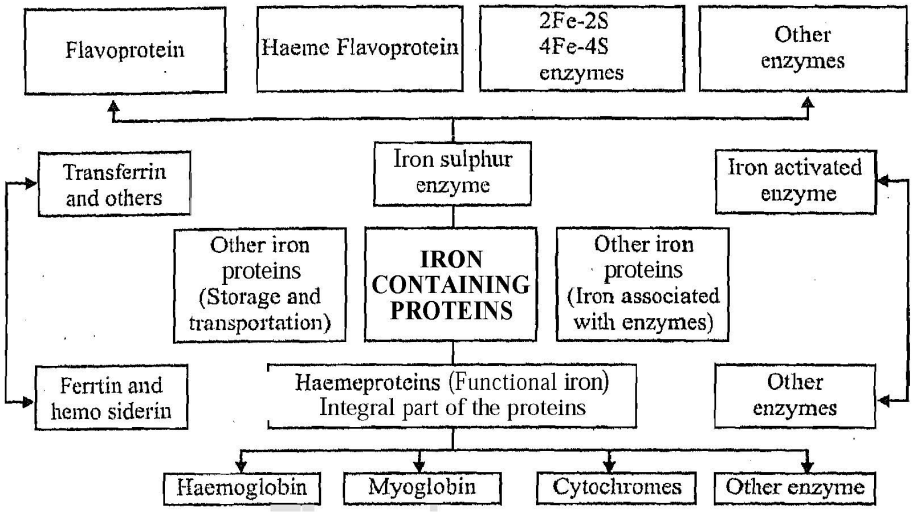

Figure 10.2: Classification of major mammalian iron containing protein

Several iron-containing enzymes, the cytochromes, have one haem group and one globin protein chain. These enzymes act as electron carriers within the cell and their structures do not permit reversible loading and unloading of oxygen. Their role in the oxidative metabolism is to transfer energy within the cell and specifically in the mitochondria. Other key functions for the iron-containing enzymes (e.g. cytochrome P450) include the synthesis of steroid hormones and bile acids; detoxification of foreign substances in the liver; and signal controlling in some neurotransmitters, such as the dopamine and serotonin systems in the brain.

As a component of cytochromes and other enzymes of electron transport chain, it is critical for conversion of food into ATP. Iron-containing molecules ensure that macromolecules like carbohydrates and fats are oxidized to provide the energy necessary for all physiological processes and movements.

Iron is a component of many. other tissue enzymes required for immune system functioning. Non-haem iron proteins, as we know, are responsible for a wide range of functions such as enzymes methane mono-oxygenase (oxidizes methane to methanol) and ribonucleotide reductase (reduces ribose to deoxyribose; DNA biosynthesis).

As a palt of haemoglobin, iron is required for the transport of oxygen, to all cells in the body. Thus, haemoglobin is critical for cell respiration. Most of the iron in the body is present in the erythrocytes as haemoglobin, a molecule composed of four units, each containing one haem group and one protein chain. The structure of haemoglobin allows it to be fully loaded with oxygen in the lungs and partially unloaded in the tissues (e.g. in the muscles), The iron-containing oxygen storage protein in the muscles, similar in structure to haemoglobin but has only one haem unit and one globin chain. As myoglobin, iron functions as a ready source of oxygen to the muscles.

Iron is thus crucial for the survival, growth and normal functioning of the human system. Let us now read about the consequences of deficiency and iron overload in the body.

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Deficiency and Iron Overload

In the following discussion, we shall cover both the deficiency and the consequences of iron overload. We shall begin with iron deficiency.

Deficiency of Iron

Iron deficien y and iron deficiency anaemia are often incorrectly used as synonyms. Iron deficiency is defined as a haemoglobin concentration below the optimunz value in an individual, whereas iron deficiency anaemia implies that the haemoglobin conceiztration is below the 95th percentile of tlze distribution of haemoglobin concentration in a population (disregarding effects of altitude, age and sex, etc. on haemoglobin concentration). Normally, iron deficiency anaemia is defined in terms of lower then normal blood haemoglobin levels and at least two of the following three: i) reduced serum ferritin, ii) increased erythrocyte protoporphyrin, and iii) increased transfemin receptors. Iron deficiency is one of the most prevalent nutritional deficiencies in the world today. It is estimated that 2 billion people worldwide suffer from different degrees of iron deficiency, about half of them, manifesting iron deficiency.

The functional effects of iron deficiency anaemia result from both a reduction in circulating haemoglobin and a reduction in iron-containing enzymes and myoglobin. These include:

fatigue, restlessness and impaired work performance,

disturbance in thermoregulation,

impairment of certain key steps in immune response,

adverse effects on psychomotor and mental development particularly in children, and

increased maternal and perinatal mortality and morbidity

Studies in animals have clearly shown a relationship between iron deficiency and brain functions. Several structures in the brain have high iron content. The observation that the lower iron content of the brain in iron-deficient growing rats cannot be increased by giving iron at a later date, strongly suggests that the supply of iron to brain cells takes place during an early phase of brain development and that, as such, early iron deficiency may lead to irreparable damage to brain cells. In humans, about 10% of brain-iron is present at birth; at the age of 10 years, the brain has only reached half its normal iron content, and optimal amounts are first reached between the ages of 20 and 30 years. Several groups have demonstrated a relationship between iron deficiency and attention, memory and learning in infants and small children. In the most recent well-controlled studies, no effect was noted from the administration of iron.

Iron deficien y also negatively influences the normal defence systems against infections. Several studies have observed a reduction in physical working capacity in human populations with longstanding iron deficiency, and demonstrated an improvement in working capacity in these populations after iron administration. Well-controlled studies in adolescent girls show that iron-deficiency without anaemia is associated with reduced physical endurance and changes in mood and ability to concentrate

Considering the ill-effects of iron deficiency, preventing this problem is crucial. Populations most at-risk for iron deficiency are infants, children, adolescents and women of childbearing age, especially pregnant women. The weaning period in infants is especially critical because of the very high iron requirement needed in relation to energy requirement. Let us then focus our attention on prevention of iron deficiency.

Prevention of Iron Deficiency

Iron deficiency anaemia accounts for approximately one-half or more of all the anaemia's seen world wide. Iron deficiency without anaemia affects a large segment of the populations, as many as with anaemia. Thus, 70% or more of the pre-school children, 90% or more of pregnant women and adolescent girls suffer from either iron deficien y or iron deficiency anaemia in India. The serious functional effects of iron deficiency anaemia on learning, cognition and physical performance in children and productivity in adults, as well as, increased maternal and pre-natal mortality in pregnant women make it imperative to prevent and or treat iron deficiency as a priority

There is a major National programme, the National Nutritional Anaemia Control Programme that aims to prevent and treat anaemia in pregnant women using a public health approach. Iron (100 mg elemental iron) and folic acid (0.5 mg) in the fom of tablets are provided to all plegnant women for 100 days during a pregnancy through the ICDS.

Severely anaemic women are given two tablets a day for 100 days as a treatment. Medicinal iron in a suitable form proves useful in treating iron deficiency at individual levels. Long-term prevention of iron deficiency must depend on improving the bio- availability of iron and increasing the iron content of the diets. Studies have shown that consumption of fillits rich in ascorbic acid such as guavas with major meals can improve haemoglobin levels. Drinking tea with meals should be avoided. At least a gap of 1 -2 hours is needed between a meal and tea for better iron absorption.

While the deficiency of iron is a common health problem; it is important to consider the causes of this problem. Nutritional iron deficiency implies that the diet cannot supply enough iron to coves the body's physiological requirements for this mineral. Worldwide, this is the most common cause of iroh deficiency. In many tropical countries, infestations with hookworms lead to intestinal blood losses that

in some individuals can be considerable.

Besides deficiency conditions, there can be situations (though rare) when there is excessive accumulation of iron in the body. Let us next discuss the consequences of iron toxicity.

Iron Overload/Toxicity

We have seen that absorption of iron is very effectively regulated. This prevents overload of the tissues with iron from diet/supplements in normal healthy individuals. However, an excessive body burden of iron can be produced by greater-than-normal absorption from the alimentary canal, ly parenteral injection or by a combination of both. For instance, people with genetic defects develop iron overload as it occurs in idiopathic haemochromatosis. It is a hereditary disorder of iron metabolism characterized by abnormally high iron .absorption owing to a failure of the iron absorption control mechanism at the intestinal level. High deposits of iron in the liver and the heart can lead to cirrhosis, hepatocellular cancer, congestive heart failure and eventual death.

African or Bantu siderosis, chronic liver disease, pancreatic insufficiency, shunt haemochromatosis and certain types of refractory anaemia have been found to be associated with iron overload. It has recently been shown that excess iron intake via overuse of iron supplements could pose a possible health risk. Cellular and tissue injury due to free radical reactions appears to be the possible mechanism. Normally iron is bound tightly to the proteins. However, it is possible that excess iron intake permits some iron to be in a free form. Associated complications may include increased risk for bacterial infection, neoplasia, arthopathy, cardiomyopathy and endocrine dysfunction.

Next, we shall learn about the indicators of iron status in the human body. These indicators/values provide valuable information to plan the subsequent course of treatment and ensure proper rehabilitation.

Assessment of Iron Status

In view of widespread iron deficiency, it is important to have reliable and sensitive measures of iron status. Iron status can be assessed by a number of methods, which are suitable for different stages of iron deficiency. These are briefly discussed below:

i) Serum Ferritin: This method is indicative of iron stores. As we know, a long term negative iron balance first results in depletion of iron stores with a fall in serum ferritin levels. Plasma femtin concentration of less than 30 microgram per litre is considered indicative of iron deficiency. In normal subjects, plasma femtin averages 100 mcg/L. Values in excess of 250 mcg/L are indicative of iron overload.

ii) Transferrin receptors: As iron deficiency progresses into second stage, the

number of transferrin receptors on the cell surface increase. Measurement of serum tranfemn receptors is thought to reflect transferrin receptors on immature red cells. Values more than 8.5 mg/L reflects iron deficienc

iii) Erythrocyte protoporphyrin: In the early stages of iron. deficiency, there is accumulation of free protoporphyrin (precursor of haemoglobin). Zinc protoporphyrin is usually measured. Levels more than 40 micro mol/mol haem is associated with iron deficiency.

iv) Transferrin saturation: As iron deficiency progresses, there is a decline in transferrin saturation. With deficiency, transferrin saturation reduces to less than 15-16%, is indicative of iron deficiency.

v) Haemoglobin and Haematocrit: In the final stages of iron deficiency, anaemia occurs. Haemoglobin and haematocrit levels indicate prevalence of anaemia. Haematocrit represents that proportion of the total blood volume that is red blood cell and is expressed as percentage (0/0). Values of these two indicators, below which anaemia is considered to exist, according to age and sex is given in the Table 10.4.

Table 10.4 : Haemoglobin and haematocrit levels below which anaemia is present

Age/ Gender Group	Haemoglobin (g/l)	Haematocrit (mmol/L)
Children 6m-59 m	110	6.83
Children 5-11 years	115	7.13
Children 12-14 years	120	7.45
Non-pregnant women (above 15 years of age)	120	7.45
Pregnant women	110	6.83
Men (above 15 years of age)	130	8.07

Source: WHO, 2001.

So, how much iron should be consumed in order to maintain an adequate iron nutriare? Let us read and find out.

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Requirements

We have already learnt about how recommended daily intakes are computed. The requirements for iron, as recommended by ICMR, for various age-groups, are given in Table 10.5. The recommended intakes are based on iron absorption of 3% in adult men, adolescent boys and children; 5% in adult women, adolescent girls, lactating women, and 8% in pregnant women.

Table 10.5: ICMR recommendation for daily iron intake for Indians

Group	Iron (mg/day)	Group	Iron (mg/day)
Adult man	28.0	Adolescents:	
Adult women	30.0	Boys 10 - 12 years	34
Pregnant Women	38	Girls 10 - 12 years	19
Lactation	30	Boys 13 - 15 years	41
Children:		Girls 13 - 15 years	28
1 - 3 year	12	Boys16 - 18 years	50
4 - 6 yeas	18	Girls 16 - 18 years	30
7 - 9 yeas	26		

Source: Recommended Dietary Allowances for Macronutrients and Minerals, Dietary Guidelines for Indians, NIN, ICMR, India **(1998).**

The FAO/WHO 2004 recommendations for iron for different dietary iron bioavailability are given in Table 10.6 for your reference.

Group Age (years)	Age (years)	Mean Body Weight	Recommended Nutrient Intake (mg/day) for a Dietary Iron Bioavailability of			
		(kg)	15%	12%	10%	5 %
Infants and	0.5-1	9	6.2"	7.7"	9.3"	18.6"
Children	1-3	13	3.9	4.8	5.8	11.6
	4-6	19	4.2	5.3	6.3	12.6
	7-10	28	5.9	7.4	8.9	17.8
Males	11-14	45	9.7	12.2	14.6	29.2
	15-17	64	12.5	15.7	18.8	37.6
	18+	75	9.1	11.4	13.7	27.4
Females	11-14[b]	46	9.3	11.7	14.0	28.0
	11-14	46	21.8	27.7	32.7	64.5
	15-17	56	20.7	25.8	31.0	62.0
	18+	62	19.6	24.5	29.4	58.8
Postmenopausal		62	7.5	9.4	11.3	22.6
Lactating		62	10.0	12.5	15.0	30.0

[a] Bioavailability of dietary iron during this period varies greatly.

[b] Pre-menarche.

In this section we read about the food sources, metabolism, functions, deficiency, toxicity of iron, as well as, important indicators of iron status and the reconlmended dietary allowances for this nutrient crucial for our survival. Let us now attempt the questions given in check your progress exercise 1 to recapitulate the concepts we have learnt so far in this unit.

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10.5 ZINC

Zinc deficiency in humans was reported by A.S. Prasad among people consuming mostly breads and very little animal protein in Middle Eastern countries. Common manifestations of zinc deficiency were reduction in growth and appearance of skin lesions. In 1974, a genetic human disease—acrodermatitis enteropathica was related to an inability to absorb adequate zinc from the normal diet. The formal recognition of zinc as an essential nutrient came in 1974, when dietary allowances for nutrients were made.

In the biological systems, zinc is always found in the divalent (+2) state. Zinc is present in all body tissues and fluids. The total body zinc content has been estimated to be 30 mmol (2 g). Skeletal muscle accounts for approximately 60% of the total body content and bone mass, with a zinc concentration of 1.5-3 grnol/g (100-200 gg/g), for approximately 30%. The concentration of zinc in lean body mass is approximately 0.46 gmol/g (30 ug/ g). Plasma zinc has a rapid turnover rate and it represents only about 0.1% of total body zinc content. This level appears to be under close homeostatic control. High concentrations of zinc are found in the choroid of the eye (4.2 gmol/g or 274 µg/g) and in prostatic fluids (4.6-7.7 mmol/l or 300- 500 mg/L).

Let us next get to know about the food sources rich in zinc.

Food Sources

Zinc is normally associated with the protein and/or nucleic acid fraction of foods. Thus, foods high in proteins are good sources of zinc. Lean red meat, whole-grain cereals, pulses and legumes provide the highest concentrations of zinc: concentrations in such foods are generally in the range of 25-50 mg/kg (380-760 pmol/kg) raw weight. Processed cereals with low extraction rates, polished rice, and chicken, pork or meat with high fat content have moderate zinc content, typically between 10 and 25 mg/ kg (150-380 gmol/kg).

Fish, roots and tubers, green leafy' vegetables, and fruits are only modest sources of zinc, having concentrations mg/ kg (<150 ymol/kg) Saturated fats and oils, sugar and alcohol have very low zinc contents. Refer to Table 10.7, where sources of zinc along with content are given.

Foods/ Food Groups	Zinc (mg/100 g) Edible Portion
Sea *Food*	
Oysters	17-91
Shrimp	1.1
Tung	0.5-0.8
Meat and Poultry	
Liver	3.1-3.9
Chicken	1.0-2.0
Beef	3.9-4.1
Pork	1.6-2.1
Eggs and daily products	
Eggs	1.1
Milk	0.4
Cheeses	2.8-3.2
Pulses and Legumes	
Legumes (cooked)	0.6-1.0
Pulses/legumes (whole)	2.8-6.1
Bengal gram/red gram dhal	0.9-1.7
Grains and Cereal	
Wheat/wheat products	0.6-2.7
Rice and pasta	0.3-.06
Bread (wheat)	1.0
Bread (white)	0.6-0.8
Nuts and Oilseeds	
Gingelly seeds	12.2
Almonds	3.6
Cashewnuts	6.0
Vegetables	0.08 - 0.68
Fruits	0.06 - 0.58

Table 10.7 : Zinc content of foods

From Table 10.7, you can see that zinc is present in high amounts in nuts and red meat. Among seafood, oysters are very high in zinc. Other good animal sources include poultry, pork and dairy products. Among the foods of plant origin, legumes, whole grain cereals and vegetables (leafy vegetables and roots) are the good sources. Refining of cereals reduce the content to a large extent.

The important aspects of absorption, storage, transport and excretion of zinc shall now be dealt in detail

Metabolism

Zinc has been found to play an important biological role in our body. Zinc ions can be chelated and precipitated by a number of chelating agents including some natural constituents of the diet. In order to take maximum benefit of this nutrient to enhance health, it is important to undeistand about its metabolism in detail. Let us begin with the absorption of zinc.

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Absorption

Like iron, zinc also needs to be liberated from food prior to absorption. During digestive process; proteases, nucleases and hydrochloric acid all appear to release zinc bound to proteins and nucleic acids.

Zinc is absorbed throughout the small intestine, with absorption being most efficient in the jejunum. Zinc given as aqueous solution to fasting subjects is absorbed to the extent of 60-70%. However, absorption from solid diets is less efficient and varies widely depending upon the content of the zinc in the meal and the composition of the diet. Tentative estimates of absorption from different types of diet have been used for estimating requirements. These are:

a) Highly bioavailable diets (low in inhibitors, high in enhancers) 50-60%

b) Normal availability—a mixed diet 30%

c) Low availability diet (high in phytate, calcium and other inhibitors) 15%

Table 10.8 presents the criteria for categorizing diets according to the potential bioavailability of their zinc.

Table 10.8: Criteria of categorizing diets according to the potential bioavailability of their zinc

Normal Category"	Principal Dietary Characteristics
High availability	Refined diets low in cereal fibre, low in phytic acid content, and with phytate-zinc molar ratio <5; adequate protein content principally from non-vegetable sources, such as meats and fish.
	Includes semi-synthetic formula diels based on animal protein.
Moderate bioavailability	Mixed diets containing animal or fish protein.
	Lacto-ovo, ovo-vegelarian, or vegan diets not based primarily on unrefined cereal grains or high-extraction-rate flours.
	Phytate-zinc molar ratio of total diet within the range 5-15, or not exceeding 10 if more than 50% of the energy intake is accounted for by unfermented, unrefined cereal grains and flours and the diet is fortified with inorganic calcium salts (>1 g Ca^{2}+/day).
	Availability of zinc improves when the diet includes animal protein or milks, or other protein sources or milks.
Low availability	Diets high in unrefined, unfermented, and ungerminated cereal grain[b], especially when fortified witli inorganic calcium salts and when intake of animal protein is negligible.
	Phytate-zinc molar ratio of total diet exceeds 15[c], high phytate, soya-protein products constitute the primar, protein source.
	Diets in which singly or collectively, approximately 50% of the energy intake is accounted for by the following high–phytate foods; high-extraction-rate (<90%), heal, rice, maize, grains and flours, and millet; chapatti flours and tanok; and sorghum, cowpeas, pigeon peas, grams, kidney beans, black-eyed beans and groundnut flours.
	High intakes of inorganic calcium salts 1g Ca^{2}+/day), either as supplements or as adventitious contaminants (e.g. from calcareous geophagia), potentiate the inhibitory effects and low intakes of animal protein exacerbates these effects.

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Like other nutrients, zinc is also first absorbed in the enterocytes and then transported across the basolateral membrane.

Let us now see how zinc enters the enterocytes and what its fate in these cells is. Zinc is absorbed into the enterocytes by a carrier-mediated process. Absorption by this process is efficient at low intakes. At high intakes, zinc appears to be absorbed by passive diffusion. Within the enterocytes, zinc has one of the following possible fates:

a) Used or stored within the enterocytes, and

b) Bound to the proteins such as cysteine rich intestinal proteins (CRIP) or metallothionein. Normally, initially absorbed zinc preferentially accumulates on CRIP. However, with the increased zinc concentrations, metallothionein concentrations rise. This is because the diets high in zinc appear to induce gene <xpression of metallothionein.

CRIP appears to mediate intracellular zinc transport while zinc bound to metallothionein is normally lost into the lumen with sloughing of these cells. These proteins can also bind other minerals especially copper in the enterocytes.

Zinc not bound to metallothionein or used within the cells is transported across the basolateral membrane with the help of zinc transporters (ZnTs). Many ZnTs have been identified in different tissues. ZnTs are found in enterocytes besides many other tissues. Look at Figure 10.3 for better clarity regarding transport of zinc. Here, as you can see, ZnT_1, binds to the unused and unbound Zn ions and transports it across the membrane.

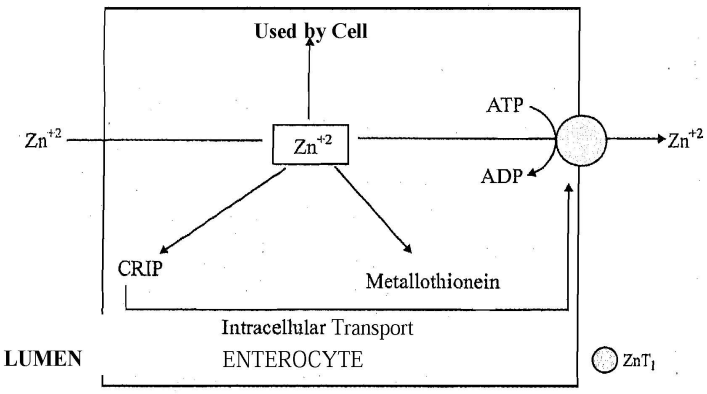

Figure 10.3: Enterocyte use and transport of zinc

The utilization of zinc depends on the overall composition of the diet. Experimental studies have identified a number of dietary factors as potential promoters or antagonists of zinc absorption. Let us learn about these factors.

Factors affecting Zn Absorption

In the last unit you have studied that absorption of various minerals (bioavailability) is influenced by number of factors. Similarly, in case of zinc, different constituents of the diet, commonly known as dietary ligands may bind to zinc and either inhibit

or enhance its absorption. It has been observed that citric acid, picolinic acid, glutathione, amino acids especially histidine and cysteine and possibly lysine and glycine serve as ligands and appear to enhance zinc absorption, especially in the presence of inhibitors. Zinc histidine and cysteine complexes are absorbed 30-40% more efficie tly than zinc sulphate. These two amino acids appear to be also the preferred ligands for zinc.

Isotope studies with human subjects have identified two factors that, together with the total zinc content of the diet, are major determinants of absorption and utilization of dietary zinc. The first is the content of inositol hexaphosphate (phytate) in the Iodine and diet and the second is the level and source of dietary protein.

Phytates are present in whole-grain cereals and legumes and in smaller amounts in other vegetables. They have a strong potential for binding divalent cations and their depressive effect on zinc absorption has been demonstrated in humans. The molar ratio between phytates and zinc in meals or diets is a useful indicator of the effect of phytates in depressing zinc absorption. At molar ratios above the range of 6-10, zinc absorption starts to decline; at ratios above 15, absorption is typically less than 15%. It has been observed that phytates, in the presence of high intraluminal calcium, has a greater inhibitory effect than phytates alone. Provisionally it has been suggested that if phytate to zinc molar ratio is greater than 15, the content of available zinc in the diet is likely to be low (less than 15%). Available evidence shows that only hexa and penta-phosphorylated forms of phytic acid inhibit zinc absorption. The phytate content can also be reduced by activating the phytase present in most phytate- containing foods or through the addition of microbial or fungal phytases. Phytases hydrolyze the phytate to lower inositolphosphates, resulting in improved zinc absorption.

The activity of phytases in tropical cereals such as maize and sorghum is lower than that in wheat and rye. Germination of cereals and legumes increases phytase activity and addition of some germinated flour to ungerminated maize or sorghum followed by soaking at ambient temperature for 12-24 hours can reduce the phytate content substantially. Additional reduction can be achieved by the fermentation of porridge for weaning foods' or dough for bread making. Thus, fermentation which promotes extensive degradation of dietary phytates can significantly improve the bioavailability of zinc.

The effect of phytate is, however, modified by the source and amount of dietary proteins consumed. Animal proteins improve zinc absorption from a phytate-containing diet. Zinc absorption from some legume-based diets (e.g. white beans and lupin protein) is comparable with that from animal protein-based diets despite a higher phytate content in the former.

As in case of iron, absorption of zinc generally is higher from foods of animal origin as compared to that from plant foods. Also, absorption appears to be enhanced by low zinc status, especially carrier- mediated mechanism. This indicates that the

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amount of zinc absorbed is homeostatically regulated.

What happens to zinc once it has been absorbed through the small intestine. Let us find out

Transport and uptake by Cells

After absorption, zinc is bound to albumin and transported to the liver. In liver, it is concentrated and then transported to different tissues ly various plasma proteins. Albumin transports 60% of the zinc, while remaining is transported by other compounds like a-2 macroglobulin, transferrin, immunoglobulin and two amino acids—histidine and cysteine.

Zinc is taken up by various tissues and is incorporated in different enzymes. Since zinc is an important component of various metallo-enzymes within the cells, enzyme synthesis and zinc uptake are correlated, However, mechanism of zinc uptake by various tissues is unknown. Multiple passive transport system including amino acid carrier systems have been proposed.

Next, we move over to the storage of zinc in the body.

Storage

Zinc is found in most organs, concentration being higher in liver, kidney, muscle, skin and bone. Zinc content of muscle, brain, lung and heart is relatively stable and does not respond to changes in dietary zinc intake. Similarly, release of zinc from bones is very slow and does not contribute zinc'to other tissues during deprivation. When dietary zinc intake is insufficient, liver metallothionein zinc appears to be mobilized and redistributed. As dietary zinc intake decreases, liver and RBC metallothionein bound zinc reduces.

Zinc which is not absorbed by our gastrointestinal tract tends to get excreted by our body. Zinc may also get lost from our body due to damage to cells/tissues of our body or as a result of normal physiologic processes. The major routes of zinc excretion are highlighted in our subsequent discussions.

Excretion

Zinc is excreted primarily through the following three routes:

i) Gastrointestinal tract: Majority of zinc is lost from the body in faeces. Endogenous zinc in the form of enzymes or metallo-proteins is secreted into the gastrointestinal tract by the salivary glands, intestinal mucosa, pancreas and liver. Some of this zinc is reabsorbed while some is excreted. Sloughed enterocytes also contribute to faecal zinc. Endogenous intestinal losses can vary from 7 pmol/ day (0.5 mg/day) to more than 45 gmol/day (3 mg/day), depending on zinc intake—the higher the intake, the greater the losses.

ii) Kidney: Very small amount of zinc is excreted in the urine (0.3-0.7 mg/day),

as most of the zinc filtered by the kidney is reabsorbed. Starvation and muscle catabolism increase zinc losses in urine.

iii) Body surface: Loss of zinc occurs due to the exfoliation of skin and sweating (0.7-1.0 mg/day). Another route of zinc loss is hair, which contains 0.1-0.2 mg Zn/g hair. Strenuous exercise and elevated ambient temperatures can lead to high losses through perspiration.

Considerable scientific efforts have been carried out to improve our understanding regarding the biological and physiological role of zinc. The important functions of this mineral are highlighted in our subsequent discussions.

Functions

Zinc is an essential component of a large number of enzymes participating in the synthesis and degradation of carbohydrates, lipids, proteins and nucleic acids, as well as, in the metabolism of other micronutrients. Zinc stabilizes the molecular structure of cellular components and membranes and in this way contributes to the maintenance of cell and organ integrity. Furthermore, zinc has an essential role in polynucleotide transcription and thus, in the process of genetic expression. Zinc also plays a central role in the immune system, affecting a number of aspects of cellular and humoral immunity. Shankar and Prasad have reviewed the role of zinc in immunity extensively. Its involvement in such fundamental activities probably accounts for the essentiality of zinc for all life forms.

These divergent functions of zinc in the body can be grouped into three categories namely, catalytic, structural and regulatory. Some of the important functions are discussed below:

1) **Component of metalloenzymes:** Zinc is unique among the trace elements in that it is a patt of enzymes for all six Enzyme Commission classes about which you may recall studying in the Nutritional Biochemistry Course (MFN-002) in Unit 4. As a component of these enzymes, it either provides structural integrity to the enzyme or participates directly in the reaction at the catalytic site. Zinc is a component of over 300 metalloenzymes and is therefore vital for many fundamental life processes. For example, as a component of carbonic anhydrase, it helps in rapid disposal of carbon dioxide; as a part of alcohol dchydrogenase, it is involved in the conversion of alcohol to aldehyde such as conversion of retinol to retinal. It is also required for protein digestion since it's a component of carboxypeptidase A and aminopeptidase, the enzymes involved in the digestion of smaller peptides released after the action of the proteolytic enzymes pepsin, trypsin and chymotrypsin. Superoxide dismutase which catalyzes the removal of superoxide radical requires two atoms of both zinc and copper. Zinc has a structural role in this enzyme.

   Delta amino levulinic acid dehydratase involved in haem synthesis also containsl zinc. Similarly, DNA and RNA polymerase and deoxykinase

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involved in nucleic acid synthesis are zinc-dependent. Zinc also influences polysome conformation and is thus involved in protein biosynthesis.

2) **Transcription Factor:** Zinc is an important structural component of DNA-binding proteins also known as 'transcription factors'. These transcription factors contain 'zinc fingers'. The term zinc finger is used mainly to denote the configuration of the protein, which looks like fingers. It contains a series of polypeptide loops resulting from twisting and coiling of the cysteine and histidine residues. Zinc is ligated to these two amino acids. The selies of loops give rise to zinc fingers.

These zinc containing transcription factors bind to promoter sequences of specific genes and regulates transcription. Example of metallothionein mRNA is illustrated in Figure 10.4.

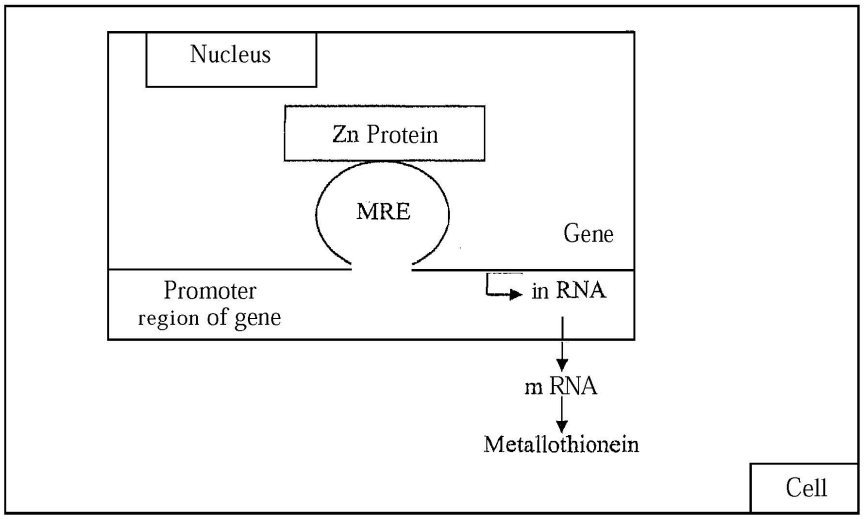

Figure 10.4: Interaction of transcription factor with zinc

Further, these DNA-binding proteins containing zinc fingers also bind to the hormones such as thyroxine, retinoic acid, I ,25-dihydroxychoIecaIiferol and other steroid hormones such as oestrogen and androgens. These proteins, with the hormones attached to them, bind to DNA and affect gene expression. More details regarding this will be covered under Unit 19.

Next, we come over to the consequences of zinc deficiency

Deficiency

Zinc deficien y was identified for the first time in 1940 when malnourished Chinese patients were found to have low concentrations of zinc in blood during war time. The clinical features of severe zinc deficiency in humans are growth retardation, delayed sexual and bone maturation, skin lesions, diarrhoea, alopecia (loss of hair or baldness), impaired appetite, increased susceptibility to infections mediated via defects in the immune system, and the appearance of behavioural changes. The effects of marginal or mild zinc deficiency are less clear. A reduced growth

rate and impairments (f immune defence are so far the only clearly demonstrated signs of mild zinc deficiency in humans. Other effects, such as impaired taste and wound healing, which have been claimed to result from a low zinc intake, are less consistently observed.

The frequency and effects of such mild and moderate deficiency in human population have not been adequately investigated. Growth limiting mild zinc deficiency has been reported in otherwise healthy male American and Canadian infants and preschool children that responded to zinc supplement. In the small areas of Egypt and the Republic of Iran, growth failure in adolescents was found to be responsive to zinc supplements. Severe zinc deficiency in humans is rare

Many studies have documented that zinc supplementation reduces morbidity from infectious diseases. Reduced activity of the zinc-dependent hormone thymulin, one of the factors responsible for reduced cell mediated immunity may contribute to the increased infectitious morbidity in zinc deficiency.

Diarrhoeal diseases are at the root of an estimated 2 million child deaths in developing countries annually. Studies have shown that an inexpensive 20 mg/day zinc supplement for 7-10 days in combination with oral rehydration therapy can reduce severity of diarrhoea by 40% and duration by 20% in children. Likelihood of future occurrence of diarrhoeal disease is also reported to be reduced by zinc supplements, It is now a routine clinical practice to administer zinc supplements to children suffering from diarrhoea.

The central role of zinc in cell division, protein synthesis and growth is especially important for infants, children, adolescents and pregnant women; these groups suffer most from an inadequate zinc intake. Zinc-responsive stunting has also been identified in several studies. Thus, prevention of suboptimal zinc status and zinc deficiency in children by an increased intake and availability of zinc could consequently have a significant effect on child health in developing countries, particularly like ours. Even though zinc is an essential requirement for a healthy body, too much zinc can be harmful. We shall now discuss the main features of zinc toxicity.

Toxicity

Only a few occurrences of acute zinc poisoning have been reported. The toxicity signs are nausea, vomiting, diarrhoea, fever and lethargy and have been observed after ingestion of 4-8 g (60-120 rnrnol) of zinc.

Gross acute zinc toxicity has been reported after consuming water stored in galvanized containers. Symptoms include nausea, vomiting and fever. These symptoms are observed after ingestion of 2 g or more of zinc.

Long-term zinc intakes higher than requirements could, however, interact with the metabolism of other trace elements. Copper seems to be especially sensitive to high zinc doses. A zinc intake of 50 mg/day (760 gmol) affects copper status.

Because copper also has a central role in immune defence, these observations should be studied further before large-scale zinc supplementation programmes are undertaken. Any positive effects of zinc supplementation on growth or infectious diseases could be offset by associated negative effects on copper-related functions.

Intakes between 25-50 mg zinc per day have been reported to interfere with metabolism of both iron and copper. FAO/WHO 2004 therefore recommended the upper level of zinc intake for an adult man at 45 mg/day (690 pmol/day) and extrapolated to other groups in relation to basal metabolic rate. For children, this extrapolation means an upper limit of intake of 23-28 mglday (350-430 gmol/day), which is close to what has been used in some of the zinc supplementation studies. Except for excessive intakes of some types of seafood, such intakes are unlikely to be attained with most diets. Adventitious zinc in water from contaminated wells and from galvanized cooking utensils could also lead to high zinc intakes.

Clinical indices/parameters which can provide useful information regarding the zinc status in the human body have been elucidated next.

Assessment of Zn Status

Sensitive indices for assessing zinc status are unknown at present. Static indices, such as zinc concentration in plasma, blood cells and hair, and urinary zinc excretion are decreased in severe zinc deficiency. A number of conditions that are unrelated to zinc status can affect all these indices, especially zinc plasma levels. Food intake, stress situations such as fever, infection and pregnancy lower plasma zinc concentrations whereas, for example, longterm fasting increases it. However, on a population basis, reduced plasma zinc concentrations seem to be a marker for zinc- responsive growth reductions. A number of functional indices of zinc status have also been suggested, for example, wound healing, taste acuity and visual adaptation to the dark. Changes in these functions are, however, not specific to zinc and these indices have not been proven useful for identifying marginal zinc deficiency in humans thus far.

Let review some of the assessment measures.

- Measurement of zinc in plasma: This is the most common method. Fasting concentrations of less than 70 W litre suggests deficiency. However, fasting plasma zinc level decreases only when dietary intake is so low that homeostasis cannot be maintained. It should be noted that while making interpretations, plasma zinc levels can also be affected by stress infections and administration of oral contraceptives.
- Measurement of zinc in RBCs and neutrophils: This method is not common.
- Metallothionein concentration: Serum metallothionein concentrations are less sensitive to zinc deficiency than levels in RBCs.
- Urinary zinc levels: Excretion of zinc in urine decreases with severe nnc deficiency. It has been suggested as an alternate method of assessing oral zinc absorption using oral dose of 10-50 mg elemental zinc.

- Hair zinc level: Low zinc may be associated with chronic low intakes of dietary zinc. However, it is important that contamination of hair with shampoo, hair collftu should be eliminated.
- Measurement of activity of zinc-dependent enzymes: In zinc deficiency, the activity of alkaline phosphatase declines faster than that of carbonic anhydrase.

It must be evident to you by now that zinc is an important element for maintaining health and performing important metabolic functions in the body. But how much amount of zinc would be required to maintain an optimum nutritional balance in the body i.e.; prevent deficiency, as well as, toxicity. Let us focus on this aspect

Requirement

The ICMR has not made any recommendation concerning zinc for Indians so far.

However, the recent dietary reference intakes for North America places the requirement for adult males at 11 mglday and adult females at 8 mglday. It is increased to 11 mg during pregnancy and 12 mg during lactation. The US Food and Nutrition Board has also derived a tolerable upper limit of 40 mglday for adults. Intakes in excess of 40 mg are undesirable.

The FAO/WHO 2004 recommended nutrient intake (RNIs) for dietary zinc to meet the normative storage requirements from diets differing in zinc bioavailability is presented in Table 10.9. We may perhaps use these for estimating zinc requirements for different populations groups in our country.

Group	Assumed Body Weight (kg)	High Bioavailability	Moderate Bioavailability	Low Bioavailaility
Infants and Children				
0 - 6 months	6	1.1[b]	2.8"	6.6[d]
7 - 12 months	9	0.8[b], 2.5'	4.1	8.4
1 - 3 years	12	2.4	4.1	8.3
4 - 6 years	17	2.9	4.8	9.6
7 - 9 years	25	3.3	5.6	11.2
Adolescents				
Females 10 - 18 years	47	4.3	7.2	14.4
Males 10 - 18 years	49	5.1	8.6	17.1
Adults				
Females 19 - 65 years	55	3.0	4.9	9.8
Males 19 - 65 years	65	4.2	7.0	14.0
Females 65+ years	55	3.0	4.9	9.8
Males 65+ years	65	4.2	7.0	14.0
Pregnant women				
First trimester	–	3.4	5.5	11.0
Second trimester	–	4.2	7.0	14.0
Third trimester	–	6.0	10.0	20.0
Lactating				
0 - 3 months	–	5.8	9.5	19.0
3 - *6* months	–	5.3	8.8	17.5
6 - 12 months	–	4.3	7.2	14.4

It must have been interesting to know about the ubiquitous presence and wide spectrum of properties of zinc. In-depth research over the past few years is unveiling the massive scope of zinc in maintaining good health. The next nutrient that we shall discuss is copper. However, before we proceed, answer the following questions for a quick recapitulation.

10.6 COPPER

As early as the times of Hippocrates, copper compounds were used to treat various diseases. However, in the 20" century, it was noticed that animals fed milk diets developed anaemia, which could not be corrected by dietary iron alone. In 1928, E.B. Hart and co-workers demonstrated that rats which developed the li.lk diet anaemia required copper along with iron to correct anaemia. It is now known that copper is a constituent of several enzymes and proteins, most of which catalyze oxidation— reduction reactions.

In the body, copper occurs in two oxidation states— Cul+ (Cuprous) or Cu2+ (Cupric). The body of a healthy adult contains a little over 0.1 g of copper with concentration being high in liver, brain, heart, bone, hair and nails. About 25 % of body copper is present in muscle, and 42% in the skeleton.

Food Sources

Foods containing more than I mg copper per 1000 kilocalories are considered high in copper and include green leafy vegetables, nuts, legumes, dried fruits, muscle meats and shellfish especially oysters. Let us look at the copper content of some important foodstuffs in Table 10.10. This information would be of great help in planning diets requiring copper restriction/enhanced intake.

Table 10.10: Copper content of some important foods

Food	Copper Content (mg/100 g)	Food	Copper Content (mg/100 g)
Dairy		*Vegetables*	
Egg, whole	0.07	Potato, without peel	0.07
Milk, whole	0.003	Potato chips	0.35
Yoghurt, low fat, plain	0.004	Potato, sweet	0.18
Cheese, Cheddar	0.04	Carrot	0.05
Meat, Fish, Poultry		Broccoli	0.03
Liver, beef	6.09	Spinach	0.08
Chicken	0.07	Peas	0.10
Pork	0.09	Lettuce	0.03
Tuna, canned	0.05	Tomato	0.06
Shrimp, cooked	0.30	Corn	0.04
Grains		Cabbage	0.01
Macaroni, cooked	0.08	*Fruits*	
Corn grits, cooked	0.01	Apple	0.03
Rice, white, cooked	0.08	Banana	0.14
Roll, white bread	0.14	Grapes	0.09
Whole wheat	0.25	Peach	0.06
Nuts		Pear	0.09
Peanut	0.68	Pineapple	0.05
		Orange	0.04
		Raisins	0.32
		Prunes	0.29

Copper though present in small amounts in the food needs to be absorbed, transported, stored and excreted efficiently so as to be able to perform its host of functions some of which are critical for other metabolic functions in our body. A brief overview regarding the metabolism of copper is being discussed next.

Metabolism

In food, most copper is present as Cu^{2+} and some as Cu^{1+}. This copper is bound to organic compounds especially protein. Gastric HCI, pepsin and some proteolytic enzymes aid in the .release of copper. Released copper forms soluble complexes with amino acids, organic acids and other chelators which are readily absorbed mainly in the upper intestinal tract. Some copper is also absorbed from the stomach; however, gastric,copper absolption contributes relatively little to the overall absorption.

As in the case of other minerals, copper absorption appears to occur by two mechanisms:

i) Saturable active mechanism, which operates when the copper concentration is low, and

ii) Passive diffusion, which occurs at a higher concentration.

Efficiency of absorption varies from 30-50% of ingested copper. Copper absorption is influenced by copper status. Absorption is significantly higher during periods of low dietary copper and vice-versa. Various dietary factors influence copper absorption.

Dietary components exerting positive effect include amino acids especially histidine, organic acids such as citric, gluconic, lactic, acetic and malic acids. Dietaw components which inhibit absorption include high intakes of several nutrients such as zinc (as you may recall studying in the last section), iron, molybdenum, calcium, phosphorus and excessive intake of antacids.

Once copper is within the intestinal cell, it may be used by the cell, may be stored in the cell or may be transported across the basolateral membrane. Copper transport across the basolateral membrane into the plasma appears to occur by a carrier- mediated active transport, specific for copper.

Copper which is not absorbed is excreted in the faeces. So, what happens to the copper which is absorbed?

After absorption, ionic copper is tightly bound to plasma proteins, namely albumin and transcuprein and is transported via portal blood to the liver. Small amount of absorbed copper is also transported to other tissues especially kidney.

In the lives, copper is incorporated into ceruloplasmin, which is then released in the blood. Ceruloplasmin constitutes 95% of the total plasma copper. Ceruloplasmin then delivers copper to various tissues. Tissues can also acquire copper from albumin, transcuprein and low molecular weight copper compounds.

Copper enters the cell directly through channels or after binding to protein transporters. Ascorbic acid enhances copper transfer. Glutathione appears to serve as a transporter of copper within the cell. In the cell, copper is incorporated into various copper enzymes and proteins such as cytochrome oxidize.

Most absorbed copper is secreted by the liver into the bile to be excreted in the faces. This process is the major regulator of copper elimination. Only small amount of copper (— 10-50 mcg) is excreted through kidney. Thus, the absorption and excretion process of copper helps in maintaining optimum levels of this element in our body so that it can help in performing a number of metabolic reactions in the body. Let us then learn about the role of copper in our body.

Functions

Copper serves as a co-factor, as well as, an allosteric component of enzymes. In many enzymes. copper functions as an intermediate in electron transfer. The list of copper -containing enzymes with their role is given in Table 10.11.

Table 10.11 : Copper-containing enzymes

Enzymes	Functions
1) Amine oxidases	Found in tissues throughout body and catabolize physiologically active amines.
a) Monoamine oxidase	Acts on serotonin, norepinephrine, tyramine and dopamine.
b) Diamine oxidase	Inactivates histamine. Also inactivates polyamines involved in cell proliferation i.e. it may play a role in limiting excessive growth. High activity in intestine, kidney and maternal plasma.
c) Lysyloxidase	Deaminates the lysine of newly formed immature elastin and collagen after which crosslinks are formed.
d) Peptidylglycine a-amidating monooxygenase	It is a newly identified cupro-enzyme involved in the synthesis of number of bioactive peptide.
2) Ferroxidases	
a) Ferroxidase *I*	Also known as ceruloplasmin. It catalyzes oxidation of ferrous iron and plays a role in the transfer of iron from storage to sites of haemoglobin synthesis.
b) Ferroxidase II	Catalyzes oxidation of iron.
3) *Cytochrome C oxidase*	It is present in mitochondria of cells throughout the body. It is involved in electron transport chain, reduces oxygen to water and allows formation oi ATP. Activity is highest in heart followed by brain, liver and kidney tissues.
4) Dopamine β-hydroxylase	It catalyzes the conversion of dopamine to neurotransmitter – norepinephrin in the brain. Its concentration is higher in grey matter than white matter of the brain. It is also present in adrenal gland.
5) Superoxide Dismutase (SOD)	Functions as a scavenger of superoxide radical and protects against oxidation Cu/Zn. SOD is present in most cells and protects intracellular components from damage. High amounts are found in brain, liver, thyroid, kidney and pituitary. ExtracellularSOD is present in high amounts in lungs, thyroid and uterus.
6) Tyrosinase	It catalyzes the conversion of tyrosine to dopamine, and oxidation of dopamine to dopaquinone, steps in the synthesis of melanin.

After going through the functions enumerated in Table 10.11, you would have realized that copper plays an important function in processes fundamental to human health. Thus, copper plays a role in bone formation and integrity of connective tissue in the heart and vascular system. It is required for the normal functioning of central nervous system and cardiovascular system. It is involved in iron metabolism. Recent evidence suggests a role for copper in Immune function. Some indices of immune function have been shown to decline with deficiency but were not reversed by increased copper intake.

In addition to the above, copper may have other roles, which may not involve enzymes. Copper appears to influence gene expression through binding to specific transcription factors. In some cases, copper has been shown to influence transcription by binding to transcriptionfactor, \8fich in turn binds to promoter sequence of DNA.

Although a very small amount of copper is required for performing the functions discussed above, its deficiency can result in serious consequences which are being discussed next.

Deficiency

Owing to the remarkable homeostatic mechanisms, copper deficiency in humans is rare. However, copper deficiency has been reported under special circumstances. The predisposing factors of copper deficiency are prematurity, low birth weight and malnutrition, especially when combined with feeding practices such as cow's milk or total parenteral nutrition. The most frequent symptoms are anaemia, neutropenia (abnormally high levels of a type of WBC's in blood) and bone fractures. Other less frequent symptoms include hypo-pigmentation, impaired growth, and an increased incidence of infections and abnormalities of glucose and cholesterol metabolism. It has been proposed that sub-optimal copper intakes over long periods may be involved in the precipitation of chronic diseases such as cardiovascular disease and osteoporosis.

While on one hand, a low intake of copper can affect our health, a very high intake or abnormally high levels of copper in the body's tissues can also be damaging to several body processes. Let us read further to find out the effects of copper toxicity.

Toxicity Acute copper toxicity in humans is rare and occurs due to inadvertent consumption of copper salts. Symptoms include vomiting, diarrhoea, haemolytic anaemia, renal and liver damage. Clinical symptoms of chronic copper toxicity appear when the capacity for protective copper binding in the liver is exceeded which include jaundice, hepatitis and liver cirrhosis.

Apart from an abnormally high or low intake, copper imbalance in various tissues may also develop as a consequence of genetic disturbances in the metabolism of copper. The most important one's being the Menke's and the Wilson's disease.

We will learn about these diseases while studying about selenium in section 10.6. Now that you have realized the importance of copper in our diet, let us now move on to the understanding of various assessment parameters of copper status.
Assessment of Copper Status

A reliable index to assess marginal copper status is currently not available. However, severe copper deficiency may be detected by one or more of the three parameters, low serum copper levels, low serum ceruloplasrnin both of which respond to copper administration; and a decline in red cell super oxide dismutase activity. Reported normal range for these parameters are as follows:

Serum copper: 64-156 mcg/dl (10-24.6 rnrnoles/L),

Ceniloplasmin: 1 8 -40 mg/dl,

Erythrocyte SOD: 0.47 mg/g

Seium copper and ceruloplasrnin are reduced to levels far below normal in severe copper deficiency. Erythrocyte SOD in severe copper deficiency has not been reported.

Sa, then what is the safe level of dietary intake for copper? Let us find out

Requirements

Safe and adequate range for copper intake is 1.5-3 mg/day.

In this section, we learnt about the salient features of copper. In our next section, we shall discuss about yet another important nutrient viz., selenium. However, before we proceed, you must attempt the questions mentioned below to recapitulate your understanding of the concepts discussed so far.

10.7 SELENIUM

The element selenium was discovered in 1817 in association with the element sulphur. However, selenium as an essential nutrient remained unrecognized for many years, although selenium toxicity in horses and cattle, "blind staggers" and "alkali disease" was known since the 1930s.

The first description of the dietary selenium deficiency in isolated populations in the People's Republic of China, was made in 1979. The disease known as Keshan disease, named for the country where it was first recognized, was characterized by cardiomyopathy affecting primarily children and young women. The disease was often fatal. The second selenium deficiency disease Kashin-Beck disease was reported in 1980. It was prevalent in China and Sino-Soviet border. Both the diseases were caused primarily due to selenium deficiency in the soil.

Selenium is a non metallic element and exists in several oxidation states which include Se2+ Se4+and Se6+. The chemistry of selenium is similar to

that of sulphur. Selenium replaces sulphur to form organic compounds such as selenocysteine and selenomethionine. Total selenium content of the body varies from 3-15 mg depending on the dietary intake. Approximately 30% of tissue selenium is contained in the liver, 15% in kidney, 30% in muscle and 10% in blood plasma. Much of tissue selenium is found in proteins as selenoanalogues of sulphur amino acids; other metabolically active forms include selenotrisulphides and other acid-labile selenium compounds.

In the body, selenium can be bound to selenium-binding proteins. It can also be directly incorporated into selenoprotein during translation at the ribosome complex using a RNA specific for the amino acid—selenocysteine. Thus selenocysteine can be considered as the 21" amino acid in terms of ribosome-mediated protein synthesis.

At least 15 selenoproteins have now been characterized. Table 10.12 provides a list of these selenoproteins. We will leam about them later in the function section.

Table 10.12: Selection of characterized selenoproteins

Protein	Tissue Distribution
Cytosolic GSHPx	All, including thyroid
Phospholipid hydroxide GSHPx	All, including thyroid
Gastrointestinal GSHPx	Gastrointestinal tract
Extracellular GSHPx	Plasma, thyroid
Thioredoxin reductase	All, including thyroid
Iodothyronine-delodinase (type 1)	Liver, kidneys, and thyroid
Iodothyronine-deiodinase (type 2)	Central nervous system and pituitary
Iodothyronine-deiodinase (type 3)	Brown adipose tissue, central nervous system, and placenta
Selenoprotein P	Plasma
Selenoprotein W	Muscle
Sperm capsule selenoprotein	Sperm tail

Food Sources

Environmental conditions and agricultural practices. have a profound influence on the selenium content of many foods. Table 10.13(a) illustrates the wide range of selenium content of the principal food groups and the variability in the selenium content of dietary constituents in selected counties. This variability is exceeded only by that found in the iodine content of foods.

Table 10.13: The selenium contents of foods and diets

a) Typical ranges of selenium concentrations (ng/g fresh weight) in food, groups

Food Group	India	United States	International Compilation
Cereals and cereal products	5-95	10-370	10-550
Meat, meat products, and eggs	40-120	100-810	10-360
Fish and marine	280-1080	400-1500	110-970
Fish and freshwater	–	–	180-680
Pulses	10-138	–	–
Dairy products	5-15	10-130	1-170
Fruits and vegetables	1-7	1-60	1-20

b) Typical distribution of selenium in dietary constituents (pg/day) in selected countries

Food Groups	China		India		Finland	United Kingdom
	Keshan Disease Area	Disease Free Areas	Low-income Vegetarian Diets	Low-income Conventional Diets		
Total diet	7.7	16.4	27.4	52.5	30.0	31.0
Cereals and cereal products	5.4	11.6	15.7	21.1	2.8	7.0
Pulses	–	–	3.9	3.6	1.1	–
Meat and eggs			–	3.7	9.2	10.0
Fish	0.6	2.2	–	18.4	9.5	4.0
Dairy products			6.9	4.8	6.5	3.0
Fruits and vegetables	1.7	2.6	0.9	0.9	0.5	6.0
other	–	–	–	–	1.1	3.0

Source: Vitamin and Mineral Requirement in Human Nutrition, FAO/WHO (2004)

Geographic differences in the content and availability of selenium from soils to food crops and animal products have a marked effect on the selenium status of entire communities. Refer to Table 10.13(b) which presents the typical distribution of selenium in dietary constituents in selected countries. As you would notice, the distribution of Keshan disease and Kashin-Beck disease in China reflects the distribution of soils from which selenium is poorly available to rice, maize, wheat and pasture grasses.

Selenium enters the food chain through plants. The concentralion of selenium

in plants is directly related to the concentration of the mineral in the soil on which plants were grown. Among the different trace elements, selenium varies greatly in its soil concentration. It has been suggested that ng/g for grain selenium and <3 ng/g for water-soluble soil selenium could be used as indices to define deficient areas. The absorption of selenium by plants is not only dependent on the concentration of selenium in the soil but also on pH, microbial activity, rainfall and the chemical form of selenium. Higher plants can absorb selenium as selenate and can synthesize selenomethionine and to a lesser extent, selenocysteine.

Owing to all above factors, the selenium content in food varies greatly. Overall, animal products, especially organ meats, are thought to contain more selenium than plant sources, as you may have noticed in Table 10.13 (a). Seafoods are also considered good sources, although availability of the mineral from fish, especially those containing mercury, is low.

Selenium occurs in foods in organic form, such as, selenomethionine, selenocysteine, selenocystine and Se-methyl selenomethionine. In general, plant foods contain greater proportion of organic selenium compounds. Inorganic forms include selenite (H_2SeO_3) and Selenate (H_2SeO_4). These forms are found in some vegetables.

Next, we shall discuss about the absorption, transport, storage and excretion of selenium.

Metabolism

Selenium compounds' are generally vety efficiently absorbed by humans and selenium absorption does not appear to be' under homeostatic control. selenium is mainly absorbed from the duodenum. Less absorption occurs in the jejunum and ileum. Inorganic forms of selenium (mainly selenate) are passively transported whereas organic forms are actively transported. Almost 50-80% of dietary selenium is absorbed, with efficiency being higher for organic forms, as compared to inorganic. Among the organic fonns, selenomethionine is better absorbed than selenocysteine.

Among the inorganic forms, selenates are better absorbed than selenites. For example, absorption of the selenite form of selenium is greater than 80% whereas that of selenium as selenomethionine or as selenate may be greater than 90%. In addition, some dietary factors appear to influence the absorption of the element. Phytates and heavy metals, such as mercury through chelation and precipitation, hinder selenium absorption. Vitamins C, A and E, as well as, glutathione enhance the absorption.

Refer to Figure 10.5 for a better understanding of selenium absorption.

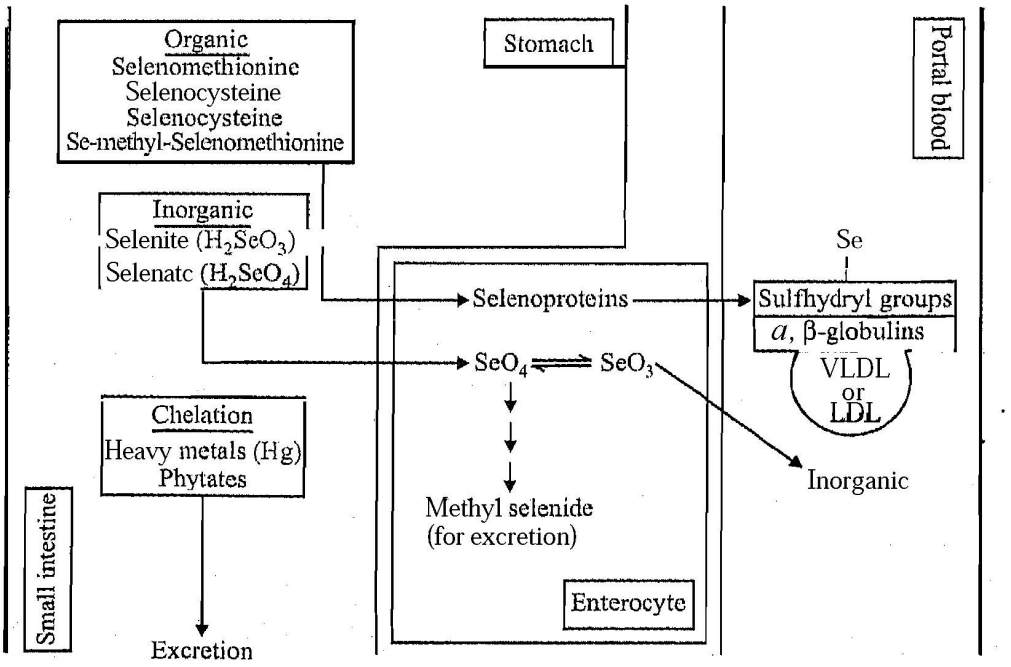

Figure 10.5: Absorption and transport of selenium

1) Selenomethionine obtained from the diet may be:

   stored as such in amino acid pool,

   used for protein synthesis, and

   catabolized to selenocysteine.

2) Selenocysteine obtained from the diet or after catabolism of selenomethionine is degraded to yield free elemental selenium. This elemental selenium may be:

   attached to tRNA charged with serine to be incorporated in selenium dependent enzymes, and

   converted into selenite which may be stored or excreted,

3) Selenate from the diet is converted to selenite. Selenite is further converted to selenide. Selenide may be:

   converted to selenophosphateto yield free selenium, which is incorporated into enzymes, and

   excreted as methyl selenide.

The above discussion can be clearly understood after going through Figure 10.6, which illustrates the metabolic fate of. selenium.

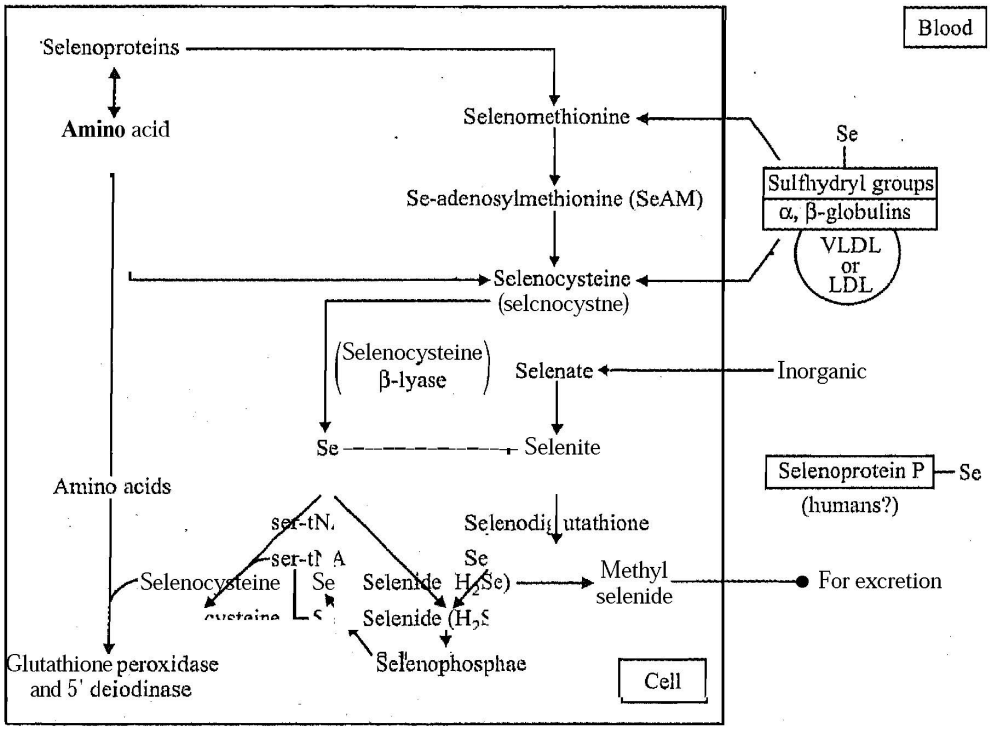

Figure 10.6: Metabolism of selenium in tissues

4) Selenium is excreted from the body almost equally in the urine (as methyl selenium) and faeces (unabsorbed selenium, biliary, pancreatic and intestinal secretion). Unlike copper, selenium is rapidly excreted in urine. Selenium losses through lungs and skin also contribute to daily selenium excretion. After having read about the presence of selenium in human body and its association with several disease conditions, it must be evident that selenium plays an important role in maintaining our health. The most salient functions of selenium have been discussed next.

Functions

Until recently, the only known metabolic role of selenium in humans was as a component of glutathione peroxidase which along with vitamin E and superoxide dismutase forms a part of the anti-oxidant defense system. However, more selenoproteins are being discovered and currently it is estimated that 50-100 selenoproteins are present in animals. Selenoproteins in animals and humans are involved in protection from oxidative damage, maintaining adequate thyroid hormone status and protection from injury by a heavy metal like mercury.

Three major enzyme systems in which selenium plays an important role have been identified in humans. These include:

a) Glutathione peroxidases,

b) Iodothyronine deiodonases, and

c) Selenoproteins P and W

Let us study them in greater detail.

a) Glutathione peroxidases: The role of selenium in the cytosolic enzyme, glutathione peroxidase (GSHPx), was first illustrated in 1973. Four selenium dependent glutathione peroxidases have been identified and named as Glutathione peroxidases 1-4 (GSHPxs 1-4). During stress, infection, or tissue injury, selenoenzymes may protect against the damaging effects of hydrogen peroxide or oxygen-rich free radicals. This family of enzymes catalyzes the destruction of hydrogen peroxide or lipid hydroperoxides according to the following general reactions:

$$H_2O_2 + 2GSH \longrightarrow {}_2H_2O + GSSG$$

$$ROOH + 2GSH \longrightarrow ROH + H_2O + GSSG$$

where, GSH is glutathione and GSSG is its oxidized form.

Thus, from the reaction above, it is evident that the main role of glutathione peroxidases is to reduce hydrogen .peroxide and free hydroperoxides in different cells and tissues by using glutathione (GSH) as the hydrogen donor. Thus, the reactive species of hydroperoxide free radicals are converted into innocuous molecules of water. $GSHP_{x-1}$ is present in virtually all cells, $GSHP_{x-2}$ is localized in the gastrointestinal tract, $GSHP_{x-3}$. is present in plasma while $GSHP_{x-4}$ is most abundant in testis but present in other tissues also.

GSHPx4 plays a major role in protecting against lipid peroxidation as it is the only intracellular enzyme that can reduce fatty acid hydro peroxide, GSHPx.3 in plasma can also perform this role.

b) Iodothyronine Deiodinases: Another group of selenoproteins are the iodothyronine deiodinases essential for the conversion of thyroxine or tetraiodothyronine (TJ to its physiologically active form tri-iodothyronine (T3).Three types of iodothyronine deiodinases have been identified, all of them being selenoproteins. When one iodine is removed from T4, it is converted T3. T_3 is more active than T_4. Thus, one of the deiodinase enzymes is involved in activating T_4. When one or more iodine is removed from T3, the resulting molecules do not have enzyme activity. Therefore, another selenium-dependent deiodinase inactivates T

Type I iodothyronine deiodinase (a selenoprotein) is found in liver, kidney

and thyroid tissue. The major role of this enzyme is to provide Ts to peripheral tissues by deiodinating T_4 secreted by the thyroid gland. Selenium deficiency causes a decline in the Type I deiodinase enzyme activity, but it may not result in hypothyroidism as there 'is a compensatory increase in plasma T_4 levels. Type II iodothyronine deiodinase, also a selenoprotein, is present in the brain, pituitary and placenta. The major function of this enzyme is to regulate T_3 levels in these tissues, and control the secretion of thyroid stimulating hormone. Type II enzyme activity is also reduced in selenium deficiency. Type III iodothyronine deiodinase, another selenoprotein, is involved mainly in degradation of the T_4 and T_3. How this enzyme is affected in selenium deficiency is not fully investigated.

Thus, these selenoprotein enzymes regulate and maintain thyroid levels. Animal studies have shown that a combined deficiency of selenium and iodine produces much more severe hypothyroidismcompated to iodine deficiency alone. Further, maternaldeficiency of selenium and iodine is implicated in cretinism in newborn— the most severe outcome of thyroid hormone deficiency during pregnancy.

c) Selenoproteins P and W: The third group comprises of selenoprotein R an extracellular constituent with multiple selenocysteine molecules. This has an antioxidant role, deactivating free radicals. Selenoprotein W, present in the muscle has a suggested role in muscular degeneration seen in combined selenium and vitamin E deficiency. Selenoprotein W gets reduced during selenium deficiency.

Another group of selenium-containing enzymes is the thioredoxin reductases. The selenoenzyme thioredoxin reductase is involved in disposal of the products of oxidative metabolism. It contains two selenocysteine groups per molecule and is a major component of a redox system with a multiplicity of functions, among which is the capacity to degrade locally excessive and potentially toxic concentrations of peroxide and hydroperoxides likely to induce cell death and tissue atrophy.

These selenoproteins catalyze the NADPH—dependent reduction of oxidized thioredoxin. Reduced thioredoxin provides reducing equivalents for various redox-dependent systems, such as, ribonucleotide reductase essential for DNA synthesis, redox regulation of transcription factors. Besides, these proteins have important functions in regulating cell growth and inhibiting apoptosis.

The above discussion clearly indicates the importance of selenium in human nutrition. Let us now find out how selenium status can have an impact on our health. We shall ,begin with the state of deficiency and then discuss the consequences of toxic levels of selenium.

Deficiency

Selenium deficiency has been linked to two regional human diseases: Keshan disease and Kashin Beck's disease.

Let us understand what these diseases are and their characteristic features.

Keshan disease: It is a cardiomyopathy (disease of the myocardium, involving heart muscle) that was identified to affect children and women of child bearing age in China. Sudden onset of insufficient heart function is characteristic of the acute form of this disease while in chronic Keshan disease, heart enlargement and insufficiency exist. Intervention trials comprising more than a million subjects in China has demonstrated the protective effect of selenium against Keshan's disease. It is important to note that selenium supplements cannot however reverse cardiac failure if it has occurred.

Kashin Beck disease: Kashin Beck disease was identified to affect growing children in parts of Siberian Russia and China. It is characterized by osteoarthritis involving degeneration and necrosis of the joints and epiphyseal-plate cartilages of legs and arms. It is possible that apart from selenium deficiency, many other factors may be contributing to the development of Kashin Beck's disease.

Suboptimal selenium status may be widespread in human population. It is accompanied by loss of immuno-competence with the impairment of both cell-mediated immunity and ß-cell function. The early preclinical stages of development of human immunodeficiency virus (HI V) infection are accompanied by a very marked decline in plasma selenium. Subclinicalmalnutrition assumes increased significanceduring the development of acquired immune deficiency syndrome (AIDS). Selenium supplementation in subjects has been shown to mark immuno-stimulant effects including increased proliferation of activated T-cells. In addition, as selenium has well recognized anti-oxidant and anti-inflammatory roles, other oxidative stress or inflammatory conditions such as rheumatoid arthritis, ulcerative colitis, pancreatitis may also benefit from selenium supplementation.

Further, enhancement of the virulence of virus due to selenium deficiency has been reported. There is a growing evidence that suboptimal selenium status may also increase risk of cancer and cardiovascular disease. However, much work is still needed in these aspects.

Toxicity

There is a narrow margin between the beneficial and harmful intakes of selenium. The level at which selenosis occurs is not well-defined but threshold for toxicity appears to be 850-900 gg per day. Symptoms of chronic toxicity include brittle hair and nails, skin lesions with secondary infections and garlic odour in the breath. Chronic selenium poisoning in people is characterized primarily by loss of hair and changes in finger nail morphology. In some cases, skin lesions may occur

Next, we shall learn about the parameters indicative of selenium status.

Assessment of Selenium Status

Blood glutathione (GSH) peroxidase activity is directly related to blood selenium

up to a level of 1.27 gmoles/L. Beyond this point, the activity of the enzyme plateaus and therefore cannot be used for assessing selenium status. As of now, GSH peroxidase remains a useful index over the assessment of usual dietary intakes but is limited by the peak level reached at 1.27 mmol/L. Plasma selenium level is index of short term status, as it has been shown to respond to selenium supplementation more rapidly in deficient individuals than whole blood selenium. Hair and nail selenium are not as yet established as valid parameters, although they are being investigated. So what level of intake should be maintained to ensure the maintenance of optimum selenium levels in plasma? Let us find out.

Requirements

The FAO/WHO 2004 recommendation for nutrient intake for selenium by groups. How do these recommendations compare with the US and the UK recommendations? Let us find out. In the (JK, the reference nutrient intake has been set at 75 and 60 mcg of selenium per day for men and women, respectively. These are based on the intakes required to saturate plasma glutathione peroxidase. In the U.S., recommended nutrient intake is 70 mcg/day for men and 55 mcg/day for women. Thus, the present FAO/WHO 2004 report represent a significant decrease in the suggested need for selenium. The lower requirements presented are physiologically justifiable and will only give rise to concern if there are grounds for serious incertainty as to the predictability of dietary selenium intake.

10.8 CHROMIUM

As you will go through this section, you will realize that compared to other minerals, the essentiality of chromium was recognized very late. Let us briefly review its history.

By the year 1948, chromium was recognized as a consistent component of plant and animal tissue. In 1950, it was recognized as an element which potentiated insulin action and restored normal glucose tolerance in rats.

In humans, studies were initiated between 1964—68, wherein chromium supplementation was shown to improve impaired glucose tolerance. Despite these studies, the essentiality of chromium in human nutrition was documented as late as in 1977, when a female patient on total parenteral nutrition (TPN) developed diabetes — like symptoms that were refractory to insulin. Chromium supplementation was shown to alleviate these symptoms and insulin was no longer required. Subsequent studies confirmed these findings

Chromium also exists in several oxidation states from Cr^{2}- to Cr^{6+}however Cr3+ or the trivalent form is also the biologically important one. Cr^{6+}, which is consumed in small amounts, comes from industrial sources. In the acidic environment of the stomach, Cr^{6+} is converted to Cr^{3+}.

NOTES

Unlike other minerals, chromium is present in small amounts in human body. The kidneys, followed by spleen, liver, lungs, heart and skeletal muscle are the tissues with greatest chromium concentration.

Let us review the rich and poor sources of chromium.

Food Sources

Chromium occurs in trivalent form in foods. Good sources of chromium include whole grains, spices and condiments, meats especially organ meats, mushrooms, cheese, prunes and tea. Brewer's yeast has a high content of biologically active organically complexed form known as the Glucose Tolerance Factor (GTF). Chromium complexes with nicotinic acid and amino acids to form GTE

We shall now brief upon the absorption, transport, storage and excretion of chromium from our body.

Metabolism

Chromium appears to be absorbed throughout the small intestine, with absorption being higher in jejunum. The mechanism of absorption has not been well defined but appears to involve processes other than simple diffusion. At normal dietary intakes (10-40 mcg(day), the absorption ranges from 0.4 to 3.0% with absorption being higher at lower intakes. As you have studied for other minerals, even in the case of chromium, an inverse relation between intake and absorption appears to be a basal control mechanism to maintain the body levels of chromium.

As comp'ared to healthy individuals, insulin-dependent diabetic patients absorb 2-4 times more chromium. It appears that these patients have an impaired ability to convert inorganic form to usable form and therefore require higher chromium. Like other trace minerals, absorption of chromium is also influenced by some factors. Enhancers and inhibitors are listed in the Table 10.15.

Table 10.15: Factors influencing absorption

Enhancers	Inhibitors
Ascorbic acid Picolinate (forms stable ipophillic ligand) Methionine and histidine (can chelate or and make it available better).	Antacids Phytates

After absorption, chromium binds to plasma proteins for transportation. Both transferrin and albumin are capable of binding absorbed Cr. It has been suggested that transferrin is the main binder of newly absorbed chromium and albumin assumes the role of chromium acceptor and transporter if transferrin

binding sites are unavailable. have studied that transferrin has two metal binding sites, one is primarily for iron and the second is involved in chromium transport. During conditions of iron excess or iron overload such as iron storage diseases, all the metal transport sites on transferrin are occupied by iron. This may explain the high incidence of diabetes in haemochromatosis patients, which may be induced by chromium deficiency.

Although transferrin and albumin play the major roles in transportation, other plasma . proteins such as a and globulins and lipoproteins are also involved.

As you will go through the next section on 'Functions', you will realize that only organically complexed chromium i.e. is active. It appears that absorbed inorganic chromium is transported to the liver, which is postulated to be the possible site for synthesis of metabolically active molecule. This molecule is held in a body pool and released as needed.

Most ingested chromium is excreted in faeces. Inorganic chromium is excreted primarily by the kidney, with small amounts being excreted through hair, sweat and bile. Organically bound chromium is excreted through bile.

The biologically active form of chromium performs several functions; the important ones are being subsequently discussed.

Functions

Active chromium as GTF potentiates the action of insulin and thus influences carbohydrate, lipid and insulin metabolism.

Let us first study the mechanism by which chromium potentiates insulin function.

Role in Insulin Formation

You are aware that insulin receptors are presentin many cells with their concentration being highest in adipocytes (cells present in adipose tissue) and hepatocytes (liver cells). Ycn also know that insulin receptor has two extracellular alpha-subunits and two extracellular beta-subunits. It is the alpha-subunit to which insulin binds. Once insulin binds to the alpha-subunit of the receptor, a specific phosphorylation of the beta-subunit occurs through a cascade of phosphorylation reactions. This leads to increased insulin sensitivity.

The enzyme partly responsible for this phosphorylation is the 'insulin receptor tyrosine kinase'. This enzyme is activated by chromium. In rats, removal Of chromium has been shown to result in the loss of kinase-potentiating activity. Besides activating the kinase, chromium also inhibits phosphotyrosine phosphatase—an enzyme responsible for inactivation of insulin receptor.

The activation of 'insulin receptor tyrosine kinase' and inhibition of 'insulin receptor tyrosine phosphatase' by chromium would lead to an increased phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity.

Since chromium improves insulin function, it is suggested that chromium may play a role in glucose and lipid metabolism. Let us now review these functions:

Role in Glucose, Lipid and Nucleic Acid Metabolism

Chromium leads to a decrease in blood glucose concentration in people with elevated glucose levels and an increase in those with low blood glucose levels. It shows no effect in the subjects with normal blood glucose levels.

Owing to its role in improving glucose tolerance, many studies having been conducted to see the effect of chromium supplementation in patients with impaired glucose tolerance, and Type 2 diabetes, however, results of different studies have been varied. From the results of various studies, it appears that supplementation level of 200 mcg/day as chromium chloride (CIC13) did not have any beneficial effect: Positive effects were observed in studies using 400 mcg Crlday as CrC13. Almost all the studies employing more bioavailable Cr picolinate have reported favourable effects with greater effect reported at 1000 mcg/day than at 200 mcg/day. Also human studies include subjects of diverse genetic and nutritional backgrounds living in environments of varying degrees of stress, all of which may affect chromium metabolism.

Similarly, improved insulin function is also associated with improved lipid profile. Although number of beneficial effects of chromium on lipid profiles have been reported, these responses are not consistent from study to study. Overall, chromium appears to reduce levels of total cholesterol, LDL cholesterol and triglycerides in blood and increase level of HDL cholesterol.

Another proposed role for chromium is in relation to nucleic acid metabolism. It is postulated that Cr^{3+} is involved in maintaining the structural integrity of nuclear strands and in the regulation of gene expression.

It must be evident from the discussions above that chromium is important for glucose, fat, protein and especially nucleic acid metabolism. Thus, its low or excessive intake over a period of time may result in the development of metabolic changes in several nutrients. Let us read further to know as to what happens when chromium intake is above or below our requirements.

Deficiency

Hallmark of marginal chromium deficiency is impaired glucose tolerance. Individuals receiving TPN without chromium have been shown to develop symptoms of deficiency such as impaired glucose tolerance with high blood glucose level and glucose excretion in urine. Peripheral neuropathy has also been reported which was reversed with chromium supplementation.

Chromium deficiency results in insulin resistance characterized by hyperinsulinemia. Hyperinsulinemia is implicated as a risk factor for coronary heart disease. Trivalent chromium, the form of chromium found in foods and

supplements, is least toxic. Oral supplements upto 800 to 1000 mcg per day appear to be safe. However, hexavalent chromium often found in paints, welding fumes and other industrial settings is very toxic. Inhalation of Cr6+ may result in respiratory disease while direct contact results in dermatitis and skin ulceration. Liver damage can also occur.

Let us then learn how to assess the chromium status.

Assessment of Chromium Status

No specific tests are currently available, which could help us to determine chromium status. Another reason being the chromium content of physiological fluids is not indicative of its status. Also urinary chromium, hair chromium concentrations and fasting plasma chromium tests do not show consistent and reliable ,results. So what level of dietary intake would suffice for our body's requirement and shall not cause any toxic effects? Let us find out this next.

Requirements of Chromium

There is no Recommended Dietary Allowance (RDA) for chromium but adequate intakes that can be used as a goal for individual intakes has been proposed by the Food Nutrition Board of the National Academy of Services, USA. These are given in Table 10.16.

Table 10.16: Suggested and / or estimated safe and adequate daily dietary intakes for

Age Group	Adequate Intake (µg/day)	Age Group	Adequate Intake (µg/day)
Infants		**Females**	
0-6 months	0.2	9-13 y	21
7-12 months	5.5	14-18 y	24
Children		19-30y	25
1-3 y	11	31-50y	25
4-6 y	15	50-70y	20
Males		> 70 y	20
9-13y	25	**Pregnancy**	
14-18 y	35	< 18 y	29
19-30 y	35	19-30 y	30
31-50y	35	31-50 y	30
50-70y	30	**Lactation**	
> 70 y	30	< 18 y	44
		19-30 y	45
		31-50 y	45

NOTES

10.9 MANGANESE

Manganese (Mn) is a transition element and can assume 11 different oxidation states, from — 3 to + 7. However, in living tissues, it is found in the + 2, +3 and +4 oxidation states. An adult man weighing 70 kg is estimated to contain 10-20 mg of the metal, with 25% of the total body stores in the skeleton. Relatively high amounts of the minerals are also present in liver, pancreas and intestine. Although not much work has been done to identify the usual dietary intake of Mn among Indians in different age groups, the diet can be estimated to be a poor or good source of Mn by knowing the food sources of this element. So let us recapitulate on the same.

Food Sources

The food sources of manganese along with their content are tabulated in Table 10.17. Here, you can see that whole cereals, nuts, leafy vegetables and tea are good sources of Mn. Indian diets high in foods of plant oiigin supply on an average 8.3 mg of Mn/day.

Table 10.17: Manganese content of selected foods and beverages

Foods/Food Group	Manganese Content (mg/100 g)
Bread, whole grains	0.50 - 2.05
Flour, whole grain	3.80
Bread, white	0.05
Flour, white	0.79
Legumes	0.24 - 0.58
Nuts	0.83 - 4.7 1
Root vegetables	0.05 - 0.62
Other vegetables	0.15 - 1.94
Fruits	0.04 - 1.60
Fruits (dried)	0.09 - 0.39
Milk and cheeses	<0.01
Cofee (brewed)	0.02 - 0.03
Tea (brewed)	0.18 - 0.22

Metabolism

Intestinal absorption of Mn occurs throughout the length of the small intestine although the exact mechanism of absorption is not clearly established.

Ingested Mn is thought to be converted into Mn3+ in the duodenum. Results of the studies suggest that mucosal uptake could be a rapidly saturable process, which appears to be mediated by a high-affinity, low-capacity active transport system.

Available evidence also suggests that mucosal transpon occurs through a

non-saturable simple diffusion process, It appears that both processes might be involved in the absorption of mineral and may operate simultaneously.

Absorption of Mn from the diet is very low. On the basis of Mn retention, it has been estimated that adult humans absorb 4.8% of ingested manganese.

Let now see which factors influence Mn absorption.

Major factors which may influence the absorption of this mineral include:

Absorption decreases with increasing intake.

Percent absorption is higher among women as compared to men.

Increased dietary iron depresses Mn absorption whereas iron deficiency increases its absorption. This could be possibly due to the competition for similar binding and absorption sites between non-haem iron and Mn.

High levels of dietary calcium, phosphoms and phytate impair the intestinal uptake of the element but these have been shown to be of limited significance.

Let us now study the fate of Mn which is absorbed.

After absorption, Mn is complexed with albumin and transpolted to the liver, which is the key organ in its metabolism. In the liver, Mn is found in both rapid and slow exchanging pools. The former is the precursor of biliary Mn, which is excreted in the faeces. The latter serves as the source of Mn for the liver and extrahepatic tissues.

Mn becomes bound as Mn2+to a-macroglobulin before traversing the liver. From the liver, some Mn2+appears to be oxidized by ceruloplasmin to Mn3+and complexes with transferrin. Transferrin bound Mn3+ is taken up by the extrahepatic tissues.

Mn is found in most organs and tissues and preferentially accumulates in the mitochondria. There is no storage form for Mn. Bone contains substantial amount of mineral but there is no mechanism to release it and thus bone Mn is considered as passive storage. It is released only as a result of normal bone turnover or in situations of accelerating bone resorption.

Mn is almost totally excreted in the faeces (92%). Excess absorbed Mn is quickly excreted by the liver into the bile to maintain homeostasis. Only trace amounts are excreted in urine. Let us now briefly review some important functions of Mn.

Functions

Like other microminerals, Mn also functions in mammalian enzyme systems. It can function both as an integral part of metalloenzymes and as an enzyme activator. Manganese containing metalloenzymes are few, as shown in Table 10.18, whereas enzymes activated by Mn are much larger in number. Most of these metal activations by Mn are non-specific, as magnesium (Mg) can substitute

for Mn. There are a few exceptions where Mn be specifically needed for activation. Examples include, activation of glycosyl transferases, phosphoenol/phruvate carboxykinase and glutarnine synthetase.

Glutamine synthetase found in high concentration in the brain catalyzes the following reaction:

NH_3 + Glutarnate + ATP + Glutamhe + ADP + Pi

Thus, glutamate synthetase converts potentially toxic ammonia into glutamine and helps in the removal of ammonia (NH3) as it is generated. It is interesting to note that even in severe Mn deficiency in animals, brain glutamine synthetase activity is maintained normal, suggesting that this enzyme has a high priority among the enzymes activated by Mn or that Mg can replace Mn.

Table 10.18: Mn activated enzymes and Mn containing metalloenzymes

Mn Activated Enzymes	Mn Containing Metalloenzymes
• Hydrolases • Kinases • Decarboxylases • Transferases • Lyases • Oxidoreductases • Ligases	• Arginase • Pyruvate carboxylase • Superoxide – Dismutase

You have seen that Mn is involved in a number of enzyme-catalyzed reactions. Therefore, it performs many important functions. These are briefly discussed herewith:

1) Antioxidant activity: As Mn is a component of mitochondrial Superoxide Dismutase (SOD), it can protect against oxidative damage. In-vitro experiments have indicated that Mn scavenged superoxide radicals at nanomolar concentration whereas hydroxy radicals were scavenged at macromolar concentrations. Thus, Mn deficiency could damage mitochondrial membrane by depressing the activity of SOD. Although, a little work has been done in humans, depressed activity of the enzyme has been reported in animals.

2) Carbohydrate metabolism: Mn is required for carbohydrate metabolism. Enzymes pyruvate carboxylase and phosphoenol pyuvate carboxy kinase involved in gluconeogenesis require Mn for optimal function.

   Further, animal studies strongly suggest a role for Mn in regulation of insulin transcription and / or in insulin mRNA turnover. Mn-deficient animals have been shown to exhibit a diabetic response to oral glucose challenges characterized primarily by impaired insulin production.

3) Integrity of cartilage: Mn plays an important role in proteoglycan

biosynthesis, which is essential for the integrity of cartilage. Bone defects have been observed in birds, rats and mice. This has been ascribed to a reduction in the activities of several Mn-dependent glycosyl transferases.

NOTES

It must be clear by now that though Mn is classified as a trace element; it is involved in the regulation of several enzyme activities and other important functions. However, what would happen during sub-optimal intake of Mn? Read further to find out.

Deficiency

Mn deficien y has been observed in many species of animals and symptoms include: impaired growth, skeletal abnormalities, depressed reproductive function and defects in lipids and carbohydrate metabolism.

With respect to humans, there is a little evidence of Mn deficiency as this mineral is widely distributed in a variety of foods. However, limited studies have reported symptoms of its deficiency after consuming experimental diets deficient in Mn. These included dermatitis, depressed growth of hair and nail, hypocholesterolemia and weight loss. Please note that sample size was very small in these limited experimental studies.

Evidence is accumulating that Mn deficiency may be present in selected groups. It has been reported in patients on long-tenn parenteral nutrition when the solutions were low in Mn content. Modest supplementation of iron can result in lowering of lymphocyte Mn-SOD activity in humans. In view of high frequency of iron supplementation by some groups, it is worthwhile to find out the incidence of Fe- supplementation-induced reductions in Mn status.

Mn deprivation has been associated with osteoporosis, diabetes, epilepsy, atherosclerosis and impaired wound healing.

While a low Mn level in body tissues can affect the human health adversely, a higher than normal intake may also influence several functions. The Consequences of toxidity are being discussed next.

Toxicity

Manganese is considered least toxic of the trace minerals through oral intake. However, some people may be at a risk to develop toxicity. For exalnple, individuals with impaired biliary and/or hepatic dysfunction are more susceptible, as dietary Mn is cleared by the liver. Similarly, total parenteral nutrition (TPN) bypasses the normal homeostatic mechanisms of the liver and gut. Therefore, patients receiving long-term parenteral nutrition are also at a risk.

Manganese toxicity, however, occurs primarily in industrial workers exposed to excess airborne Mn such as in case of industries manufacturing steel, alloys and iron products. Airborne Mn is also contributed by the Mn containing antiknock

compounds in gasoline fuel. Majority of Mn 'toxicity cases have been reported from individuals exposed to airborne Mn in industrial areas in excess of 5 mg per cubic meter (m3). Mn toxicity is a serious health hazard; in its severe form it results in serious psychiatric symptoms such as hyperirritability, violent acts, hallucinations and poor coordination. Several abnormalities occur in the central nervous system, the morphological lesions being similar to Parkinson's disease. In workers exposed to less than 1 mg/m3, impaired motor coordination and impaired memory have been reported. The symptoms of Mn toxicity are apparently due to excessive tissue oxidative damage by Mn.

So which clinical indicators can help in identifying the Mn status of an individual? Read and find out.

Assessment of Mn Status

The body Mn status has not been yet established by laboratory tests. Though the normal range of serum Mn concentration is found out to be 0.04 to 1.4 mcg/dl, it has been shown that Mn supplementation significantly increased lymphocyte SOD activity and serum Mn concentrations.

You must have understood by now that an optimum intake of Mn is imperative for maintaining good health. However, what level of dietary intake per day would help in maintaining equilibrium between the intake and requirements? Let us find out.

Requirements

You have studied in Unit 1 that there are no RDA for certain nutrients including Mn. Instead there is an average intake (A1) value established by US Food and Nutrition Board which is presented in Table 10.19.

Table 10.19: Average intake (AI) values for manganese

Age Group	Requirements (mg/day)
Infants (< 6 months)	0.003
Infants (7 - 12 months)	0.6
Children (1 - 3 years)	1.2
Children (4 - 8 years)	1.5
Boys (9 - 13 years)	1.9
Boys (14 - 18 years)	2.2
Girls (9 - 18 years)	1.6
Adult Men	2.3
Adult Women	1.8
Pregnant Women	2.0
Lactating Women	2.6

In this section, you studied about nutritional significance of chromium and magnesium for maintaining human health. In our next section, two very important nutrients viz., iodine and fluorine shall be dealt in detail. However, before we proceed, you must perform the check your progress exercise 5. You may have to read certain aspects again to clear your concepts.

NOTES

10.10 IODINE

Iodine derives the nutritional importance as a constituent of thyroid hormones, tetraiodo-thyronine (thyroxine or T 4) and 3,5,3 tri iodo-thyronine (T3).The thyroid hormones are indispensable for normal growth and development in humans and animals. Synthesis of the iodine containing thyroid hormones occurs exclusively in the thyroid gland. Goitre was known to the ancient Indians, Chinese, Greeks and Romans. Iodine as an element was discovered only in 1811; however, its presence in the thyroid gland was discovered by Bauman et, al in 1895. The relation between iodine deficiency and enlargement of the thyroid gland or goitre was shown early in the 20th century when it was reported by Marine that the thyroid gland became hyperplastic (increase in number of normal cells in an organ and therefore an increase in volume/size of the organ) with low level of iodine in the body. Subsequently in 1922, Marine and Kimball demonstrated that administration of small amounts of iodine could prevent or substantially reduce endemic goitre among school children in Ohio.

Introduction of iodized salt as a public health measure to prevent goitre was first introduced in Switzerland and Michigan. Following this, the incidence of goitre and cretinism fell rapidly in these countries. Another major development for the population at-risk of severe iodine deficiency in inaccessible mountainous areas, was the iodized oil (1 ml containing 480 mg iodine) which can be given once in three years. Oral iodized oil is also effective but the effects may last only for one year.

Iodine is a non-metallic element of the halogen group with common oxidation states of —1^{-1} (iodides), 1^{+5} ,KI03 (iodates), KI04 (periodates) and less common states of +1 (iodine monochloride) and +3 (iodine tlichloride). In humans, iodine is typically found and functions in its ionic form, iodide (I-').

About 15-20 mg iodine is found in human body, of which 70-80% is present in the thyroid gland. The thyroid gland weighs 15-25 grams and has a remarkable ability to concentrate iodine. In the iodine deficient individual, enlarged thyroid gland may contain only I mg iodine.

So, how can we consume adequate amounts of iodine in our diet? Let us get to know about the food sources, next:

Food Sources

Please note that unlike other minerals studied so far, like selenium, the iodine concentration in foods is highly variable and also depends on the concentration of iodine content of soil in that region. The iodine present in the upper crust of the earth is leached by glaciation and repeated flooding, and is carried to the sea. Seawater is, therefore, a rich source of iodine. The seaweed located near coral reefs has an inherent biological capacity to concentrate iodine from the sea. The average iodine content of foods (fresh and dry basis) is given in Table 10.20.

The amount of iodide in drinking water is an indicator of the iodide content of the rocks and soils of a region and it parallels the incidence of iodine deficiency among the inhabitants of that region. In general, iodine deficient areas have water iodine levels below 2 mcg/L as in Nepal and Sub-Himalayan India (0.1— l.2 mcg/L) compared with levels of 9 mcg/L in the city of Delhi, which is not iodine deficient.

Table 10.20: Average iodine content of foods (mg/kg)

Food	Fresh Basis		Dry Basis	
	Mean	Range	Mean	Range
Fish (fresh water)	30	17-40	116	68-194
Fish (marine)	832	163-3180	3715	471-4591
Shellfish	798	308-1300	3866	1292-4987
Meat	50	27-97		
Milk	47	35-56		
Eggs	93			
Cereal grains	47	22-12	65	34-92
Fruits	18	10-29	154	62-277
Legumes	30	23-36	234	223-245
Vegetables	29	12-201	385	204-1636

In addition to water, iodine is also contributed by sea foods, as mentioned above., However, a large difference in the content exists between sea water fish and fresh water fish. Sea fish contain about 300-30,000 mcg iodine/kg in contrast to only 20-40 mcg iodine/kg in fresh water fish.

Also, food additives used as bread dough oxidizers or conditioners can contribute to the iodine content of the diet.

You must be acquainted with the physiological significance of iodine by now. Let us find out how the dietary iodine that we consume gets absorbed, transported, stored and if required, excreted from our body.

Metabolism

Now, we will very briefly study how iodine is absorbed, distributed in the body and excreted out. Like other nutrients, dietary iodide is either found free or bound to amino acids. It is primarily found as iodide or iodate. The latter form is reduced to iodide by glutathione in the gut. Iodide is rapidly and completely absorbed throughout the gastrointestinal tract and very little iodine appears in faeces.

Iodine bound to amino acids is also absorbed but less efficiently. The thyroid hormones: thyroxine (TJ and triiodothyronine (TD are also absorbed unaltered. Therefore, T4 medication can be administered orally.

After absorption, free iodide appears in the blood and circulates to all tissues. Thyroid gland traps most of the ingested iodide (80%). This is achieved against an iodide gradient (often 40 to 50 times plasma concentration) by sodium-dependent active transport system. This mechanism is regulated by thyroid stimulating hormone (TSN) secreted by pituitary. Thyroid gland takes up almost 120 mcg of iodide per day. Other tissues such as salivary glands, gastric mucosa, choroid plexus and mammary glands also concentrate the element by a similar active mechanism.

Several sulphur-containing compounds such as thiocyanate, isothiocyanate and goitrin inhibit active transport mechanism by competing for uptake with iodide. Thus, iodide uptake by thyroid gland may be reduced. These are called goitrogens and their goitrogenic activity can be overcome by iodine supplementation, Refer to Box 10.1 for better understanding of goitrogens.

Box 10.1 Goitrogens

Goitrogens are substances that interfere with iodide metabolism in any way that inhibits thyroid hormone synthesis. As a result, there is augmentation in TSH release and subsequent thyroid gland enlargement. These active goitrogens are released by plant enzymes from thioglucosides or cyanogenic glucosides found in cassava, kale, cabbage, broccoli, turnips, rapeseeds and mustards. Most important of these is cassava, which can be detoxified by soaking in water and cooking it well. Tobacco smoke also contributes thiocynate.

Unutilized iodide is excreted via kidneys, which forms the major route of iodide excretion (80-90 %). The urinary output of iodide correlates closely with the plasma iodide concentration and has been used to monitor iodide status. Some iodide is also lost in sweat, especially in the hot tropical regions.

Iodine, as we all know, performs some very important functions in our body particularly those pertaining to the thyroid gland. We will now discuss the ntnctions of iodine in detail.

Functions

Iodine is an essential constituent of the thyroid hormones: thyroxine (T 4) and triiodothyronine (T_3), which have a key role in growth and development. Let us first briefly review how these hormones are synthesized and released from the thyroid gland.

Biosynthesis and Secretion of Thyroid Hormones

Histologically, the functional cells of the thyroid gland are arranged in follicles,

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which surround a central lumen containing a colloid in which the hormones are stored in the form of thyroglobulin. Thyroglobulin (refer to Figure 10.7) is a glycoprotein and is synthesized in the follicular cell as prothyroglobulin and the tyrosine units are iodinated in the intact protein.

As you may have noticed in Figure 10.7, the iodide actively transported into the cells from extracellular fluid (ECF) is released from the thyroid cells into the colloid follicle where it is oxidized by thyroperoxidase in the presence of hydrogen peroxide.

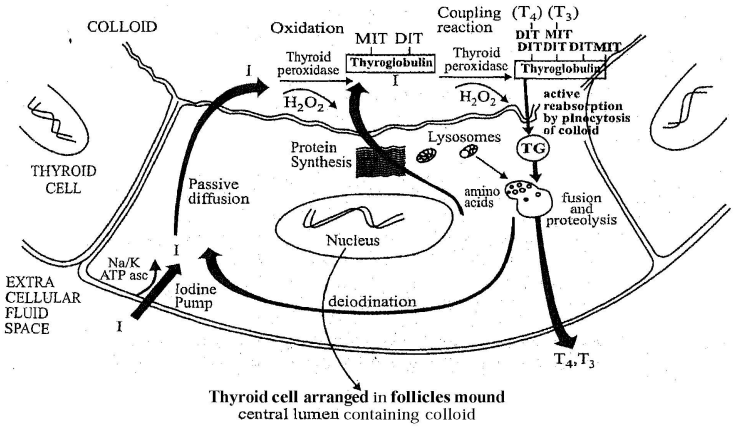

Figure 10.7: Biosynthesis and secretion of thyroid hormones

The oxidized iodine is then combined with the amino acid tyrosine in thyroglobulin to form mono and di-iodotyrosines (MIT/DIT), which are again catalyzed by thyroperoxidase. These are then coupled to form triiodo to thyronine and tetraiodo-thyroxine. The iodinated thyroglobulin is absorbed back into the cells by a process known as pinocytosis. The iodinated thyroglobulin is hydrolyzed within the cells by the cellular proteolytic enzymes to release T4 and T3 into the blood circulation. Un- utilized mono- and di-iodotyrosines are not released into the blood but are conserved within the gland for further incorporation into thyroglobulin.

In blood, these hormones bind to transport proteins mainly thyroxine-binding-protein and are distributed to the target cells in the peripheral tissues. All phases of biosynthesis and secretion of thyroid hormones are stimulated by thyroid-secretary hormone (TSH), which is secreted by anterior pituitary gland in response to low levels of thyroid hormones.

Let us next review the physiological functions and metabolic effects of thyroid honnones, in order to understand the importance of iodine in humans.

Physiologic Functions of Iodine

Thyroid hormone performs multiple functions as regulator of cell activity and growth. The hormone has crucial metabolic roles in the foetus, and in the infant post-natally. It promotes growth and maturation of peripheral tissues in the human embryo, the most visible effect seen in the skeletal growth. Delayed bone

development has been seen in hormone deficient human embryos. Thyroid hormone influences neuronal cell growth and dendrite development in the embryo. A major effect of foetal iodine deficiency is cretinism, characterized by mental deficiency and deaf mutism.

Postnatally, linear growth, i.e. stature and bone inaturation are critically dependent on thyroid hormone. Both are retarded when there is a deficiency of the hormone due to low iodide intakes. The hormone plays an important role in the provision of energy to most cells in the body; the best indicator of this is the energy available for utilization in the basal state, i.e. the basal metabolic rate. In thyroid hormone deficiency, the BMR is lower, slowing the overall cellular activities. Iron deficiency in children is characteristically associated with goitre.

In the endemic iodine deficient regions of India, school children have been shown to have general IQs 10 points lower than children in non-iodine deficient areas. A high degree of apathy has also been noted in adults living in the iodine deficient areas in India. Even domestic animals in these areas have been reported to display apathetic behaviour. Reduced mental function is widely prevalent in thyroid hormone deficien y in the iodine deficient endemic areas, highlighting the key role of this hormone in neuronal and brain development and function. Iodine deficiency is a major obstacle to human and social development and should be prevented as a priority.

Some important aspects of the metabolic influences exerted ly thyroid hormones are being highlighted in the subsequent text.

Metabolic Effects of Thyroid Hormones

The deiodination of (T 4) and (T3) takes place in extrathyroidal tissues, mainly liver. Let us now proceed to learn about the health effects of a low iodine intake which continues to be a serious public health problem even today despite concerted efforts being laid down by our government to alleviate this nutritional deficiency disorder.

Deficiency

Iodine deficiency affects all populations at all stages of life, from the intrauterine stage to old age. However, pregnant women, lactating women, women of reproductive age, and children younger than 3 years of age are considered the most important groups in which to diagnose and treat iodine deficiency, because iodine deficiency occurring during foetal and neonatal growth and development leads to irreversible damage of the brain and central nervous system and, consequently, to ilreversible mental retardation. Thus, its deficiency causes a wide spectrum of disorders. These include:

- Mild goitre, i.e., a larger thyroid gland than normal. The mildest form of goitre ranges from those only detectable by touch (palpation) to very large goitre that can cause breathing problems. The enlargement of glands occurs from

stimulation of thyroid cells by TSH and without ability to increase hormones production owing to iodine deficiency.

- The most severe form is endemic cretinism, which is characterized by congenital, severe irreversible mental and growth retardation.
- Hypothyroidism, which is accompanied by low BMR, apathy, slow refle relaxation time with slow movements, cold intolerance and myxoedema (skin and subcutaneous tissues are thickened because of accumulation of mucin and become dry and swollen).

Collectively, these manifestations of iodine deficiency are termed 'Iodine Deficiency Disorders' (IDD) .

The symptoms of IDD differ depending on the life stage at which iodine deficiency occurs. For example, iodine deficiency in foetus has most severe consequences and results in cretinism. There is severe mental retardation, deaf-mutism (defects (f hearing and speech), squint, disorders of stance and gait and stunted growth.

However, varying degrees of intellectual or growth retardation are apparent Mhen iodine deficiency occurs in infancy or childhood and adolescence.

Apart from cretinism, hypothyroidism and goitre, other features linked to IDD are the decreased fertility rates, increased stillbirths and spontaneous abortion rates and increased perinatal and infant mortality.

Epidemiological studies have indicated that an ingestion of 100-200 mg of iodine daily is sufficient to prevent deficiency except among individuals suffering from a genetic disorder. However, excessive iodine load may develop due to continued administration of iodine doses for a long time or pharmacological/dietary reasons. The effects of iodine overload are being discussed next.

Toxicity

A wide range of iodine intakes is tolerated by most individuals, owing to the ability of the thyroid to regulate total body iodine. This tolerance to huge doses of iodine in healthy iodine-replete adults is the reason why WHO stated in 1994 that, "Daily iodine intakes of up to I mg, i.e. 1000 gg, appear to be entirely safe". This statement, of course, does not include neonates and young infants.

Over 2 mg iodine/day for long periods should be regarded as excessive or potentially harmful to most people. Such high intakes are unlikely to arise from natural foods, except for diets that are very high in seafood and/or seaweed or comprising foods contaminated with iodine. In contrast to iodine-replete individuals, those with IDD or previously exposed to iodine-deficient diets may react to sudden moderate increases in iodine intake, such as from iodized salt. Iodine-induced thyrotoxicosis (hyperthyroidism) and toxic modular goitre may result from excess iodine exposure in these individuals. Hyperthyrodism is largely confined to those over 40 years of age and symptoms are rapid heart rate, trembling, excessive sweating, lack of

sleep, and loss of weight and strength. Individuals who are sensitive to iodine usually have mild skin symptoms.

Thus, the level of iodine in the body can be a vital biochemical indicator for assessing the impact of a sub-optimal iodine intake and for outlining an appropiiate patient care process. Let us find out which parameters can be helpful in the field and clinical settings.

Assessment of Iodine Status

Iodide nutritional status is generally directed at population living in areas suspected to be iodine deficient. The assessment is based on both the physical examination and chemical testing of individuals. It includes:

- Total population count, including the number of children below 15 years of age. It is estimated that about 10 million people are exposed to the risk of IDD in India, they live in iodine deficient endemic areas.
- Incidence of goitre, as established by physical examination and cretinism in the population of the 150 million at risk stated above, 55 million are reported to have goitre and 22 million suffer from cretinism.
- The quantification of urinary iodide excretion. Urinary concentration less than 50 mcglg of creatinine are considered at-risk. Urinary iodide less than 10 mcg/dl is considered deficient. While above 10 mcg/dl is normal. The quantification of iodide in the drinking waler. Less than 2 mcg/L of water is indicative of iodine deficient endemic area.
- Determination of serum (T4) levels in various age groups. Normal levels are 4-12 mcgldl.
- Detemzination of serum TSH: Values less than 1 10 4 micro unitslml is considered normal. TSH is elevated in iodine deficiency disorders.
- Determination of T4 and TSH: Both are used in assessing the iodine status of the newborn in endemic areas. A new born infant with T_4 less than 3 mcg/dl and TSH 50 micro units/ml or higher is conside ed to have neonatal hypo thyroidism.

Requirements

The minimum amount of iodide to prevent goitre is estimated between 50 and 75 mcglday or 1 mcglkg body weight. The 1989 ICMR recoinmended RDA is 150 mcglday for adults of both sexes. Although the recommendations are the same for both males and females, iodide needs are higher during pregnancy and lactation. Therefore, the recommended intakes during pregnancy and lactation are 175-200 mcg iodine per day.

Refer to Table 10.21 which presents the daily iodine intake recommendation by the WHO, UNICEF and the International Council for Control of Iodine Deficiency Disorders.

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Table 10.21: Daily iodine intake recommendationsly the World Health Organization, United Nations Children's Fund, and International Councell for Control of Iodine Deficiency Disorder

Group	Iodine Intake	
	(µg/day)	(µg/kg/day)
Infants and children, 0 - 59 months	90	6.0 - 30.0
Children, 6 - 12 years	120	4.0
Adolescents and adults, from 13 years of age through adulthood	150	2.0
Pregnant women	200	3.5
Lactating women	200	3.5

We shall finally review the key aspects of yet another important trace element of nutritional significance i.e., fluorine, which is very often implicated with dental health. You may also have read or heard about fluorine toxicity which arises due to the presence of fluorin in high amounts (>1 ppm) in drinking water. Let us get know more about this important aspect.

10.11 FLUORNE

Fluorine is potentially a toxic element. Its essentiality for humans is not established although the role of fluo ide in providing protection from dental caries in human has been demonstrated. Fluorine (F)is a gaseous chemical element, while its ion, fluoride (F^{-}) is composed of fluorine bound to a metal, non-metal, or an organic compound. Examples are magnesium fluoride, hydrogen fluoride, fluro/benzene fluoride. Fluoride predominatesin nature and in body, it is deposited in bones and teeth. Its incorporation into tooth enamel markedly increases the hardness and resistance to decay.

Let us next study about the food sources of fluoride.

Food Sources

The major source of fluor de in most diets is water, with foods providing only about 25%of total intake. These include tea and marine fish, ready-to-use infant formulas made with fluoridated water. Other foods which significantly contribute to fluoride in our diet are given in Table 10.22.

Table 10.22: Sources of fluorid

Food Group	Fluoride Content (ppm)
Dairy products	0.05 - 0.07
Meat, fish, poultry	0.22 - 0.92
Grain, cereal products	0.29 - 0.41
Potatoes	0.08 - 0.14
Green leafy vegetables	0.10 - 0.15
Legumes	0.15 - 0.39
Root vegetables	0.09 - 0.10
Other vegetables	0.06 - 0.17
Fruits	0.06 - 0.13
Fats, oils	0.13 - 0.24
Sugar	0.21 - 0.35

Metabolism

Soluble fluo ides, even at high intake levels are allnost completely absorbed from gastrointestinal tract. These include aqueous solutions of fluorides, sodium fluoride (NaF) used in toothpastes, and sodium fluorosilicate used in water fluoridation. However, its availability from solid foods is only about 50%-80% of that absorbed from aqueous solutions. This is because in foods, it may be bound to proteins and on hydrolysis by enzyme proteases, may still be less available for absorption, Peak plasma concentrations occur within 30-60 minutes of ingestion. Fluoride absorption occurs through diffusion.

Once absorbed, the fluoride passes into the blood for distribution chiefly to the calcified tissues. Most of the ionic fluoride enters the bone and developing teeth where the fluoride ion replaces the hdroxyl or bicarbonate in the hydroxyapatite and forms fluoroapatite. About half of the fluoride absorbed each day is deposited in the skeleton or teeth within 24 hours. Nearly 99% of the fluoride in the body is in the calcified tissues. Fluoride in the bone is in a reversible pool and can exchange for other ions such as hydroxyl ions during the process of bone remodeling. The only positive role clearly demonstrated for fluoride, however, is in the prevention of dental caries. Let us learn about this important function next.

Functions

The only beneficial role demonstrated for fluoride is in reducing the prevalence and severity of dental caries in children and adults. This is enumerated next.

Fluoride and dental cavies: There are three ways in which fluoride may act to prevent tooth decay. When fluoride is incorporated into the tooth early in life at the time of tooth emption, the enamel containing fluoroapatite becomes more resistant to dissolution by acids. Secondly, in normal course, the enamel gets demineralized by contact with food acids and demineralization occurs to ensure that enamel structure is maintained.

Topical application of fluoride enhances demineralization and maintains the integrity of the enamel. Lastly, fluoride inhibits glycolysis and then reduces acid fonnation from sugars on the teeth, helping to prevent enamel demineralization and tooth decay. For these reasons, fluoride is considered as a beneficial element

for humans, but it is not an essential element. Drinking water fluoride levels of 0.7 to 1.2 mg/L is considered safe. Levels above this can cause several health risks and should be avoided.

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In regard, let us discuss the effects on health of fluoride toxicity.

Toxicity

Fluoride is a cumulative toxin. Ingestion of fluoride 1.0-1.5 mg/L for several years may produce dental fluorosis, i.e. browning and pitting of teeth known as mottling, as you may recall studying in the Public Nutrition Course (MFN-006). Chronic high level of fluoride in the range of 2-5 mg/L can cause skeletal fluorosis. Crippling skeletal fluo osis can occur where drinking water containing higher than 10 mg/L is consumed over several. years.

The severe forms of skeletal deformity in toxic fluorosis include kyphosis (abnormal curvature of the spine), fixed spine and other joint deformities. Hyper parathyroidism secondary to high fluoride intake has been reported, which induces calcification of soft tissues. You may recall that PTH is a hormone involved in calcium homeostasis, releasing calcium from the bone into the blood when blood calcium levels tend to fall. An abnormal increase in PTH can add calcium to the soft tissues, hardening them in the process.

A form of severe skeletal flourosis known as "Genuvalgium" (knocked knees) has been reported from part of India, China and African countries. The condition is characterized by severe skeletal fluorosis and osteoporosis of the limbs. Chronic ingestion of excess fluoride coupled with low calcium and high molybdenum intakes appear to increase fluoride retention in the bone. While hyper-parathyrodism and increased levels of PTH result in calcium removal from the bone, explaining the osteoporosis of the limbs.

With this, we end our study of micro minerals. Indeed that was an exhaustive study,

10.12 LET US SUM UP

In this unit, we studied about 8 physiologically important micro minerals namely, iron, zinc, copper, selenium, chromium, manganese, iodine and fluorine. We learn1 about their history, food sources along with content, their physiology of metabolism inside our body. We also focused on their vital functions, the deficiency and toxicity levels.

We also got to know about the various testsfmethods used to assess their status in our body. Also, we learnt about their recommended level of intake of requirements which are essential to carryout various physiological roles.

10.13 GLOSSARY

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Acrodermatitis Enteropathica : a genetic human disease related to an inability to absorb adequate zinc from the normal diet.

Alopecia : an autoimmune disease in which the immune system mistakenly attacks the hair follicle leading to hair fall on the scalp) loss of hair or baldness.

Arthopathy : any disease or disorder involving a joint.

Bradykinesia : slowness of movement.

Cardiac arrhythmias : an abnormal rate of muscle contractions in the heart.

Cardiomyopathy : a disease of the heart muscle that causes it to lose its pumping strength.

Ceruloplasmin : a Cu-containing protein.

Chelators : compounds that bind to metal ions to fonn a complex.

Dystonia : abnomal muscle tone of one or more muscles.

Glucose Tolerance Factor : a compound containing chromium that aids insulin in regulating blood sugar levels.

Goitrogens : substances that interfere with iodide metabolism in any way that inhibits thyroid hormogenesis.

Haematocrit : proportion of the total blood volume, that is, red blood cell; expressed as a percentage.

Haem iron : iron found in foods (f plant origin.

Hypoxia : insufficient oxygen, especially as applied to cells.

Micro minerals : minerals which comprise less than 0.01% of the total body weight and are required in concentration of Ippm or less.

Mobilferrin : an iron-binding protein.

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10.14 CHECK YOUR PROGRESS

1) Enumerate a few dietary factors which affect iron absorption.

2) How does our body maintain iron balance?

3) What are the consequences of iron deficiency

4) List the various methods by which one can assess iron status.

5) Why is zinc referred to as the most abundant intracellular trace element?

6) Describe the term 'Zinc Fingers'.

7) Which components aid in the release of Cu in the gastrointestinal tract?

8) Enumerate the dietary component affecting Cu absorption.

9) What is Wilson's disease?

UNIT

11

FOOD COMPONENTS OTHER THAN ESSENTIAL NUTRIENTS

STRUCTURE

11.1 LEARNING OBJECTIVE

After going through this unit, you will be able to:

- describe what are functional foods/nutraceuticals,
- classify the functional foods,
- discuss the potential health implications and mechanisms of action of functional foods, and
- explain the various adverse effects of these substances.

11.2 INTRODUCTION

In the previous units so far, we have read about the six major nutrients, which are essential for us. Though these vary in their requirements and roles, they have significance in our daily diets. Apart from these nutrients, there are certain health- promoting essential nutritional factors which have protective and

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preventive functions. In this unit, we will be studying about what are these and their beneficial, as well as, adverse health effects.

The idea that food can be health-promoting beyond nutritional value is gaining a wide acceptance. This broad view of nutrition has led to the concept of 'functionality'. The American Dietetic Association (ADA) has taken the position that specific substance in food e.g. phytochemicals may benefit health when consumed as a paxt of a varied diet. Many common foods contain non-nutritive components that may provide protection against chronic diseases. It is believed that 'nutraceuticals' or 'functional foods' will help to provide an increased 'health span', that is, medical benefits, including the prevention and treatment of disease.

These substances are bioactive (extra-nutritional) constituents of foods which can act as 'chemopreventers7 i.e. have anticarcinogenic and other beneficial properties evoking physiological, behavioural and immunologic effects. This unit deals with such health promotive nutritional factors and bioactive constituents—their potential health implications and mechanisms of action to the extent that has been elucidated so far. While reading this you should bear in mind that despite animal research and some clinical trials, there is still uncertainty about the absolute safety and long-term benefits of supplementing the diet with some of these constituents. While functional foods in general have promoting properties, some of them may have an adverse effect on absorption or utilization of certain nutrients. We shall learn about these effects in this unit.

11.3 FUNCTIONAL FOODS

The term 'functional food' was born in Japan. Functional foods are actually products formulated with naturally occuning chemicals or a combination of these. They are found in many fruits, vegetables, grains, herbs and spices to provide a health benefit, lower the risk of certain diseases or affect a particular body process. To be precise, these are the food substances, beyond basic nutrients that are designed to lower tlze risk or delay the onset of certain diseases. The Japanese were the first to observe that food could have a role beyond nutrient supply. Thus, a functional food must be a food and not a drug. Beneficial effects should be obtained by consuming normal amounts that is within the parameters of a 'normal' diet.

In Japan, several functional foods are available in the market. It was the first country to legislate these products (FOSHU stamp—Foods of Specified Health Use). Europe and the American countries incorporated later the concept of an added value of food. There is no consensus between Europe and the USA regarding a concrete definition. Therefore, we have several different terms such as: nutraceutical, designer food, vita foods, pharma food medicinal foods, prescriptive foods, therapeutic foods, super foods, foodiceuticals and medifoods. Nutraceutical is the preferred term in USA. European experts decided to adopt the term 'functional food' with a consensus definition. You may refer 10 Box 11.1 and Box 11.2 for a

detailed European and Japanese perspective on functional foods.

According to Japanese criteria, functional foods are not capsules, pillslpowder, however, in some countries functional foods (prebiotic products) are marketed in the fonn of powder or liquid suspension. Now then having gone through the European- and Japanese perspective on functional food, it must be coining to your mind that what is present in a food that makes it to be classified as a functional food. Let us find out.

So far, the most important components that have been identified and can be added to food are:

- **Probiotics:**A mono or mixed culture of living organisms, which when ingested in certain amounts, has a positive impact on host health, beyond conventional nutritional effects. You may recall reading about them earlier in the Food Microbiology and Safety Course (MFN-003) as well in Unit 1. These stimulate the growth of certain other bacteria in the colon, thereby improving health. Bacteria most often used as probiotics are Lactobacilli and Bifidobacteri which can be given along with the fermented foods e.g. yoghurt, fermented vegetableslmeat.
- **Prebiotics:** Ingredients/compounds that have a benefici l effect on microflor in the large intestine of the host e.g. fibre, fructo oligosaccharides, lactulose, sugar alcohols. Generally, they are carbohydrates that may be fermented in the large bowel and stimulate growth of potentially beneficial bifidobacteria

Several beneficial effects of functional foods have been reported, which include effects such as antioxidant, anticarcinogenic, blood glucosellipid-lowering, regulation of intestinal transit, prebiotic effect, anti-bacterial, anti-viral and immunopotentiating. A reduced risk of several chronic diseases such as CVD, cancer, diabetes, hypertension, osteoporosis has also been reported.

A wide variety of functional foods are available in the market. Functional foods can be identified/selected on the basis of their properties, clinical significance or composition. Discussed below are some of the common methods employed for classifying functional foods.

11.3.1 Classification

Functional foods may be classified in various ways. From the nutritional viewpoint, they can be categorized as nutrients and non-nutrients. Have a look at the Table 11.1, which presents this classification.

Table 11.1: Classification of functional foods

Nutrients	Non-Nutrients
• *Lipids* n-3 fatty acids Conjugated linoleic acid	• *Fibre* Insoluble and soluble fibre • *Phenolic compounds*

• *Vitamins* Folates Vitamin E Carotenoids: β-carotene and a-carotene Vitamin C • *Minerals* Selenium	Phenolic acids Flavonoids Isoflavones Catechins Tannins • *Non-digestible Oligosaccharides (NDO)* Fructans Galacto oligosaccharides Isomalto oligosaccharides Xylo oligosaccharides Soy oligosaccharides • *Phytosterols* • *Glucosinolates* • *Carotenoids* Lutein Cryptoxanthine • *Lycopene* • *Organosulphur compounds*

Here we will not be discussing nutrients classified as functional foods, since these have already been dealt with in the earlier units of this course. We will only focus on the non-nutrient category. But first we shall look at the other classifications of functional foods.

Another classification is by the target organdsystenz benefited. This is of clinical relevance especially with regards to treatment and management of various diseases. Examples of functional foods, on the basis of their beneficial impact on different organ systems, are given in Table 11.2.

Table 11.2: Classitication based on orgadorgan system

Organ/Organ System	Food Component
Gastrointestinal tract	Prebiotics (NDOs), soluble fibre Insoluble fibre Probiotics Polyphenols Phytatc n-3 fatty acids Micronutrients
Cardiovascular system	n-3 fatty acids Polyphenols Micronutrients Soluble fibre
Immune system	Prebiotics Probiotics Nutrients n-3 fatty acids Polyphenols
Skeletal system	Fructans
Kidney	Fructans

Besides classification based on orgadorgan systems, another classification is based on origin or source i.e. plant, animal or microbial. Some compounds/substances included in each group are listed herein Table 11.3.

Table 11.3: Classification based on origidsourc

Source	Components
Animal	Conjugated linolenic acid (dairy products)
	Chitosan
	Fish oils (ω L-fatty acids)
Microbial	Probiotics
Plant	Fibres (all components)
	Polyphenols
	Fructans
	n-3 fatty acids
	Phytates
	Carotenoids
	Non-glycerides in edible oils

Some foods are inherently functional and do not require much modification whereas others do. Foods may be made functional by:

elimination of components e.g. toxins or allergenic proteins,

increasing the concentration of a natural component e.g. fortific tion, addition of components with beneficial effects e.g. non-vitamin antioxidants,

addition of beneficial microbes e.g. some yeasts, bacteria

replacement of a component, usually a macronutrient e.g. fat replaced widi modified or emulsified carbohydrates, a

enhancement of bioavailability of components.

Thus, a number of substances or components can be added to food to make it more appropriate for the treatment of a disease or management of health. Next, we move on to the study of functional foods. We will begin with the bioactive substances especially those present in protein-rich foods.

11.4 BIOACTIVE SUBSTANCES FROM PROTEIN FOODS

Bioactive substances are derived from living organisms that can be used by humans for a variety of applications. They are constituents in foods or dietary

supplements, 'other than those needed to meet basic human nutritional needs and are responsible for changes in health status. Let us in this section learn About these as present in protein foods and their possible health effects.

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The main function of dietary protein, as we know, is to supply the body with essential amino acids and organic nitrogen. However, proteins also supply bioactive peptides that are released by proteolysis in vivo (within the living body) and in vitro (in an artificial environmentoutside the living). Casein-derived peptides have found applications as dietary supplements and pharmaceutical preparations.

Peptides originating from food proteins should be considered as potential modulators of various regulatory processes in the body. A number of in vitro studies have shown anti-carcinogenic and anti-tumor activity for many of these in addition to the antimicrobial activity of the whey proteins.

Let us next get to know more about edible oils and fats and how they act as bioactive components.

11.5 NON-GLYCERIDES IN EDIBLE OILS

You may be aware of the fact that the glyceride fraction (an ester of glycerol and fatty acids that occurs naturally as fats and fatty oils) in edible oils and fats is about 90-98% and the remaining 2-10% is the non-glyceride fraction and that it contains a variety of components. These are: Sterols, terpene alcohols, tocopherols, hydrocarbons, long chain alcohols including waxes, carotenoid pigments, sulfur- and nitrogen-containing flavour compounds. They possess nutritional and physiologic functions. These components are present in the crude extract and are destroyed/ reduced during the process of concentration or chemically modified during refining.

A brief review on these non-glyceride fractions follows:

- Sterols: These constitule a major proportion of the non-glyceride component while tocopherols, carotene pigments and flavour compounds are minor compounds.
- Aliphatic alcohols: These are water-insoluble, with their content varying from 0.5-7% of the unsaponifiable matter. Rice bran oil contains a mixture of ferulic acid, esters of slerols and triterpene alcohols, 'Oryzanol' which is considered to have a hypocholesterolemic effect.
- Terpene alcohols: Partly free, partly esterified e.g. ferulic acid; these are found in significant amounts in rice bran oil, wheal germ oil, soybean oil, linseed and olive oil. Commonly used edible oils e.g. groundnut, sesame, safflower, corn, coconut, sunflower and palm oils contain only —10-20% of the amount found in rice bran oil. A hypocholesterolernic effect has been seen in animals and humans. Blends of rice bran oil and safflower oil have been shown to reduce cholesterol and LDL aside from the effects of PUFA and MUFA.

So far we have read about functional foods, bioactive substances present in protein foods and the non-glyceride fractions in edible oils which have been found to have health promotive properties. We shall learn about some other food components in our subsequent discussions. However, before we proceed, it would be a good exercise to recapitulate about the concepts learnt so by answering the questions mentioned in the check your progress exercise l.

11.6 PROBIOTICS AND PREBZOTICS

We all have read or heard about probiotics and prebiotics at some point of time. However, what exactly do we mean by these terms? When were they identified? What are the benefits of these components and which foodslfood products would contain them? These are a few questions which shall be answered through the discussions to be followed next.

Well, during the initial stages, research and development of functional foods was confined to mostly those to which certain components such as micronutrients were added. However, one of the most promising current targets for functional food development is the gastrointestihal tract (GIT). The human large intestine is inhabited by very large numbers of microorganisms. The resident microflora through their metabolic activities exerts important physiological action relevant to health and disease. This and other possibly beneficial effects to other target organs have led to an intensive study of probiotics and prebiotics.

We shall now begin our study about pro and prebiotics by first defining these terms.

11.6.1 Definition and Characteristics

An early definition of probiotics is 'organisms and substances which contribute to intestinal microbial balance'. Later the word 'substances' was removed since these could include antibiotics and microbial stimulants that are categorized as prebiotics. The revised definition is a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbicd balance. It has been suggested that the definition should be expanded to include other areas of the body e.g. skin, vagina and respiratory tract. Thus, the beneficial effect of probiotics can be mediated through the gut microflora by ingesting viable micsoorganisms. According to the definition, probiotics include not only preparations but also traditional yoghurts and other fermented foods.

Prebiotics, on the other hand, are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.

Let us now move on to the understanding of the characteristics of probiotics and prebiotics.

Characteristics of Probiotics and Prebiotics

The characteristics of probiotics and prebiotics are highlighted in Table 11.4.

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Table 11.4 : Characteristics of probiotics and prebiotics

Probiotics	Prebiotics
Are microorganisms	Are non-digestible dietary/food ingredients
	Are not hydrolyzed/absorbed in the upper GIT, reach the large intestine in an intact form and have a specific metabolism therein – directed towards beneficial/advantageous bacteria than those which are adverse/detrimental for host health
Promote a healthy intestinal microflora	Fermented in colon
Ensure colonization resistance to pathogens	Alter composition of colonic microbiota towards a healthier community
Destruction of genoioxins and mutagens Immune system function	May induce systemic effects beneficial to host

11.5.2 Probiotics: Dietary Sources and their Mode of Action & Effects

We can have specific preparations designed for robotic use, as well as, foods. Probiotic products which are marketed are in the form of powders, tablets and liquid suspensions. Among the various organisms, lactic acid bacteria, streptococci and bifidobacteri are commonly used.

It is not clear how probiotics influence the flora and produce a beneficial effect. However, colonization of the gut appears to be a prerequisite for the probiotic effect. Important relevant features may be:

resistance to low pH and bile acids, and

ability to adhere to intestinal epithelium.

However, ability to adhere to intestinal epithelium does not ensure that an organism will permanently colonize the gut. Also, there is a continuous interchange of species with one strain being replaced by another, which is possibly better suited. Since some strains are more suitable than others. Organisms such as Saccharomyces boulardii are effective although they do not grow in the gut. For such organisms, continuous administration is required to ensure the presence of large numbers of metabolizing cells in the GIT.

As a dietitian, you must be now curious to know which foods contain probiotics. Let us read further and find out.

Probiotics in Foods

Yoghurts have been supplemented with probiotic strains of bifidobacteria and lactobacilli. Milks fermented solely by intestinal isolates of lactic acid bacteria have also been developed. Other fermented milk products like cottage cheese, sour cream etc. contain viable organisms and may have an incidental probiotic effect.

We will mw examine the health effects of probiotics.

Health Effects related to Probiotics:

Several lines of evidence support the conclusion that normal gut microflora are involved in resistance to disease, especially gastrointestinal infections.

These are:

- germ-free animals are more susceptible to infection than animals having complete gut flora
- orally administered antibiotics increase susceptibility of animals to infection (antibiotics are known to destroy gut microflora), and
- administration of enemas of faecal suspensions from a healthy adult can control antibiotic-associated diarrhoea (AAD).

Let briefly examine the effects that have been reported (remember most of it has been on animals):

- In animals, probiotics may control tumour production.
- In humans, probiotics can reduce incidence of intestinal infections. The possible mechanism of action is: the probiotic has some antagonistic effect (direct/indirect) on the pathogen: either through direct chemical antagonism, competition for nutrients or an indirect effect via the immune system by competition for receplors on the epithelial surface.
- 50% reduction in AAD observed in patients given Saccharomyces boulardii.
- Significant reduction in diarrhoea incidence among children aged 4-45 months after administration of L.casei GG. The effect was more pronounced in patients with confirmed rotavirus infection.
- Can have an antifungal effect. During chemotherapy for leukemia. Treatment with a milk preparation containing L. acidophilus and Bifidobacterium sp. markedly reduced the faecal count of Candida.

Now that we have understood the benefits and usage of probiotics, let us look at the details of prebiotics in the next sub-section.

11.5.3 Prebiotics: Dietary Sources and their Mode of Action/ Health Effects

We have already seen how prebiotics are defined. Let us go a little in-depth about them. Prebiotic fermentation should favour growth of potentially health promoting bacteria especially Lactobacilli and Bifidobacteria which are indigenous to the

gastrointestinal tract. In a way, the approach is similar to that of dietary fibre or resistant starch. However, prebiotics will affect bacterial growth selectively. Also, efficient prebiotics will reduce/suppress the numbers and activities of possibly pathogenic microorganisms.

Since prebiotics are fermented by the gut microflo a, they may have physiological effects on the GIT such as:

- control of transit time and motility,
- regulation of epithelial cell proliferation,
- influence on nutrient bioavailability
- modulation of immune function, and
- modulation of endocrine function.

In addition, they may exert systemic effect by influencing carbohydrate or lipid homeostasis.

Our subsequent discussion would be pertaining to soine itnportant types of prebiotics such as Non-digestible oligosaccharides.

Let us read about them.

Non-Digestible Oligosaccharides (NDO)

Among the various food components, the best prebiotic effects seem to be exerted by the NDOs. They are oligomeric carbohydrates, which a n resistant to hydrolysis by intestinal digestive enzymes but NDOs can be metabolized by colonic bacteria. What will be the products of bacterial fermentation? Well, these are:

short chain carboxylic acids (short chain fatty acids),

gases; and

organisms also increase metabolic energy, growth and proliferation.

Generally, these carbohydrates are a mixture of oligomers of differing chain lengths. Oligosaccharides with prebiotic effect are:

fruct ooligosaccharides (FOS) or inulin-type fructans

soybean oligosaccharides e.g. stachyose and raffinose

galacto oligosaccharides

malto oligosaccharides

galactosylsucrose

palatinose condensates

xylooligosaccharides

Many prebiotic oligosaccharides are being used in Japan. Among these, FOS have been the most studied. We will now highlight some interesting features of filicto-oligosaccharides or fiuctans

Fructans

It is a general term for any carbohydrate in which one/more fructosyl fructose link constitutes the majority of glycosidic bonds. They are linear or branched fmctose oligopolymers i.e. # -2,1 fructosyl fructoselinked inulins or ß -2,6 linked levans. Inulins are mainly of plant origin, containing 2->70 units, whereas levans are mostly produced by some fungi and many bacteria. Fungal/bacterial inulins have a much higher degree of polymerisation (DP) (upto 150). Oligofiuctose (DP 2-10) is produced by enzymatic hydrolysis of inulin. Thus, as food ingredients, they are available either as native inulin or high molecular weight inulin, or the enzymatically produced hydrolysate oligofructose. Synthetic fmctans are mainly ß-2,1 linked fiuctose with DP 2-4, industrially obtained by enzymatic synthesis from sucrose. Inulin type fmctans are present in significant amounts in a variety of edible fiuits and vegetables e.g. plant families such as Lilliaceae, Amaryllidiaceae, Graminae, Conzpositae e.g. asparagus, artichoke, garlic, leek onion, banana, chicory roots.

Fructans can be ingested by consuming these foods, e.g. in cereals, aerial parts of many Graminae particularly young seedlings contain upto 70% of their dry weight. Estimated daily intake in Western countries is 3-11g/day, depending on the type of food consumed.

Because of their configu ation, inulin-type fmctans are resistant to human digestive enzymes, and in the ileum due to microbial activity and/or enzymatic hydrolysis, with the remaining 86-88% of the ingested fructans being left undigested. Isomaltooligosaccharides are partially hydrolyzed by isomaltose in the jejunum whereas the soybean oligosaccharides raffinose, stachyose and palatinose are not hydrolyzed much. Galactooligosaccharides appear to be metabolized.

The functional/technological attributes that give them a potential for incorporation into foods and the health benefits of fructans are enumerated next. A) Health Benefits of Fructans The health benefits of fiuctans includ

- Bifidogenic Effect: Fructans selectively stimulate the growth of Bifidobacteria and Lactobacilli, while decreasing concentrations of E.coli, Clostridia and bacteroides. Predominance of these bactetia is achieved within two weeks, with effects lasting as long as the fmctans are consumed. Daily doses of 4-40 g increased the bifidobacteria upto 1095 per gm of faeces. But what are the benefits of increasing the growth of bifidobacteri

  Bifidobacteria displaces potential pathogens selectively, showing an antibiotic like effect, which is unrelated to the changes in short chain fatty acids (SCFA) and PH. Due to fennentation, the carboxylic acids produced—acetate, propionate, butyrate—have both systemic and physiological effects. Also, these end products of fermentation allow the host to salvage a part of the energy of NDO and may play a role in regulating cellular metabolism, cell division and cell differentiation. Look at Table 11.5, which presents the physiological effects of bacterial growth and acid produced.

NOTES

Table 11.5 : Physiological effects of fermentation

Acid Causes:	Bacterial Growth Causes:
• decrease in faecal pH • hyperplasia of intestinal mucosa • increased wall thickness in small intestine and cecum • increased blood flow in the tissue • the lowered pH in a micro niche makes it unfavourable for pathogens	• increased bacterial biomass • increased faecal mass • competition effects towards colonization sites and available nutrients • excrete natural anti-microbial agents which can affect a variety of organisms • may themselves function as anti-infective agents through occupation of pathogen colonization or receptor sites

Thus, prebiotics help to attain an appropriate balance of microflora and help in resisting the effects exerted by the various pathogens.

Mineral absorption: NDOs affect mainly calcium/magnesium absorption and balance. Acidification of colonic contents increases the concentration of ionized minerals, particularly calcium and magnesium, thus favouring passive diffusion. Formation of soluble salts of organic acids and colonic hypertrophy facilitates increased absorption of these minerals. Similar effects have been observed in animals (but not yet in humans) for iron and zinc.

Glycemia/lnsulinemia: Preliminary research evidence indicates that there may be beneficial effects in terms of decreased fasting blood glucose/hepatic glucose production. This may be due to delayed gastric emptying, increased transit time, which may be dose-dependent. Alternatively, hepatic metabolisin of glucose may be modified, mediated by the SCFA, especially propionate. Propionate inhibits gluconeogenesis probably via its conversion to methylmalonyl CoA and succinyl COA, both of which inhibit pyruvate carboxylase. Propionate enhances glycolysis and may lower plasma fatty acid concentrations.

Lipid Metabolism: Animal studies consistently show a hypotriglyceridemic effect although equivocal results have been seen with healthy humans. Hypotriglyceridemia is due to decreased VLDL concentrations. Animal studies show a decreased de novo lipogenesis in the liver due to reduced acuvity (almost 50%)of all lipogenic enzymes, possibly through modification of lipogenic enzyme gene expression. Inhibition is mainly attributable 10 propionate. Limited studies show possible lowering of serum total and LDL cholesterol. Uremia and Nitrogen Disposal: In animals, faecal and renal nitrogen were enhanced and decreased uremia was seen in normal and nephrectomised animals.

The mechanisms proposed are: increased colonic biomass and consequent nitrogen fixation with acidification and conversion of diffusible ammonia into less diffusible ammonium ion, due to NDO's osmotic effect, urea transfers into distal ileum and large intestine is accelerated. In the large intestine, ureolytic

microflora may act. When fermentable carbohydrate intake is high, the amount of ammonia required may become insufficient and blood urea is used as a substrate, and inhibition of ureagenesis in the liver by propionate.

Once again it should be emphasized here that these are inferences drawn from animal studies and verification in humans will have to wait until relevant studies are carried out.

Enumerated below are the potential uses of fructans.

B) Fructnns as Food Ingredients

Oligosaccharides have several functional/technological attributes that give them a potential for incorporation into foods. They can:

- modify freezing point and moisture content,
- have variable stability to acid, on storage and processing,
- have bacteriostatic prope ties,
- may stabilize proteins,
- retain flavour, aroma,
- affect colour formation,
- variable sweetening power, thus variable energy density and carcinogenicity,
- can be used as fat replacers since they confer mouth feel and texture similar to fat, and
- can be used as bulking agents.

Thus, to summarize, we can say that a good prebiotic should have the following properties:

- be active at a nutritionally feasible, as low a dose as possible,
- lack side effects,
- be able to exert fine control of microflora modulation
- persist throughout the colon including distal areas,
- have varying viscosity,
- have good storage/procéssing stability,
- have differing sweetness, and
- inhibit adhesion of pathogens.

In this section, we learnt about pro- and prebiotics. The discussions highlighted the different types of these substances, their properties and uses in the food industry. It must have been interesting to learn about non-digestible oligosaccharides particularly, fructans. We shall continue to learn further about some more bioactive non-nutritional components such as polyphenols. However, let us first revise our concepts by performing the following exercise given in check your progress exercise 2.

11.7 POLYPHENOLS

We now come to a group of compounds, which were until recently considered to adversely influence nutrient absorption or giving colour to foods e.g. anthocyanins. Today they are among the most popular and commonly consumed nutraceuticals. More than 4000 phenolic phytochemicals have been identified so far including tocopherols and tocotrienols. They are ubiquitous in all plant organs and therefore are an integral part of the human diet. Let us find out what are these

11.7.1 Definition and Glassif'ication

Polyphenols are the compounds that contain an— ON group attached to the benzene rizy. The main classes are: flavonoids, phenolic acids and polyphenols (tannins). They arise from common intermediates phenylalanine or its precursor shikimic acid. Natural phenolic compounds range from simple ones like hydroxybenzoic acid to highly polymerized ones e.g. tannins. They arc glycosylated by one or more sugar residues. The OH groups linked can be glucose, galactose, rhamnose, xylose or arabinose, glucuronic or galacturonic acids.

The various classes are:

a) Phenolic acids and derivatives

b) Flavonoids such as Flavonols and Flavones, Isoflavones and Flavanols

c) Tannins

d) Stilbenes

e) Lignans

We will now describe each of these one by one.

A) Phenolic Acids and Derivatives

Two families of phenolic acids are widely distributed in plants: a range of benzoic acid derivatives and those derived from cinnamic acid, both occuning in a conjugated or an esterified form. Examples are:

- **Hydroxybenzoic acid:** e.g. ellagic and gallic acids, which are hydrolyzable tannins, present in berries and nuts.
- **Hydroxycinnamic acid:** e.g. caffeic and ferulic acids, which are heat-sensitive. Caffeic acid is a precursor of lignin. Caffeic with qunic acid gives chlorogenic acid. They occur in fruits, vegetables notably seeds, coffee beans, grains, sunflower seeds. Among these, curcumin and chlorogenic acid have been studied more. Anticarcinogenic effects are attributed to caffeic and ferulic acid. They may act in two ways:

  a) prevent formation of carcinogens from precursors, and

  b) block reaction of carcinogens with critical cellular macroinolecules.

B) Flavonoids

Flavonoids constitute the largest group of plant polyphenols, generally arc the compounds of low molecular weight, bound to sugar molecules. You may be familiar with some of these plant pigments. Anthocyanins (red, blue and purple pigments) are flavanoids. We also have anthoxanthins, which' include flavonols, flavones, flavanols and isoflavones All of these are colourless/white/yellow. We will look at each briefly:

- **Flavonols and Flavones:** These are the most widely distributed among the flavonoids. The most commonly occurring are Quercetin, Myricetin and Kaempferol. Quercetin is quantitatively the most important and is present in onions, apples, kale and tea. It is concentrated in the outer exposed parls of plants and its concentration is proportional to the greenness. Losses vary; average cooking methods result in less than 200/0 losses whereas other processing methods lead upto 50% losses.

- **Flavanols:** Examples are catechin and epicatechin. You may have heard of the benefits of tea. Some of them are due to gallic acid, which is combined with epicatechin. Flavonols constitute 30% of dry matter from tea solutions. In fruits, legumes and grains, they exist as condensed polymers and are concentrated more in immature fruits. Fruits stored over winter lost approximately half their content.
- **Isoflavones** These are usually treated separately from the other five subclasses and are an area of considerable research interest. Isoflavones are found almost exclusively in the legume family but occur in high amounts only in soybeans. Genistein and Daidzein are found in soybeans. They are heat stable, slightly water-soluble. The content in dry soybeans ranges from 1600-2400 mg/kg. The third polyphenol covered in this section are tannins.

C) Tannins

Long known for their inhibitory effects on iron absorption, recent research indicates that tannins do have beneficial effects. Tannins are compounds of high molecular weight. In fact, the astringent taste that you find in some foods is due to the reaction of tannins with mouth proteins. Figure 11.1 highlights some of their characteristic features.

D) Stilbenes

Stilbenes contain 3 phenyl compounds connected by a 2-carbon methylene bridge and occur in nature in restricted distribution. In plants, they act as anti-fungal phytoalexins, usually synthesized only in response to infection/injury. The most extensively studied is trans-reservatrol, present in grapes, wine and peanuts. Red wine contains 1.5-3.0 mg/L.

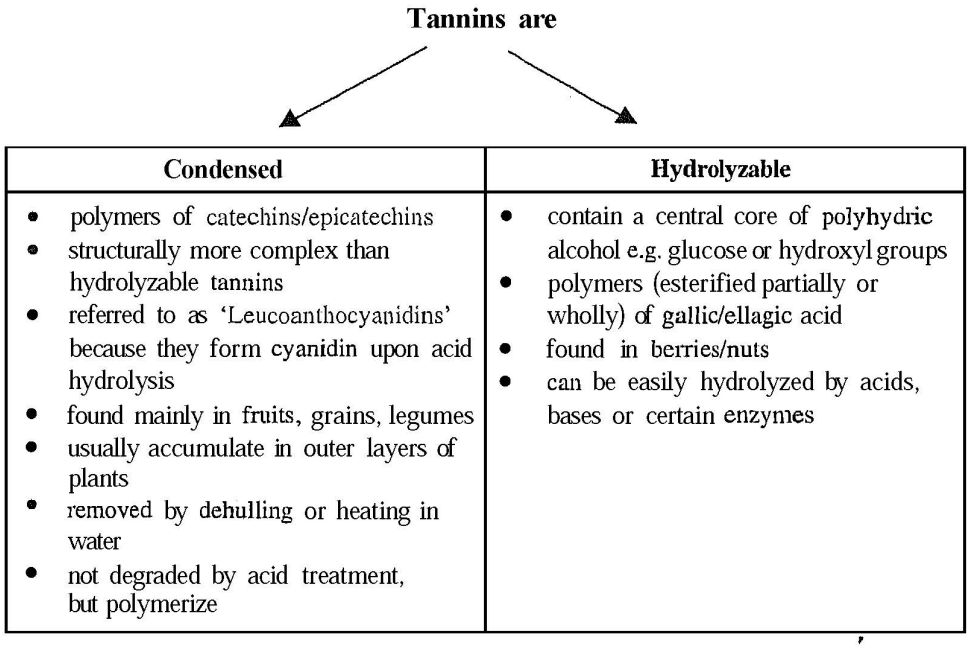

Figure 11.1: Characteristics of different forn~s of tannins

E) Lignans

Lignans are diphenolic compounds formed by dimerization of 2 cinnamic acid residues. Most lignans apparently pass through the GIT as fibre. Some lignans may be converted by intestinal microflora to mammalian lignans-enterodiol and enterolactone, which are absorbed through enterohepatic circulation. Flaxseed meal and flour are said to be the richest sources of 2 lignans-SecoisolariciresinoI diglycoside (SDG) and matairesinol. Other good sources of lignans are pumpkin seeds and sunflower seeds. Next, we shall read about the absorption/bioavailability of polyphenols.

11.7.2 Bioavailability of Polyphenols

What do you mean by the term 'bioavailability'? You would recall reading about it earlier in this course. We suggest you to go back and refer to its definition in Unit 7 and 8 and then proceed. further.

We need to consider bioavailability before studying the functions because their nutritional significance depends on their behaviour in the digestive tract. Some of the salient aspects related to bioavailability have been elucidated herewith:

i) their digestion and utilization depends on their snucture, degree of glycosylation/ acylation, conjugation with other phenolics, molecular size and stability,

ii) in vitro studies and animal experiments show that upto 1/3rd of extractable polyphenols are excreted, however, the percentage of non-extractable polyphenols excreted are twice or three times more,

iii) some phenolics like aglycones,simple phenols and flavonoidsare directly absorbed into the small intestines. Glycosylated polyphenols are hydrolyzed by glycosidases present in food/produced by the GIT mucosa or they are acted upon by microflora, after which they are absorbed in the colon. Intestinal bacteria have been found to solubilize non-extractablepolyphenols, and

iv) absorption in rats is low (20-34%). In humans, the absorption is appmently influenced by the chemical nature, thus the extent varies from as much as 24- 52% for Quercetin, 9-21% for isoflavones to as little as 0.2-0.9% for catechin.

Human studies on bioavailability indicate that plasma levels of flavonoids are close to 0.55 gm01/L but do not exceed 1 gmol/L when the dose was close to dietary intakes.

With a brief understanding about the bioavailability of polyphenols, next we shall the influence of polyphenols on macronutrients and minerals,

11.7.3 Infl ence of Polyphenols on Macronutrients and Minerak

Let us study in this sub-sectionhow the polyphenols affect the digestion and absorption of various macronutrients such as proteins, carbohydrates, lipids and minerals.

A) Proteins

You know that tannins are considered as anti-nutritional because their presence is usually accompanied by a reduced protein digestibility and a subsequent inueasein the faecal nitrogen. Decreased protein digestibility may be due to the formation of 'protein-tannin complex', as well as, inhibition of proteolytic enzymes like trypsin by polyphenols. Polyphenols have exhibited a highly significant and negative conelation with in vitro digestibility of proteins. However, this may have a beneficial effect in overweight or obesity, since tannins bind to endogenous proteins in the intestinal tract such as digestive enzymes like lipase and amylase and inhibit them, resulting in lower energy availability.

B) Carbohydrates

Binding of proteins may indirectly affect carbohydrate absolVtion. Inhibition of amylolytic enzymes and subsequent reduction of dietary carbohydrate hydrolysis can decrease the postprandial glycemic response, which can have a beneficial effect for diabetics.

C) Lipids

The effect of food polyphenols on lipid metabolism has not been extensively studied.

D) Bioavailability of Minerals

Polyphenols can form complexes with metal cations through their carboxylic or

hydroxylic groups, and thus interfere with the intestinal absorption of minerals like iron, copper, sodium and aluminum. The important negative interaction in the Indian setting is the iron absorption vs. polyphenols, as Indian diets are deficient in iron. In view of the impact of polyphenols on the metabolism of several macro and micro nutrients, research has been carried out to explore their potential in the treatment, management and prevention of vafious diseases. Enumerated next are some of their health benefits.

11.7.4 Health Benefits of Polyphenols

Various health benefits have been attributed to polyphenols. These include:

anti-microbial
anti-viral
anti-oxidant
hypotensive
hypoglycemic
anti-carcinogenic
anti-mutagenic
oestrogenic
anti-ulcer .
anti-inflammatory
prevent expression of adhesion molecule
inhibit replication of HIV

Most of these properties (health benefits) are due to their anti-oxidant activity. Both in vitro and in vivo studies have been conducted to elucidate these effects. Let us read further 10 understand the various properties of polyphenols in detail.

A) Antioxidant Action of Polyphenols

The properties of polyphenols due to which they have been identified to act as antioxidant is because they:

act as terminators of free radicals by rapid donation of H atoms,
chelate metal ions like iron and copper,
act as terminators of propagation,
quench reactive oxygen species and reactive N2 species,
inhibit lipoxygenase and cyclo-oxygenase enzymes, and
inhibit damage by haemprotein/peroxide mixtures.

The antioxidant function depends on the number of hydroxyl groups and their positions. Among the various derivatives, flavonoids are the most potent and retain their scavenging capacity even after chelation with the metal ions. Non-extractable polyphenols are apparently 15-30 times more effective than simple

phenols. A point to note is that their ability to chelate metals also makes them act as pro-oxidants-in situation when tissue injury causes release of iron/ copper. The most important antioxidant role of polyphenols identified so far has been with respect to the treatment, management and prevention of several degenerative diseases

B) Cardiovascular Effects

You must have heard of the 'French Paradox'. The lower incidence of heart attacks in certain areas of France despite higher prevalence of factors like smoking and high fat intake was attributed to the red wine consumption in these areas. Subsequently, the 'Zutphen study' in the Netherlands showed an inverse relation between the incidence of CHD/ stroke in elderly men with the dietary intake of flavonoids especially quercetin, which originated mainly from tea, fruits and vegetables. Average total daily consumption of flavonoids was at least 23 mg (16 mg quercetinlday) and the average vitamin E intake was 7-10 mg.

Phenols have been found to consistently decrease several risk factors/CVD indicators — plasma LDLc was less susceptible to oxidation, contained lower amount of lipid peroxides. There was lower plaque formation in spontaneously hypertensive rats, consumption of wine polyphenolic extracts improved aortic blood pressure and vessel mechanical properties.

Next, we move over to the prevention and inhibition of cancer.

C) Cancer and Inhibition of Tumorigenesis

Polyphenols appear to play a preventive role although the molecular mechanisms of action and applicability to human cancer prevention are unclear. Various studies appear to suggest that they may be effective when given in the post initiation period i.e. they are more helpful in inhibiting tumor promotion and progression. Most studies have been conducted either in vitro or in vivo in animals. Hence, we must be cautious in extrapolating these observations to humans. The observations from studies are summarized as:

i) caffeic acid, ferrulic acid, chlorogenic acid and curcumin inhibited tumor promotion —curcumin inhibited colon tumorigenesis.

ii) multiplicity of invasive and non-invasive adenocarcinoma was lower.

iii) apoptosis of colonic tumor cells was higher.

iv) expression of oncoprotein was decreased.

v) in mammary tumors, these compounds cause inhibition directly or by modulating oestrogen action.

These effects have been observed with tea catechins and related compounds, caffeine, quercetin and other flavonoids, isoflavones and lignans, reseveratrol and other grape constituents. How do they confer beneficial effects? Well, this is through the following mechanisms:

Inhibit activation of carcinogens,

facilitate elimination of certain carcinogens or their reactive intermediates,

inhibit the metabolism of arachidonic acid—decreased production of pro-inflammatory or mitogenic metabolites like certain prostaglandins or reactive oxygen species,

modulate hormone-dependent carcinogenesis,

modulate different oncogenes, suppressor genes, signal transduction pathways. Thus, they inhibit cell proliferation, transformation and induce apoptosis, and

promote terminal differentiation of human tumors.

It must be evident to you by now as to why polyphenols have become popular nutraceuticals world wide and are being consumed frequently as an over the counter food supplement. Let us now move on to the next group of compounds, phytoestrogens.

But before that, you need to quickly review what we have learnt till now by answering the questions included in the check your progress exercise 3.

11.8 PHYTOESTROGENS

You may be aware of the surging interest in phytoestrogens (PE) especially in connection with osteoporosis. This section briefly discusses these compounds. As the term implies, they are the oestrogenic compounds found in plants. They exert oestrogenic effects on the central nervous system, induce estrus and stimulate growth of the genital tract of female animals. In a broader sense, they are chemicals showing effects suggestive of oestrogenicity e.g. binding to oestrogen receptor (ER), inducing specific oestrogen-responsive gene products and stimulating ER-positive breast cancer cell growth.

Phytoestrogens can be divided into 3 main classes: isoflavones, coumestans and lignans. All are diphenolic compounds with structural similarities to natural md synthetic oestrogens and anti-oestrogens. Our subsequent discussions highlight the major forms of phytoestrogens and their food sources.

11.8.1 Dietary Sources and Chemical Forms

Isoflavones and coumestans are the most common compounds. Soybeans and soyfoods are the most important sources, containing approx. 0.2- I .6 mg per gram dry weight; although chick peas and other legumes also contain them. Second generation soy foods e.g. products like tofu yoghurt contain 6-20% of the isoflavones present in the whole beans.

Isoflavones may be present in unconjugated form (aglycones) e.g. daidzein, genistein, or as glycosides such as daidzin, genistin.

Non-fermented soy foods like tofu contain greater levels of glucosides whereas fermented foods e.g. tempeh have higher amounts of aglycones due to enzymatic hydrolysis during the fermentation process.

A large number of cournestans e.g. coumestrol in alfalfa have been isolated from plants but only a few possess uterotropic (stimulating growth of the uterus) activity. The highest amounts of coumestans are present in clover and alfalfa sprouts (5.6 and 0.7 mg/g dry weight). Other sources are split peas, kala Chana, lima beans and soy bean sprouts (15-80 mcg/.g dry weight).

Lignans do not induce estrus but are considered to be phytoestrogens because they have oestrogen-like actions. They are present in plant foods and human biological fluids, plant lignans being converted by bacterial action to mammalian lignans in the GIT. Secoisolariciresinol and matairesinol are plant dietary precursors of the mammalian lignans, enterodiol and enterolactone.

The content of lignans in various foods is shown in the Table 11.6, oilseeds being the richest plant sources.

Table 11.6: Lignan content of selected foods

Plant Source	Content (mg per 100 g wet wt)
Flaxseed	0.8 mg secoisolariresionl per g dry wt
Unhulled soybeans	20.5
Dried sea weed	0.9
Whole legumes	0.6
Cereal brans	0.5
Legume hulls	0.4
Whole grain cereals	0.3
Vegetables	0.14
Fruits	0.03

The potential role of phytoestrogens with respect to maintaining good health is being discussed next.

11.8.2 Physiological Effects

Little is known about the biologic and physiologic effect of phytoestrogens in humans. Animal studies suggest the following physiological effects of phytoestrogens:

hormonal effect, like stimulation of uterine growth in a manner similar to oestrogen (whether phytoestrogens have oestrogenic or anti-oestrogenic effect will depend on the amount of endogeneous oestrogen present), and

antioxidant effects by increasing the activities of antioxidant enzymes such as catalase superoxide dismutase, GSH peroxidase and GSH reductase.

Soya isoflavones may also act directly as anti-oxidant

The health benefits ascribed to phytoestrogens are for protection against cancer, relieving symptoms of menopause like hot flus es, prevention of osteoporosis (through prevention of bone resorption and promoting increased bone density) and prevention of heart disease in postmenopausal women probably acting as oestrogen agonists (mimicking the effect of oestrogens), producing effects on lipoproteins similar to those caused by oestrogen.

Let us now look at the characteristic features of other food components with antinutritional effects. You may be familiar with the terms phytate and trypsin inhibitor.

Let us discuss these and others.

11.9 OTHER DIETARY FACTORS WITH ANTINUTRITIONAL EFFECTS

In the above sections, we have learnt about a variety of food components having a host of health promotive properties. Let us now have a look at a few factors with antinutritional effects. These factors in foods include protease inhibitors physic acid, phenolic compounds, amylase inhibitors and saponins. The well known anti nutritional effects of these factors are discussed first. These factors are present in foods that we consume regularly such as whole wheat, other whole grains, legumes and soyabeans. A few noteworthy points:

The concentration of antinutritional factors is much lower in the refined cereals from which nearly all the bran and much of the endosperm has been removed. Further, some of the anti-nutritional factors such as, protease inhibitors in soyabean and some legumes, are heat labile and therefore proper cooking will inactivate them. Household processes such as soaking and fermentation will also remove many of the antinutritional factors.

The traditional methods of cooking and processing all have the effect of reducing the antinutritional factors in our diets. Therefore. you will notice that although several adverse effects are documented chiefly in animal models for these antinutritional factors, in actual practice, the cooking and processing of foods for human has evolved in such a way as to keep these antinutitional factors low in our diets so that we do not suffer from the ill effects. Occasionally, however, the consumption may reach levels at which ill effects become manifest. It is important, therefore, to be aware of these adverse effects.

Following the adverse effects of each of these constituent, the currently known beneficial effects are listed. At the current time what we do not know is the amount of these to be consumed to maximize the beneficial effects and minimize the adverse effects.

So then let us begin our study of these factors with protease inhibitors.

11.1 Protease Inhibitors

These are protein in nature and are abundant in raw cereals and legumes, especially soybeans. It would be interesting to note here that since they are proteins, they can be denatured by heat. However, in commercial soy products, 5-20% of the activity has been detected.

What are the effects of protease inhibitors?

In experimental animals, they have been found to be associated with growth inhibition and pancreatic hypertrophy. A negative feedback mechanism in the small intestines has been postulated for these effects. In the presence of trypsin inhibitors, inactivation and loss of intestinal trypsin can take place. These can trigger the release of cholecystokinin (CCK) from the intestinal mucosa. CCK then can induce the pancreas to produce more trypsin. However, excess of trypsin inhibitors can reduce the protein available thus explaining the gwwth inhibition seen in animals, as well as, the pancreatic hypertrophy. Moreover, trypsin is rich in sulphur-containing amino acids; hence increased synthesis of trypsin (the more the inhibitor, the more trypsin that is made) increases the requirements for these amino acids, ultimately leading to weight loss. Also, the stress of the pancreas results in pancreatic hypertrophy and hyperplasia of the acinar (exocrine) cells.

Feeding purified trypsin inhibitor or raw soy flour containing protease inhibitors potentiated the effects of pancreatic carcinogens. It must be noted that most of the effects have been observed in some species of animals only, whose pancreas constitute a fairly higher percentage of body weight (0.29-0.8%) e.g. in rats, mice, chickens, hamsters and guinea pigs but not in large animals with a small pancreas (0.06-0.24% of body weight) e.g. dogs, calves, monkeys.

In human subjects, provision of raw soy flour or purified trypsin inhibitor directly to the duodenum, increased secretion of pancreatic enzymes and serum level of CCK. This suggests that a negative feedback mechanism also exist in humans. However, it is interesting that among populations with fairly high intake of soybeans or other foods rich in protease inhibitors, e.g. in Japanese and Seventh Day Adventists, the incidence of pancreatic cancer is lowel. Another category of food components which may influence human health are the saponins. A few characteristic features of saponins are discussed below. 11.8.2 Saponins

These are a diverse group of compounds commonly found in legumes like soybean, lentils, chickpeas, peanuts and alfalfa sprouts. They are also present in some plants which we use as flavouring agents such as herbs spices e.g. fenugreek, nutmeg, ginseng, sage and thyme.

Let us briefly understand their chemical nature Food Components other than Essential Nutrients

Their structures are characterized by the presence of a steroid or triterpene group, i.e. an aglycone linked to one or more sugar molecules. Since these compounds have both polar (the sugar moiety) and non-polar (steroid or triterpene) group, obviously they will have surface-active properties. These properties are responsible for whatever effects saponins exert.

You should remember that saponins have both adverse, as well as, beneficial biological effects. Let us first list the adverse effects.

The adverse effects of saponins may be described as under:

- A well-known toxic effect is 'erythrocyte lysis' since they interact with the cholesterol in the erythrocyte membrane.
- In mammals, intravenous adnlinistration causes local inflammation
- In large doses, it results in death due to nassivere lease of erthyrocyte debris.
- A reduction in oxygen-carrying capacity of blood.
- It can lyse other cells e.g. of the intestinal rnucosa and thus affect nutrient absorption.
- High saponin intake results in decreased weight gain. This has been attributed to a number of reasons:

  bitter taste

  decreased nutrient absorption and utilization because of inhibition of metabolic and digestive enzymes such as amylase, lipase, protease and cholinesterase. These effects have been observed with soy saponin.

Alfalfa sprouts have been found to inhibit chymotrypsin, protease, succinoxidase, as well as, bind zinc.

Now let us study the beneficial effects of saponins. Saponins may have some anticarcinogenic effect by binding primary bile acids, formation of secondary bile acids and thus the promotion of tumorigenesis is reduced. They also enhance the immune response and have been used as adjuvants for oral vaccines.

Another group of substances of interest are the commonly consumed amylase These are most frequently consumed in view of the fact that they are present in several cereals and legumes and we know that Indian dietaries are principally cereal based.

11.8.3 Amylase Inhibitors

Inhibitors of the enzyme a-amylase are found in wheat, rye, beans, mango, legumes, potatoes, sorghum (jowar) and oats. Most amylase inhibitors from plants are active against animal amylase.

Let us see how these inhibitors act.

The inhibitor forms a complex with amylase, which in turn reduces starch

digestion. Complex formation is influenced by pH, ionic strength, temperature, time of inactivation and inhibitor concentration. Other effects observed are pancreatic enlargement and hyperplasia.

When starch digestibility is reduced and in case starch intake is limited, you may expect growth to be adversely influenced. However, observations on animals provide confl cting data. It is possible that amylase inhibitors from different sources may have different effects due to pH sensitivity and sensitivity of the pancreas to different amylase inhibitors.

In humans, slightly different effects have been observed e.g. diarrhoea, nausea and vomiting. It is noteworthy that these effects were observed after intake of 'starch blockers' which may not be pure amylase inhibitors and other antinutritional factors like lectins and protease inhibitors also caused some of these effects.

Yet another category of food substances which are not conducive to good health include lectins and haemagglutinins. These terms may be relatively new to you. Let us understand some of their salient characteristic features.

11.8.4 Lectins or Haemagglutinins

These are sugar binding proteins, having the ability to bind and agglutinate red blood cells (RBCs). Yut will find that they occur in most plant foods including those, which may be eaten raw. Lectins are specific in the sugar they bind to and also in their toxicity. Of great interest would be the fact that lectins from horse gram, lima beans, kidney beans, mung, winged beans and castor beans are toxic when orally consumed but lectins from soybeans and peanuts are not.

What are their toxic effects?

Well, these can cgüse growth inhibition in animals and diarrhoea, nausea, bloating and vomiting in case of human beings. When injected lectins agglutinate RBCs, haemolysis and death occurs in extreme cases. Several outbreaks in England after consuming improperly cooked beans have been related to lectins although other antinutritional factors may have played a role. Since lectins are proteins, they are denaturated by heal: however, low temperature or slow cooking may not completely eliminate their toxicity.

Toxic effect of lectins also relates to their binding with specific receptor sites on intestinal mucosal cells. This results in lesions, disruption and abnormal development of microvilli. Other effects include reduced activity of brush border enzymes viz. peptidases, disaccharidases, alkaline phosphatase, as well as, pepsin and pancreaticl salivary amylase. Secretion of mucin and increased weight/number of intestinal mucosal cells in presence of lectin has also been observed.

Since the enzymes secretion/activity are affected, carbohydrates and proteins are not completely digested. When these substances reach the colon, they act

as substrates for the colonic microflora, which subsequently ferment them and produce short chain fatty acids and gases. This is the underlying reason for some of the gastrointestinal symptoms associated with intake of raw beans/purified lectin.

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Bacterial overgrowth may also occur and may contribute to lectin toxicity. This has been linked to thinning of the jejunal mucosa and damage to duodenal. microvilli. Increase in bacterial colonization by lectin may be due to its polyvalent nature, which allows lectin to bind to both mucosal cells and bacteria simultaneously. This would 'fix' the bacteria close to the intestinal mucosa. If the mucosa is disrupted, it may allow translocation of the bacteria and/or endotoxin and cause a toxic response. In addition, there are reports that lectins themselves may be internalized, causing systemic effects such as increasing protein catabolism, breakdown of stored glycogen and lipid, as well as, disturbing mineral metabolism.

Yet another type of food components which may influence nutrient absorption/ health include phytates. You must have read about them before especially with respect to iron absolption. We will now discuss some salient features of phytates.

11.8.5 Phytates

We are familiar with phytates as an inhibitor of mineral absorption (calcium, iron etc.) especially in the vegetarian diets that are cereal-based. This sub-section deals with the well-known nutritional implications which have been long researched, as well as, the health benefits, which have been in focus more recently. Let us begin our study with the chemistry and occurrence of phytates.

Chemistry and Occurrence

Most plant foodstuffs contain inositol which is present in the form of Inyo-inositol hexakisphosphate i.e. phytic acid and its salts. In seeds, inositol is the storage form of phosphate and 60-90% of phosphate is present as phytate. Phytic acid (PA) is generally complexed with minerals and/or proteins. The complexed fonn with minerals is known as 'Phytate'. Various cations can strongly chelate between two phosphate groups or weakly within .a phosphate.

Our subsequent discussions will elucidate the interaction of phytates with nutrients, as well as, their health benefits. We will begin with influence of phytates on mineral absorption.

Nutritional Implications

We have already discussed about the influence of polyphenols on the various macronutrients and minerals earlier in Unit 9 and 10. Let us in this sub-section once again review the nutritional implications of these components.

Phytate and Mineral Interaction: Phytic acid occurs as a crystalline globoid inside protein bodies in the bran of cereal grains. It is negatively charged over a wide pH range. This will enable it to react with the positively charged ions. Thus, PA binds

to mineral cations such as Ca^{2+}, Fe^{2+}, Fe^{3+} Zn^{2+} and Cu^{2+} and forms strong complexes which render them unavailable for absorption. The effects of PA on mineral availability depends on numerous factors:

- the amount of PA present,
- concentration of the minerals,
- molar ratio of PA to minerals,
- size and valency,
- association of PA with protein,
- pH,
- presence of other metal ions,
- presence of other substances which can bind minerals, e.g. fibre, tannins, oxalic acid, and
- processing methods used.

At the pH values between 5 and 7 which are similar to those in the duodenum, PA binds and form insoluble chelates with divalent cations. At pH 7.4, the order of complexation in decreasing order is Cu > Co > Mn >Fe >Ca.

As phytates accumulates in various storage sites, other minerals apparently chelate to it forming the complex salt 'phytate'.

Studies on animals show that phytate inhibits zinc and calcium absorption, the maximum inhibitory effects being shown by 'myoinositol hexaphosphate.' The inhibitory effects appear to be greater for Zn than for calcium. It appears that at least 5 of the 6 possible sites need to be phosphorylated in order to exert its inhibitory effect. In vitro studies on availability of iron and zinc from North Indian diets indicate that it is very low—3.3 to 4.4% for iron and 7.8 to 8.7% for zinc, with a negative correlation between availability and PA content.

Next, we will discuss the influence of phytates on protein metabolism. Phytate and Protein Interaction: You may be more familiar with phytate's role in mineral absorption. However phytates also bind with starch and protein. Depending on the pH, 2 types of complexes are formed—at acidic pH, a binary protein-phytate complex and as the pH approaches neutrality, a ternary protein-mineral-phytate complex. Strong electrostatic attraction between negatively charged phytates and proteins with a net positive charge results in the formation of protein-phytate complexes. Apparently most such complexes are formed de novo in the gastrointestinal tract. Also phytates can interfere with digestive enzymes and their substrates, thus adversely affecting digestion of dietary protein and increasing endogenous losses of amino acids.

With this, we end our discussion of phytates. Our study on other factors with antinutritional effect, shall not be complete without a brief mention about the health benefits of these factors. Yes these factors can be beneficial to health. Let us quickly review the health benefits

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11.10 HEALTH BENEFITS OF OTHER DIETARY FACTORS WITH ANTINUTRITIONAL EFFECTS

Despite the predominantly nutritional antagonistic effects of the factors described above, there is some evidence accumulating to show that these may be associated with some health benefits as well. Some of the benefits noted with these factors appear to be similar to those observed for fibre e.g. lowering blood glucose/blood lipids and lowering the risk of developing cancer. These are briefly reviewed below.

- **Hypoglycemic effects:** Of the different carbohydrate foods tested for starch digestibility and blood glucose response, those rich in anti-nutrients e.g. legumes show the lowest values. Effects were best seen with the soluble whey fraction, which is rich in anti-nutrients like tannins, lectins and phytic acid. Amylase inhibitors can reduce blood glucose and raise insulin levels.
- **Reduction of blood lipids:** This effect have been especially observed with saponins. Diets containing saponin-rich foods (300-500 mg saponins/day) e.g. soya, alfalfa, chickpea, bean meal reduced plasma cholesterol by 16-24%. However, other substances in these foods like phytosterols, isoflavones, protein and fibre may also have contributed. Cholesterol reduction may be due to saponin binding dietary cholesterol thus preventing its absorption and/or binding with bile acids and increasing their faecal excretion.
- **Reduction in cancer risk:** Different cancers, especially colon and breast cancer, has been linked not only to phytates but also to protease inhibitors. In vitro studies show that they suppress malignant transformation of cells. Among the protease inhibitors, the most effective are those with chymotrypsin inhibitor activity in foods like soybean, chickpea and potato. Soybean also has the Bowman- Birk inhibitor which inhibits/prevents development of chemically induced liver cancer.

What are the mechanisms possibly responsible for these effects?

There are several possibilities: reduced availability of amino acids to cancer cells by reversing the carcinogen-induced change in oncogene expression, or by inhibiting formation of superoxide radicals, hydrogen peroxide formation by neutrophils which is induced by tumor promoters.

Research has indicted that phytates inay have some beneficial aspects as well. Let us le'arn about them.

Benejcial effects of phytates: Soine of the health promotive aspects of phytates include:

1) Phytic acid is a known antioxidant. Colonic bacteria produce oxygen radicals in appreciable accounts. Dietary phytic acid suppresses free radical mediated damage to intestinal epithelium.

2) Protective benefits are seen particularly in relation to carcinogenesis,

particularly against colon cancers. Complexing of iron by phytate may reduce iron-catalyzed production of free radicals and reduce lipid peroxidation. Also, phytate-containing foods have a higher fibre content. Studies show that signal-transductionpathways, cell cycle regulat01Y and differentiation genes, oncogenes and tumor-suppressor genes may be involved in phytate's anti-neoplastic' effects.

3) Lowering blood glucose and lipids.

4) Binding amylase and reducing starch digestion.

5) Lowering plasma cholesterol and triglycerides. In the last two section(s) we read'about celtain food components such as protease/ amylase inhibitors, saponins, lectins and phytates, which are at times referred to as antinutritional factors. These food coinponents have been found to inhibit nutrient absorption and a few substances also are health promotive. Research however needs to be conducted to further ascenain their health benefits especially with regards to their type and dosage. We hope that it must have been a good learning experience for you. A list of references has been mentioned at the end of the course for you to learn further.

You may now need to perfonn the check your progress exercise 4 to recapitulate the details of the food components discussed in this section.

11.11 LET US SUM UP

In this unit, we studied about the health benefits adverse effects of several food components apart from the nutrients. We got to know about the concept of functional foods and which components make them healthier food choices. Subsequent discussions highlighted the characteristic features of several nutraceuticals/ bioactive substances/ food components such as probiotics, prebiotics, non-glycoride components of edible oils, phytoestrogens etc. Their mode of action, potential beneficial health effects food sources and clinical uses have been elucidated in this unit. We also saw their interactions with nutrients such as proteins and minerals, especially in the case of phytates. In the subsequent sections, we learnt that the physiological effects of the various substances will depend on their level of intake, presence of other dieta1Y constituents and the nutritional/health status. Benefits and risks need to be balanced. However, considerable work is required before we can issue recommendations in terms of amounts of these to be consumed for the population at large.

11.12 GLOSSARY

Adenocarcinoma : cancer that begins in cells that line certain internal organs and that have secretory properties.

Angiogenesis : the growth and proliferation of new blood vessels.

Apoptosis : one of the types of programmed cell death that is the deliberate suicide of an unwanted cell in a multicellular organism.

Fructans : a general tern for any carbohydrate in which one/more fructosyl fructose link constitutes the majority of glycosidic bonds.

Functional foods : the food substances beyond the basic nutrients that are designed to lower the risk or delay the onset of certain disease.

Lectins : sugar binding proteins, having the ability to bind and agglutinate RBCs.

Non-digestible oligosaccharides: oliogomeric carbohydrates which are esistant to hydrolyzed by colonic bacteria.

Phytate : complexed form of phytic acid with minerals.

Phytoestrogens : oestrogenic compounds found in plants.

Polyphenols : compounds containing an —OH groups attached to the benzene ring.

Prebiotics : non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial in the colon.

11.13 CHECK YOUR PROGRESS

1) What are functional foods? Where are these found?

2) What are the functions of functional foods, as per the Japanese'FOSHU' criteria?

3) The food components for benefiting the immune system. Explai

4) What are the major components of non-glyceride fraction in edible oils and fats

UNIT

12

MENU PLANNING

NOTES

STRUCTURE

12.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

present the rationale behind the interesting and challenging task of menu planning,

enumerate the factors which influence our food choices, and hence need to be considered in menu planning,

describe the aims of menu planning and the steps involved,

apply the knowledge of the menu planning to plan and also quickly calculate the

nutritive value of the menus for various conditions,

explain the various factors to be kept in mind while planning diets for adults,

critically comment on the scenario of health and the nutrition situation of women at various levels, and

plan a few low-cost menus for adults.

12.2 INTRODUCTION

You have learnt from the previous units that our body's many functions, be it

physical activity, mental exercise, growth (in the case of children) or convalescence after an illness, require various nutrients delivered by an array of foods that we eat have also seen that the nutrients work in a perfect harmony, much like the keys of a piano; one key not reaching the perfect pitch could mean a discordant note! For example, bone formation requires, besides calcium (Ca), phosphorus (P) and vitamin D also in specific amounts—a lack of any one would mean improper bone formation—indicating that a perfect symphony of all the nutrients is required to ensure a good health.

We have also learnt that factors such as age, gender, physique, physiologic conditions and the level of physical activity influence the requirements for various nutrients. Apart from these, climatic conditions, growth and pathological stress also influence the need for the various nutrients. It is not enough if we, as dietitians, have just in- depth knowledge of the nutrients and the nutritive value of foodstuffs. We must be able to apply this knowledge to plan and also quickly calculate the nutritive value of the menus for various conditions served to the people under your care with the help of a simple device known as an 'exchange list'. In this unit, we will learn about the exchange list and the rationale for menu planning. What is menu planning? Why do we need to plan menus? What factors should be considered while planning menus? What are the steps involved in it? These are a few issues highlighted in this unit, Finally, we shall learn about menu planning for adults with respect to their nutrient needs.

With women playing important role in providing nutritious meals both at home and in the healthcare units, it is desirable that we have a basic awareness of the scenario of health and nutrition situation of women at various levels, This is the other important aspect covered in this unit.

12.3 MENU PLANNING

Any individual who carries the responsibility of providing meals has to take decisions regarding what to serve, how much to serve, how much to spend, where to shop, how much to buy, how to prepare food, how to serve meals, at what hour to serve meal and so on. All such decisions are a part of planning meals. Extending this concept further, one could define meal planning as a simple practical exercise which involves applying the knowledge of food, nutrient requirement and individual preferences to plan adequate and acceptable meals. In other terms, meal planning means planning for adequate nutrition.

Remember meal planning is just not an exercise of selecting the right kind of foods to help meet the nutrient needs. It also concerns with preparing/ planning attractive and enjoyable meals for all persons. Meals must taste good, smell good. Because food is seen before it is tasted, the eyes have a role as well, in food acceptance. Meals must 'look good' to be tasted to be enjoyed. To do this, the planner does not have to be knowledgeable only, but also imaginative and

creative. The aft of skillful blending of foods in terms colour, texture and flavour must be known. In this context, therefore, it is said that meal planning is an art. It is an art which develops through thought and inspiration. Meal planning, in fact, is a skill which improves with practice.

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12.3.1 Rationale for Menu Planning

'Menu', as we all know, is nothing but a list of dishes planned for preparation, and forms the very core of all activities in the food service establishment. Although it may seem a simple exercise of providing something to eat and drink, in practice, good menu planning requires a lot of skill. It involves planning of balanced meals that are colourful, appetizing, palatable and within the economic means of the individuals concerned. When a food has to be bought, prepared and served in large quantities to people of varying tastes and requirements, as is the case in hospital food service, due consideration needs to be paid for this activity. It is essential to provide appetizing, nourishing and attractive meals to the people at a reasonable price. This is possible only if the meals are planned in advance; for example, price advantage can be obtained buying seasonal foods and in quantities which carry discount.

What are the other advantages? Can you list a few of these? Well. planning in advance helps to determine quantities of different foods accurately. Food buying can thus be controlled through advance buying because the quantities need to be calculated beforehand. Time and effort spent on haphazard ordering, shopping and receiving of food materials is saved to a large extent. Planning in advance helps to avoid monotony in the menus drawn; variety in terms of colour, flavour and texture and different methods of cooking could be given due consideration if the menu is planned in time. If the meal does not satisfy the budget, it cannot be put into practice. Bulk purchasing, including seasonal foods all help in this; this means that menu planning has to be done in advance. The dietitian is responsible for giving clear- cut instructions to the kitchen staff to ensure harmony among the staff involved in preparation. This is possible only if the menus are planned in advance. The quantity of nutrients for the day for patients with various diseases, its distribution between the various meals of the day all need due consideration so that the people are satisfied with the service provided. This is not possible without planning menus in advance.

Having understood the rationale for menu planning, we will learn the factors that affect the food choice, next.

12.4 FACTORS AFFECTING FOOD CHOICE

As a dietitian, it is necessary to understand how our food choices are affected. Everyday we make food choices which influence our health for better or worse. Every day's choice may benefit/harm our health only a little, but when these choices are repeated over years and decades, the rewards and consequences can

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become major.

Various factors influenc our food choices. In this section, we shall review these factors. We begin with the nutritional factors.

12.4.1 Nutritional Factors

Food choices made based on sound principles of nutrition will be conducive to good health while carelessness about nutrition can contribute towards many of the today's most prevalent chronic degenerative diseases of later life, such as heart diseases. Remember, we don't consume nutrients as such, but as meals/dishes made up of foodstuffs containing the nutrients in various amounts. Knowledge of food groups will help one to formulate a healthy diet. The various foods in a food group are similar in a general chemical (nutrient) composition, and hence contribute almost similar types of nutrients to the diet, although not always in the same proportion. At this point, it is worthwhile to learn about the evolution of the concept of Food groups.

In the 1940s, nutritionists began translating RDA into more practical terms so that people with no special training in nutrition could still estimate whether their nutritional needs were being met. A seven-food-group plan was one of the early formats. Daily food choices had 10 include food from each food group. This plan was simplified into five- food-groups

By the mid-1950s, a four-food-group plan was established that included Iti.lk group, meat group, fruit-vegetable group and bread and cereal group. In 1979, the names of the groups were revised, and a fifth group containing fats, sweets and alcoholic beverages was added as a part of the "Hassle-free Daily Food Guide". Caution needs to be urged in consuming this last group, though it can supply essential fatty acids and vitamin E.

The following discussion briefly summarizes the nutritive value of each of these food groups. Let us begin our discussion with cereals.

1) Cereals and Bread Group

- Cereals form the staple of the Indian diet.
- These grains are the main source of energy in the Indian diets contributing as they do 60-70% of daily energy intake of majority of Indians. This is because they are rich sources of carbohydrates.
- Proteins in cereal grains, as you may recall studying earlier, are partially complete as cereals are low in one or two essential amino acids — lysine and threonine. However, cereals when eaten with pulses, as is the common practice in India, the protein quality improves due to mutual supplementation between the cereal and pulse proteins, the former being deficient while the latter (pulse) being rich in lysine.
- Cereals are low in fat, but contain 1-3% omega-3 fatty acids.

- Cereals in general, cannot be considered lich sources of minerals. However, ragi is rich in calcium (i.e. 344 mg/ 100 gm); bajra, and whole wheat flour are high in iron content. The non-nutrient factors such as phytates, oxalates and fibres which are present in them interfere with the absorption of calcium and Iron.
- Cereals, particularly the whole grains, are important sources of B-vitamins. Since most of these vitamins reside in the outermost layer of the grains, they are lost depending on the extent of polishing and refining. Parboiling, which involves soaking in water and subsequent steaming of paddy, results in seeping of vitamins present in outer layer into the grain; thus parboiled milled rice retains much of the vitamins.

Cereals are neither rich in vitamin A nor C; they don't contain any vitamin B_{12} either; however, whole grain cereals are rich in the other B-vitamins.

2) Pulse/Meat, Poultry/Sea Food Group

They are excellent sources of protein, containing 25% protein, but varying from each other in other respects. Let us discuss each of these groups and find out what these differences are.

a) Pulse group

- Pulses are rich sources of proteins (20-25 g/ 100 g), the limiting amino acid being methionine. However, protein quality can be improved by mutual supplementation with cereals. Soybean has exceptionally high protein content (43 g/100 g). Besides, they have carbohydrates in fair amounts.
- Pulses are fairly rich in iron, with soybean, cowpea, black gram and horse gram being exceptionally rich.
- Sprouting or germination of legumes, a practice common in our households, brings about beneficial effects. Vitamin C, which is practically absent in dry pulses, increases in significant amounts upon sprouting; folic acid also increases threefold. Interestingly, sprouting brings about a decrease in flatus-forming compounds originally present in non-germinated pulses. Sprouted pulses require a much shorter time to get cooked. The antinutritional factors such as trypsin inhibitors, are inactivated by sprouting, thus rendering them more easily digestible.

b) Fish and Sea-foods group

- They are rich sources of proteins (20-25%) of a high biological value. Dry fishes contain more (60%) proteins since most of the moisture is lost.
- Dried fishes have exceptionally high amounts of calcium since it is consumed with the bones.
- Some varieties of fish such as hilsa, seer, katla, pomfret and mackeral are rich in omega-3 fatty acids, which are known to protect
- against cardiovascular diseases.

c) Meat and Poultry group

- Meat and poultry are rich sources of proteins of high biological value.
- They do not contain carbohydrates.
- All the meats except egg yolk contain haem iron; therefore, the iron is well absorbed. However, egg yolk contains non-haem iron; the phosvitin which is present in egg yolks interferes with iron absorption but consuming vitamin C in the same meal helps 10 overcome this problem.
- Egg yolk is rich in vitamin A and p-carotene, while liver is rich in vitamin A.
- Red meats are rich in saturated fats, while fish and poultry contain very small amounts of fats. Lean meats contain less fat.
- Organ meats such as liver, kidney and brain and egg yolks are rich in cholesterol. Including large amounts of such foods in the diet, especially along with saturated fats in the diet has been shown to result in high serum cholesterol which is a risk factor for coronary heart diseases.
- Flesh foods are rich in iron, zinc and vitamin B12, but are devoid of fibre and vitamin

3) Dairy/milk Group

This first food of mammals is rich in body-building proteins and bone-forming calcium, besides being the only source of vitamin B12 for the vegetarians. However, milk does not contain vitamin C, besides being deficient in iron. Dairy milk of varying fat contents is available in the market, the highest fat milk being known as full fat milk, the next known as standard milk and the lowest is skim milk. Low fat dairy milk is better suited for adults, especially the ones who want to watch their weights and have a check on their cholesterol levels. Curds are an ideal substitute for people who have problem in digesting milk due to the deficiency of the enzyme lactase.

4) Vegetable-Fruit Group

The vegetables and fruits add colour and variety to our diets in addition to providing a host of essential nutrients and phytonutrients that help to prevent chronic degenerative diseases. The fruits are also high in potassium and help to establish a proper balance between the sodium and potassium content of our diets.

An often-neglected group, this group provides for the water-soluble vitamins and minerals, so vital for the proper functioning of the body's various mechanisms. These delicious natural capsules of vitamins and minerals offer protection against many diseases, especially, heart diseases and certain types of cancer. Most important is the fact that it offers a variety in terms of texture, colour and flavour and thus helps to avoid monotony in the meal.

Green leafy vegetables are rich sources of various nutrients such as iron, calcium, p-carotene, folic acid and vitamin C, the amount being much more in the darker

leaves. Their contribution to energy intake is very low, usually less than 2-3%. Yellow-orange coloured vegetables are rich in p-carotene. They must therefore be included at least four to five times in our diets.

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We can say adding colour to our diet will add colour to our life'.

The citrus fruits such as oranges, sweet-lime (mosambi) and also, papaya and guavas are rich in vitamin C and the yellow-orange ones such as mango and papaya are rich in p-carotene. Fruits with high water content such as melons have low energy content, while dry fruits such as dates and raisins are high in energy.

5) Fats, Oils and Sugar Group

This group imparts flavour to the items and thereby improves the palatability. Items incorporating them do melt in the mouth , it has been very aptly said 'a minute on the lips, forever on the hips'.

The fats and oils are generally the most expensive among the dietary items and therefore intakes are determined by the economic affordability. A deficit in the intake of fats and oils is rare in the affluent population while an apparent surfeit in this group is often responsible for obesity, heart ailments and certain types of cancers. Hence one needs to use caution in the amounts used.

Each of these groups provides some but not all of the nutrients. No single natural food supplies all the essential nutrients and the phytonutrients in proper proportions to maintain health, nor is a food group more important than the other. A meal plan that includes adequate amounts of foods from the different groups provides the foundation for good health which needs to be amply supported by food hygiene, clean drinking water and a clean environment.

Besides nutritional factors, the other factors affecting food choices are enumerated next.

12.4.2 Other Factors

Although people are aware and realize that their food choices affect their health, they often choose food for other reasons. Let us review these factors.

- **Personal Preferences:** Often people choose foods because they like certain flavours. While we Indians enjoy strong curry spices, the Western cuisine does not include them. Similarly, asafoetida (hing) features in the South Indian preparations while garam masala features in the North Indian cuisine.
- **Habit:** We often select food just out of habit. While idli and dosa feature in South Indian breakfast, paranthas feature more commonly idli the North Indian cuisine.
- **Social Interaction:** Food signifies friendliness. Meals are social events, and

the sharing of food is a part of hospitality, Social customs almost compel people to accept food or drink offered by a host or shared by a group. When your friends are going out for pizza or ice cream, how can you refuse to go along?

- **Availability, Convenience and Economy:** People eat foods that are accessible, quick and easy to prepare, and within their financial means. Convenience is valued highly by the consumers, as reflected in their choices of meals they can quickly prepare the recipes with few ingredients. Many people frequently eat out or have food delivered, which limits food choices to the selections on the restaurant's menu.
- Seasonal availability of food is particularly important aspect which influences the food choices, particularly for lower income group families.
- **Positive and Negative Associations:** People tend to like foods with happy associations — such as sweets during Diwali and cakes during Christmas. By the same token, we often develop intense dislike to foods that we have to eat when we are sick or when forced to eat when not hungry.
- **Emotional Comfort:** Some people eat in response to an emotional stimulus for e.g. to relieve boredom or depression or calm anxiety. A lonely person may choose to eat rather than to invite a friend and risk rejection. Eating in response to emotions can easily lead to over-eating and obesity but may be appropriate at times.
- **Body Image:** Sometimes, people select foods which they believe will improve their physical appearance and avoid those that may be detrimental. Such decisions can be beneficial when based on sound nutrition and fitness knowledge but undermine good health when based on faddism or carry to extremes.

Now that we have well-understood the factors that influence an individual's food choice, let us move on to discuss the concept of food exchange list. But first let us recapitulate what we have learnt so far.

12.5 EXCHANGE LIST VS. FOOD COMPOSITION TABLES FOR MENU PLANNING

A dietitian is frequently expected to make quick, yet reasonably accurate estimation of the nutritive value of diets or calculate diets that must be controlled for one or more nutrients. The nutritive value may be calculated from the Food Composition Tables (given in the Nutritive Value of Indian Foods by Gopalan et. al., NN, Hyderabad). By 1940s, dietitians and physicians were aware that Food Composition Tables used to calculate therapeutic diets were cumbersome, time-consuming and needlessly precise and that the dietitian does not have the time to calculate for each day the energy and nutrient composition of the food required to fulfill the dietary prescription. Thus, an Exchange List was evolved. What is the exchange list? It is a grouping of foods in which specified amounts of all the foods provide approximately equal amount of (the same amount) carbohydrate, protein and fat and hence, energy content. Specific foods within the group may vary

slightly in nutritive value from the averages stated in the group. These differences in composition tend to cancel out because of the variety of foods selected from day to day. Thus, any food within a given list can be substituted or exchanged for any other food in that list in the given quantities.

Food exchange system allows one to choose a variety of foods with adequate nutrients. The food exchange system is important in planning a nutritious diet. Essentially, the Food Exchange System allows variety to be introduced into the diets without altering the energy or the macronutrient contents. The exchange lists are especially useful in planning diets for metabolic diseases and are very useful in the management of obesity.

Let us then quickly review the steps involved in planning/developing an exchange list. This will help you plan meals using the exchange list.

12.5.1 Steps in the Development of Exchange List

As mentioned above, when we group together similar food items so that each supplies a constant amount of a particular nutrient, we call the group a food exchange. Given herewith are the steps which when followed, will guide you in developing the exchange list. You will realize that developing an exchange list for Indian foods is a difficult task as our dishes defy any attempt at standardization. Nevertheless let us try.

1) An important first step in developing an exchange list is the standardization of serving or portion sizes. The portion sizes vary considerably in India. Idlis, dosas, chapattis and puris of different sizes in different states and in different households is a common scene. Despite this, some attempts have been made to define portion sizes.

2) The second step is to calculate the energy, carbohydrate, protein and fat content of one serving or portion size of the different dishes. This can be done by converting the cooked weight of one serving of a dish into raw weight of the ingredients that have gone into it. Although allowances should be made for cooking losses, this has not been done. Future exchange lists must I-ale care of this. From the raw weights of the ingredients in one serving and using the Indian Food Composition tables, the energy, carbohydrate, protein and fat content of one serving can be calculated.

3) The third step is to create an exchange list of different dishes in terms of standard portion sizes that would provide approximately the same energy or carbohydrate or fat as the case may be. Since foods contain widely varying amount of the macronutrients, serving or portion sizes are defined for a group of more or less homogeneous foods. For example, all cereals provide approximately the same number of calories, approximately 350 per 100 g raw weight and about the same amount of carbohydrates, about 70 g per 100 g raw weight (Refer to Table 12.1). Therefore, cereal exchanges are grouped together. Similarly,

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there are vegetable, fruits, milk and meat exchanges. Within each of these food groups, the composition of the different items in terms of carbohydrate, protein and fats remain similar,

Food Group	Energy (Kcal)	CHO (g)	Protein (g)	Fat (g)
Bajra	361	67.5	11.6	5.0
Jowar	349	72.6	10.9	1.9
Maize, dry	342	66.2	11.1	3.6
Ragi	328	72.0	7.3	1.3
Rice, raw	345	78.2	6.8	0.5
Parboiled	346	79.0	6.4	0.4
Flakes	346	77.3	6.6	1.2
Puffed	325	73.6	7.5	0.1
WWF	341	69.4	12.1	1.7
Maida	348	73.9	11.0	0.9
Semolina	348	74.8	10.4	0.8
Vermicelli	352	78.3	8.7	0.4
Mean	344	73.5	9.1	1.5
Bread, White	245	51.9	7.8	0.7
Brown	244	49.0	8.8	1.4

Table 12.1: Nutritive values used in the development of the exchange list for cereals

4) An example is provided in Table 12.2 from a comprehensive exchange list developed by the Lady Irwin College. Another list, originally developed by the Dietary Department of CMC, Vellore and subseqnently added to by many other institutions; consists of six exchange groups. These are cereals, pulses, milk, meat, limits and vegetables A and B. A brief review of these exchanges follows:

- Cereal exchange per serving, provides 85 Kcals, 20 g carbohydrate and 1.6 g protein
- Milk exchange provides per serving 65 Kcals, 4 g carbohydrate, 3 g protein and 4 g fat.
- Meat exchange provides per serving 85 Kcals and varying amounts of CHO, protein and fat.
- Fruit exchanges provide per serving 40 Kcals and 10 g carbohydrate.
- The vegetable A group exchange provides 30 Kcals while the B group provides 30-50 Kcals.

Exchange (Food Group)	No. of Exchanges	Amount* (g)	Energy Content (Kcal)	Protein Content (g)
(Energy Giving group)				
Cereals	1	20	70	2
Roots and tubers	1	60	70	2
Sugar and Jaggery	1	5	20	-
Fats and oils	1	5	45	-
(Body-building group)				
Milk	1	250 ml	170	8
Pulses	1	30	100	7
Meat/fish/poultry/egg	1	40-50	70	7
(Protective/regulatory group)				
Green leafy	1	100	Negligible	Negligible
Vegetables	2 #	200	40	2
Other vegetables	1	100-150	40	2
Fruits	1	80-100	40	Negligible

*Basis of each exchange; cereals 15 g carbohydrate; roots and tubers 15 g carbohydrate; fats and oils 5 g fat; milk 8 g protein: meat/fish/poultry/egg 7 g protein; fruits 10 g carbohydrates.

#2 exchanges of green leaf vegetables is equivalent to one exchange of other vegetables.

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Using the steps elaborated above, we hope you will be in a position to use the exchange system to calculate a diet pattern, which calculates the diet order in kinds and number of servings of food exchanges to be consumed by any individual or a patient each day.

Although the exchange system, you would have noticed, reflects average and not specific energy and nutrient values, the therapeutic success that results when the values are used to calculate the diet pattern demonstrate that the method is accurate enough to serve this purpose.

An adequate diet, providing all nutrients, is needed throughout our lives. An adequate and balanced diet is one that meets all the nutrient needs of an individual for maintenance, repair, the living processes, and growth or development. A balanced diet provides all the nutrients in required amounts and proper proportions. It can easily be achieved through maintaining variety in foods and including foods from the different food groups discussed above. The quantity of food needed to meet the nutrient requirements vary with age, gender, physical activity etc., as we will learn next, in the section focusing on planning for adults.

12.6 PLANNING FOR ADULTS

The term 'adult' refers to any individual in the age group of twenty years and above. The period beginning from twenty years and extending through old age till the time of death is considered the period of adulthood. Adulthood represents the stage in life when an individual has completed his/her growth in terms of body size. The nutritional need is for maintenance of body functions rather than for growth.

As an individual ages, there is a gradual and progressive change in body functioning. Why does this happen? This is because there is an increased breakdown of tissues and the renewal of worn out tissue is also much less. These changes associated with ageing are common to all individuals, but, there is a great variation from person to person. In some individuals, the changes become significant relatively early, whereas, in other cases these changes appear much later in adulthood. All these factors influence the nutrient needs of adults. We shall review the nutrient requirements for adults, next.

12.6.1 Recommended Dietary Allowances (RDA)

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The recommended dietary allowances, are estimates of nutrients to be consumed daily to ensure the requirements of all individuals are met in a given population. You may recall studying about this concept and the RDAs earlier in Unit 1.

Growth is no longer an energy-demanding factor in adulthood as mentioned above, and BMR is relatively constant among population groups of a given age and gender. Consequently, habitual physical activity and body weight are the main determinants for the diversity in energy requirements, in particular for adult populations with different lifestyles. Table 12.3 presents the ICMR recommended dietary intakes of adults.

Nutrient	Sedentary Work	Moderate Work	Heavy Work
Energy (Kcal)	2425	2875	3800
Proteins (g)	60	60	60
Calcium (mg)	400	400	400
Iron (mg)	28	28	28
Vitamin A (mcg)			
Retinol	600	600	600
Or			
β-carotene	2400	2400	2400
Thiamine (mg)	1.2	1.4	1.6
Riboflavin (mg)	1.4	1.6	1.9
Niacin (mg)	16	18	21
Ascorbic acid (mg)	40	40	40
Folic acid (mcg)	100	100	100
Vitamin B_{12} (mcg)	1	1	1

Table 12.3: Recommended dietary intakes for adults

MAN (Weight-60 kg)

Nutrient	Sedentary Work	Moderate Work	Heavy Work
Energy (Kcal)	1875	2225	2925
Proteins (g)	50	50	50
Calcium (mg)	400	400	400
Iron (mg)	30	30	30
Vitamin A (mcg)			
Retinol	600	600	600
Or			
β-carotene	2400	2400	2400
Thiamine (mg)	0.9	1.1	1.2
Riboflavin (mg)	1.1	1.3	1.5
Niacin (mg)	12	14	21
Ascorbic acid (mg)	40	40	40
Folic acid (mcg)	100	100	100
Vitamin B_{12} (mcg)	1	1	1

WOMAN (Weight-50 kg)

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In the Table 12.3, you would have 'noticed that:

- The nutrient requirements for adults are given under the three categories based on activity level — sedentary, moderate and heavy work, and
- The nutrient requirements for men and women are given separately. For computing RDA, the ICMR has taken body weight of 'reference man' as 60 kg and that of 'woman' as 50 kg.
- The requirements for proteins are based on body weight. The requirements are expressed as kg protein per kg body weight.
- RDIs for thiamin, riboflavin and niacin are dependent on RDAs for energy. The relationship between the RDAs for these vitamins and energy, as also mentioned earlier in Unit 8 is as follows:

RDA for thiamin = 0.5 mg/1000 Kcal; RDA for riboflavin 0.6 mg/ 1000 Kcal, RDA for niacin = 6.6 mg/ 1000 Kcal.

These recommendations given by ICMR are likely to be revised in the light of the new FAO/WHO human energy requirement report published recently in 2004. According to FAO/WHO, energy requirements for younger and older adults and the elderly should be calculated on the basis of physical activity level (PAL) as indicated in Table 12.4. In adult men and non-pregnant, non-lactatingwomen, BMR times PAL is equal to total energy expenditure or the daily energy requirement.

Category	PAL value
Sedentary or light activity lifestyle	1.40 - 1.69
Active or moderately active lifestyle	1.70 - 1.99
Vigorous or vigorously active lifestyle	2.00 - 2.40*

* PAL values > 2.40 are difficult to maintain over a long period of time.

Table 12.4: Classification of lifestyles in relation to the intensity of habitual physical activity, or PAL

*PAL values > 2.40 are difficult to maintain over a long period of time

The examples of lifestyles with different levels of energy demands as given in Table 12.4 are enumerated herewith. You may also recall studying about these lifestyles earlier in Unit 2.

- **Sedentary or light activity life styles:** These people have occupations that do not demand much physical effort, are not required to walk long distances, generally use motor vehicles for transportation, do not exercise or participate in sports regularly, and spend most of their leisure time sitting or standing, with little body displacement (e.g. talking, reading, watching television, listening

to the radio, using computers). One example is male/female teachers, office workers (executives, clerks, typists etc.) in urban areas, who only occasionally engage in physically demanding activities during or outside working hours. Another example is housewives living in urban areas, with access to energy saving devices and domestic help to carry out most of the manual chores and other moderate energy activities.

- **Active or moderately active lifestyles:** These people have occupations that are not strenuous in terms of energy demands, but involve more energy expenditure than that described for sedentary lifestyles. Alternatively, they can be people with sedentary occupations who regularly spend a certain amount of time in moderate to vigorous physical activities, during either the obligatory or the discretionary part of their daily routine. For example, the daily performance of one hour (either continuous or in several bouts during the day) of moderate to vigorous exercise, such as jogging/running, cycling, aerobic dancing or various sports activities. Other examples of moderately active lifestyles are associated with occupations such as servants, house cleaners, masons and construction workers, or rural women in less developed traditional villages who participate in agricultural chores or walk long distances to fetch water and fuel wood.
- **Vigorous or vigorously active lifestyles:** These people engage regularly in strenuous work or in strenuous leisure activities for several hours. Examples are women with non-sedentary occupations who swim or dance an average of two hours each day, or non-mechanized agricultural labourers who work with a machete, hoe or axe for several hours daily and walk long distances over rugged terrains, often carrying heavy loads. Other examples of vigorously active occupations include rickshaw pullers, mine workers, coolies etc.

For FAO/WHO 2004 recommendations for energy requirements, we suggest you look up Tables 2.11, 2.12, 2.13 and 2.14 given earlier in Unit 2 for men and women aged 18 to 29.9 years and 30 to 59.5 years, respectively. Tables 2.15 and 2.16 (in Unit 2) presents the recommendations for elderly male and female, respectively over 60 years.

Now that we have learnt about the nutrient requirements for the adult, let us focus our attention on how to translate these needs in terms of balanced diets/ meals for adults.

12.6.2 Planning for Adults: Some Menu Plans and Dietary Guidelines

Now that we have a thorough and complete understanding about food exchange lists and the nutrient requirements for adults, we shall review a few regional menus and critically analyze them from nutritional point of view. But first, we would like you to study the dietary guidelines for Indians developed by National Institute of Nutrition (NIN), ICMR. These guidelines presented in Tables 12.5, 12.6 and Table 12.7 provide information as to the number of portions and actual diets that need to be consumed in order to ensure optimal health for Indian adult man and women.

These diets, you would notice, are based on locally available foods within the reach of the people and generally are in conformity with our tradition and custom. Using these guidelines, we can plan diets for adults.

Food Groups	G/Portion	Type of Work					
		Sedentary		Moderate		Heavy	
		Man	Woman	Man	Woman	Man	Woman
Cereals & millets	30	14	10	16	12	23	16
Pulses	30	2	2	3	2.5	3	3
Milk	100 ml	3	3	3	3	3	3
Roots & tubers	100	2	1	2	1	2	2
Green Leafy vegetables	100	1	1	1	1	1	1
Other vegetables	100	I	1	1	1	I	1
Fruits	100	1	1	1	1	I	I
Sugar	5	5	4	8	5	11	9
Fats and Oils (visible)	5	4	4	7	6	11	8

Table 12.5: Balanced diet for adults (Sedentary/Moderate Heavy Activity): Number of portions

For non-vegetarians substitute one pulse portion with one portion of egg/ meat/ chicken fish. Source: Dietary Guidelines for Indians - A Manual. National Institute of Nutrition, Indian Council of Medical Research, Hyderabad (1998).

Meal Time	Food Group	Raw Amounts	Cooked Recipe	Servings
Breakfast	Milk	100 ml	Milk or	1/2 cup
	Sugar	15 g	Tea or	2 cups
			Coffee	1 cup
	Cereals	70 g	Breakfast	
	Pulses	20 g		
Lunch	Cereals	150 g	Rice	2 cups
			Chapati	2 nos.
	Pulses	20 g	Dal	1-2 cup
	Vegetables	150 g	Veg-cuny	3/4 cup
	Vegetables	50 g	Veg. salad	7-8 slices
	Milk	100 ml	Curd	1/2 cup
Ten	Cereals	50 g	Snack	
	Milk	50 ml	Tea	1 cup
	Sugar	10 g		
Dinner	Cereals	150 g	Rice	2 cups
			Pulkas	2 Nos.
	Pulses	20 g	Dhal;	112 cup
	Vegetables	150 g	Veg curry	3/4 cup
	Milk (curd)	50 ml		1/2 cup
	Vegetables	50 g	Veg raita	1 medium
	Fruit	100 g	Seasonal	

Table 12.6: Sample meal plan for adult man (sedentary)

Note: For non-vegetarians — substitute one pulse portion with one portion Of egg/ meat/ chicken/fish Use 20 g visible fat per day

- **Breakfast items:** Idli- 4 Nos./ Dosa — 3 Nos. / Upma —1-2 cup/ Bread — 4 Slices/Porridge — 2 Cups.Com flakes with milk — 2 cup
- **Snacks :** Poha — I cup / Toast — 2 slices , Samosa — 2 / Sandwiches — 2 / Biscuits —5. Council of Medical Research, Hyderabad (1998).

Meal Time	Food Group	Raw Amounts	Cooked Recipe	Servings
Breakfast	Milk	100 ml	Milk or	1/2 cup
	Sugar	15 g	Tea or	2 cups
			Coffee	1 cup
	Cereals	70 g	Breakfast	
	Pulses	20 g		
Lunch	Cereals	150 g	Rice	2 cups
			Chapati	2 nos.
	Pulses	20 g	Dal	1-2 cup
	Vegetables	150 g	Veg-cuny	3/4 cup
	Vegetables	50 g	Veg. salad	7-8 slices
	Milk	100 ml	Curd	1/2 cup
Ten	Cereals	50 g	Snack	
	Milk	50 ml	Tea	1 cup
	Sugar	10 g		
Dinner	Cereals	150 g	Rice	2 cups
			Pulkas	2 Nos.
	Pulses	20 g	Dhal;	112 cup
	Vegetables	150 g	Veg curry	3/4 cup
	Milk (curd)	50 ml		1/2 cup
	Vegetables	50 g	Veg raita	1 medium
	Fruit	100 g	Seasonal	

Table 2.7: Sample meal plan for adult woman (sedentary)

Note: For Non-Vegetarians — Substitute one pulse portion with one poi-tion of egg/meat/ chicken/fish

Use 20 g visible fat per day.

- **Breakfast items:** Idli- 3 Nos./ Dosa — 2 Nos. / Upma —I cup/ Bread — 3 Slicesl Porridge — 1-112 Cups/Corn flakes with milk — 1-112 cup
- **Snacks :** Poha — I cup / Toast — 2 slices . Samosa — 2 / Sandwiches — 2 / Biscuits —5,

Having studied the dietary guidelines, let us now review a typical South Indian Menu plan and critically analyze and give justification of the food items selected

MENU (SOUTH INDIAN)

NOTES

Breakfast

- Ragi Kanji
- Ragi
- Sugar

Mid-morning

- Rice flakes (roasted and sweetened
- Guava

Lunch

- Rice
- Roti
- Dal
- Aloo Palak, (Palak, Potato and Tomato)
- Dry fish chutne

Tea

- Lemon rice (with groundnuts)

Dinner

- Pongal Rice
- Mung dal
- Drumstick leaves Bhaji

Put down your comments related to the menu in the space provided herewith: Menu Planning

Now compare your comments, with the justification presented herewith

Justification of the plan

- Ragi Kanji is given forms a good source of calcium in diet.
- Rice flakes forms one of fairly good sources of iron and to aid for good absorption of iron, Guava is given, which is one of the cheapest sources of vitamin C.
- Lunch has normal staple diet like rice, dal and roti which is accompanied by aloo palak (bhaji) — one of the sources of green leafy vegetable in diet and dry fish chutney, which forms a good source of protein
- Lemon rice is given, which is typical to South Indian inenu and forms one of the sources of vitamin C. Lemon should be squeezed just before consumption to avoid oxidation of vitamin C. It also contains peanuts, which adds protein and calories to the diet.
- Pongal forms a good supplementation of protein through vegetarian sources due

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to mutual supplementation of rice and pulse, which completes the inadequacies of each other.

- Dinner also contains drumstick leaves chutney which forms one of sources of calcium. Curds form good source of protein.

Let us consider another typical North Indian Menu Plan and its justification from a nutritional standpoint. This menu is planned for a pregnant lady, who is anaemic, doing household chores and belongs to a low socio-economic groups, So let us proceed and find out what nutrients considered and which food items have been selected to fulfill the above listed criteria

MENU (NORTH INDIAN)

Breakfast

- Moong sprouts
- Potato Parantha - Groundnuts, wheat four, fat
- Tea - Milk, sugar
- Fruit - Sugar

Lunch

- Bajra Roti (Bajra flour, fat
- Dal (Masoor dal, onion, tomato, fat)
- Dry fish chutne
- Vegetables (Yam, onion, tomato, french beans, fat)
- Plain curds

Tea

- Tea - Milk, sugar
- Masala roti (Wheat flour, groundnuts

Dinner

- Plain rice
- Dal (masoor dal, tomato, fat)
- Vegetable (amaranth, potato, onion, tomato, fat)
- Butter milk

Justification of the Plan

The plan is for a anaemic pregnant lady, from a lower socio-economic level and doing moderate level of work, hence selection of foods is made accordingly.

- Among cereals, along with rice, whole wheat flour, some amount of Bajra is

also incorporated to fulfill the iron requirements

- Among pulses, as already to her low economic level, rationale for pulses is a big restrictive. Hence, it has been made a point to incorporate sprouts to provide for some additional vitamins and minerals.
- There is also an accommodation made for nuts (groundnuts, being cheap) to meet her energy requirements along with calcium, iron, and protein.
- Milk is very important for her condition as milk is a very good source of calcium which is required ill highest quantities.
- In flesh, dry fish has been incorporated, which is a cheaper than other fish foods and at the same time, the best source of iron and calcium, which are the basic requirements of a pregnant woman.
- There is a need to give good amount of fruits and vegetables in the diet (increased need for vitamins, minerals, antioxidants, fibre). But looking at her socio-economic status, care has been taken to give her fruits/vegetables which are cheaper yet an enriched source of many nutrients.

We would finally end our study with tips on how to plan low cost menus

12.6.3 Planning a Low Cost Menu

In this sub-section, you will find examples of a few low cost menus. We would like you to critically analyze these menu from the nutritional point of view. So go ahead and study these menus. Menu 1

Breakfast

- Poha (with potato and moong sprouts)
- Tea
- Guava

Lunch

- Chapati
- Rice
- Masoor dal
- Yam Bhaji
- Dry fish chutne
- Cucumber raita

Tea

- Ragi Porridge
- Puffed rice and groundnut laddu
- Papaya

Dinner

- Bajra Bhakri
- Dry fish chutne
- Palak dal gravy
- Buttermilk

So then what is your analysis? Compare your analysis with the analysis presented herewith.

Analysis

On analyzing of the menu, you would have noticed that:

1) Guava is served at breakfast containing rice flakes; vitamin C in guava will help in the absorption of iron (in rice flakes)

2) Ragi is given, which will supply calcium.

3) There is a combination of all the food groups at both lunch and dinner.

4) DIY fish is a cheap source of good quality protein, calcium and iron

5) Raw foods in the form of raita and fruits are incorporated in the menu.

Let's look at another menu for a woman from a low socio-economic group.

Menu	Items
Breakfast	Bajra Bhakri, Colocasia leaves and potato bhaji
	Papaya
	Tea
Mid- morning	Sukha Bhel
Lunch	Roti
	Khichadi
	Dry fish chutney
	Aloo methi bhaji
	Pumpkin raita
Snacks	Rajgira Laddu
	Tea
Dinner	Roti
	Rice
	Dry fish chutney
	Aloo methi bhaji
	Cucumber raita

On critically analyzing the menu, you would observe that:

- Bajra used in the breakfast is a cheap and rich source of iron.
- Colocasia leaves are rich in iron, calcium, ß-carotene and vitamin C.
- Papaya is an exceptionally rich source of ß-carotene, besides being rich in vitamin C. The advantage of dry fish in a menu is already known to us
- The menu for both lunch and dinner are almost same, and hence are ideally suited in the menu of the woman from the low socio-economic group.

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With this, we end our study on planning diets for adults. Before we move on to the next unit, we would like to present another critical analysis on the nutritional profile of women in our country

12.7 NUTRITION OF WOMEN

During the post-war years, the people in the developed world recognized that women were at a disadvantaged position and felt the need to improve their condition. The technical advances (such as birth control) and the labour-saving technological means (which helped to free the women from drudgery and gave adequate time for self- development) helped in the emancipation of women. The year 1975, known also as the "International Women's Year" was devoted to promote equality between men and women. The decade 1976-1985 is also designated as the United Nations Decade for Women: Equality, Development and Peace. In contrast to this, the majority of women in developing countries have inferior social status to men. They have less educational opportunities than men in the same society. The global literacy rates for adult female population are only 32% as against 52% for men; this gap is much wider in Asia and also Africa. Sex discrimination in nutrition and health care appears to increase the vulnerability of female children to infectious diseases. Female children receive less nutritional and health care with consequent higher mortality rate.

Women in many developing countries face social and cultural disadvantage in terms of health, nutrition, education and economic status compared to women in developed countries, as well as, men in their own societies. Half-a-million women die annually of causes related to delivery, and most of these are preventable. Maternal mortality rates are estimated as 8.74 per 1000 live births in rural Andhra Pradesh, India compared lo 0.02 in Sweden. There are more deaths in India (from causes related to pregnancy and childbirth) in one week than there are in the whole of Europe in one year.

Child bearing in the third world involves a high risk of death. Maternal mortality accounts for almost 25% of deaths among women of child-bearing age in developing countries compared with 1%in the USA. According to WHO, up to 60 women die every hour worldwide due to problems associated with child birth. In the developing world as a whole, the life time risk of dying is I in 40 as compared to 1 in 40,000 in the developed world.

The World Health Organization estimates that 21 million low birth weight infants are born in the world each year and that a vast majority of such births occur in the third world. The incidence is around 17% in the developing countries compared Lo 7% in the industrialized world. Low birth weight is closely associated with maternal malnutrition; maternal malnutrition, especially in the last trimester of pregnancy, reduces the baby's ability to put on weight, a phenomenon which subsequently limits their chances for survival or growth.

Nutritional anaemia widely affects menstruating and pregnant women in the third world. The WHO estimates that nearly 500 million young women suffer from some degree of nutritional anaemia. It is alarming to know that almost one out of every two young women in the third world is likely to be anaemic. Iron deficiency has been identified as a common and important cause of nutritional anaemia in both pregnant and nonpregnant women in low-income populations which severely affects women's health and productivity. Anaemia is frequently caused by a combination of factors, particularly low iron intake and absorption, and is often aggravated by malaria and hookworm infestation.

Women's health and well-being in the low-income income families are seriously affected by too many pregnancies, prolonged lactation, long hours of work, poor diet repeated exposure to diseases and limited access to adequate health care. The combination of work and reproduction exert substantial stress on women for many years in their lives. Repeated pregnancies and prolonged lactation often result in a physiological depletion and stress, while long hours of work put them under constant physical stress.

We all know that breastfeeding ensures adequate food and care for the infant. This demands that the mother should be ensured of special care which include besides adequate diet, reduction in her workload and knowledge of family planning options for adequate child spacing. This would ensure not only the mother's health but also her wellbeing; she needs to feel that she is as important as her infant.

There are several unique examples of successful nutrition intervention in almost every part of the world through the hard work of so many people. Thailand is one of them. Thai has been recognized by the nutrition community for its ability to eliminate severe and moderate malnutrition among children less than 5 yrs of age, and reduce overall malnutrition from 51% to about 19% within a decade. This was possible due to policies and programmes created to reduce poverty, as well as, malnutrition. Grounded with a primary health care philosophy, a good technical background and strong management skills, a group of academics and practitioners formed a core group for nutritional programme. This body helped merge nutrition

Work into the national poverty alleviation plan. The massive scale of implementation and high levels of volunteer recruitment at the village level, results were communicated widely and this helped to raise awareness. Both men and women were in nutrition policy implementation. These people acted individually

and collectively 10 alert the public about nutrition problems and their burden for the nation's future. These leaders, from the very beginning realized that nutrition is not only a human disease, but a societal problem that can only be improved by collaborative efforts. Also, Thai husbands are proud to leave decisions regarding household management, including family food and nutrition to their wives. This often includes money to be used in the family. With access to appropriate information, the women are decisive in nutritional matters and because of this background, women are key factors for nutrition in Thailand.

Gender-sensitive nutrition action is important for all Asian countries and it is especially significant for India. Systematic and concerted efforts are needed to create a critical mass of leaders — especially women leaders — who can understand the importance of this at various levels. As a professional trained to translate nutrition in terms of appropriate foods, you will be in a position to bring about changes in diet habits of people, particularly women — both the apparently healthy and the sick.

12.8 LET US SUM UP

In this unit, we .got introduced to the meaning of the term 'menu' and to the concept of menu planning. We saw the various benefits of menu planning and the nutritional and non-nutritional factors affecting. people's food choices.

Further, to facilitate the process of menu planning, we learnt about food exchange lists and food composition tables. We also learnt the steps involved in the development of food exchange list and planning a few low cost menus along with its nutritional analysis, where we saw how meals must be planned for them based on the important nutrients, physical activity, gender and income level. Also, we got to have a look at a few sample menu plans along with their nutritional justification

12.9 GLOSSARY

Balanced meal : a meal including different types of foods in such quantities and proportions that the need for calories, vitamins, minerals and other nutrients is adequately met.

Essential Amino Acids : amino acids that cannot be synthesized by our body and hence need to be supplied through diet.

Exchange list : a grouping of foods in which specified amount of all foods are of approximately equal proximate principles and energy content.

Food group : a number of food items sharing common characteristics.

Menu : a list of dishes planned for preparation.

Menu planning : planning of balanced meals that are colourful, appetizing, palatable and within the economic means.

Mutual supplementation : a nutritional strategy in which vegetable foods with low contents of amino acids are eaten together with a food that is high in that same amino acid.

Packed lunch : any food preparation carried to the place of work which is consumed in the afternoon.

Parboiling : to cook partially by boiling for a short period of time.

Satiety : a feeling of satisfaction and fullness after consuming meals.

Staple food : foods used frequently or daily, for example, rice (in the South) or wheat (in the North).

Texture : the structure, appearance, consistency of foods or food items. Crisp, smooth, soft, hard or chewy are some of the textures of the food.

12.10 CHECK YOUR PROGRESS

1) What do you understand by the terms 'menu' and 'menu planning'? Why is menu planning considered an important activity in a food service organization?

2) Discuss the nutritional significance of

   a) Fruits and vegetables

   b) Pulses

3) Enumerate the various factors affecting choice of food items.

4) What are the two major aspects that must be kept in mind while planning meals for:

   a) A rikshaw puller

   b) A Sportsperson

NOTES

UNIT

13

PREGNANT AND LACTATING MOTHERS

STRUCTURE

13.1 LEARNING OBJECTIVE

After studying this unit, you should be able to:

- describe the various physiological changes during pregnancy,
- describe foetal growth and development and understand the importance of nutrition,
- identify determinants of poor pregnancy outcome,
- explain what is IUGR and LBW and their consequences,
- discuss the various aspects about lactation and importance of human milk,
- elaborate the nutritional requirements during pregnancy and lactation,
- state dietary considerations to be followed to ensure successful pregnancy and
- lactation, and
- counsel mothers as per their individual requirements.

13.2 INTRODUCTION

In the previous unit, we learnt about the basic principles of meal planning and the various considerations and guidelines that must be kept in mind while planning the diets for adults. In continuation with our discussion on adults, let us move on to study about the nutrient requirements during the periods of pregnancy and lactation, Pregnancy and lactation are unique periods in the life cycle. They occupy a critical place in the life cycle and have health and social importance for individuals, families and society. This intergenerational significance has led all societies to recognize these as special periods and to make provisions for their care. This unit discusses the various issues pertaining to these two important physiological stages such as meeting the nutritional requirements during these periods. It focuses on nutrition in preparation for, and support of, pregnancy and lactation. As you read on, it will become evident to you that there are heavy demands on the mother during pregnancy and lactation.

What modifications should be made to meet the increased needs? Which foods must be included in the diet of pregnant/lactating women? Let proceed with our discussion and find out all these aspects

13.3 PREGNANCY AND LACTATION – CRITICAL STAGES IN THE LIFECYCLE

You must be aware that the situation of women is far from optimal and it is necessary to give attention to their nutrition and health. The National Family Health Survey (NFHS-2, 1998-99) indicates that the mean BMI for women is 20.3. More than 1/3rd women have a BMI below 18.5 indicating high prevalence of chronic energy deficiency. Asia has the highest prevalence of anaemia in the world with about half of all anaemic women living in the Indian subcontinent, where 88% of them develop iron deficiency anaemia during pregnancy.

Undernutrition in children is strongly associated with undernutrition in mothers. It often starts in utero and may extend throughout the life cycle. It occurs during pregnancy, childhood and adolescence and has cumulative effects. Undernutrition, especially in the mother, is associated with poor pregnancy outcome including a higher incidence of low birth weight, maternal mortality, foetal and infant death and disability. Malnourished women or adolescent girls give birth to stunted and thin babies. Thus, undernutrition is handed down from one generation to another. Such children may not show catch-up growth in the later years and are more likely not to perform well in school. As adults, they may be less productive and are more likely to suffer from chronic degenerative diseases. Chronic undernutrition accounts for a large proportion of child deaths, poor pregnancy outcomes, poor quality of life and lost productivity among earning adults and spanning generations, At no other period is the well-being and future

of an individual completely dependent on the health and nutritional status of another as is during pregnancy and early periods of lactation. The mother's nutritional status is a crucial factor affecting pregnancy outcome. Her diet must be carefully planned to supply the nutrients needed to maintain her health, support the physiological changes in her body and provide for the rapid growth and development of her unborn baby while protecting her from deficiency or excess of nutrients.

The goal is not just survival, we must try and ensure that every woman who is pregnant has the opportunity for a safe and successful pregnancy and the ability to deliver and care for an infant whose physical and mental potential are not impaired. Once a child is born, she must be adequately nourished to continue to depend on their mothers for nourishment. Lactation has high nutrient costs; hence the mother's diet must be nutritionally adequate. Let us then understand these two physiological conditions in greater details. We begin with pregnancy.

13.4 PHYSIOLOGICAL CHANGES DURING PREGNANCY

A whole new life begins at conception. Organ systems develop rapidly and nutrition plays many supportive roles. Pregnancy from conception to birth usually lasts 40 weeks (10 lunar months/menstrual cycles) in humans. During this period, the unborn child grows from a single cell to an infant that is ready for life outside the womb. Many physical changes also take place in the mother to support her developing offspring, regulate her own (maternal) metabolism and prepare her for labour, birth and lactation. Changes in the mother are anatomical, physiological and complex, affecting almost every function of the body. They are an integral part of the maternal — foetal system, which creates the most favourable environment possible for the developing child. Many of these changes are apparent in the very early weeks.

Let us briefly look at the important physiological effects, which will help you to understand the basis of nutritional requirements.

13.4.1 Expansion in Plasma Volume and Red Cell Mass

In this sub-section we shall review the expansion in blood volume and in the red cell mass accompanying pregnancy.

- **Plasma:** In a non-pregnant woman, average plasma volume is 2600 ml. Plasma volume begins to increase by end of the first trimester and reaches a peak by 34 weeks, when it is about 50% greater than it was at conception. The physiologic dilution accompanying the expansion in blood volume is known as haemodilution. Haemodilution is responsible for the decline we see in several blood parameters during pregnancy especially in the second and third trimesters.

Individual variations are seen in plasma volume — multigravidas and in mothers with multiple births, usually have a greater increase. Increase in plasma volume is conflated with obstetric performance. Women with an increase smaller than the average have higher risk of still births, abortions or low birth weight babies. This has been seen in women with hypertension, renal disease, low weight gain during pregnancy, undernutrition, smoking, pre-eclampsia, diuretic treatment and smoking.

- **Red Cells:** Production of red cells is stimulated and their numbers gradually rise. However, as compared to the expansion in plasma volume, their increase is not as large; there is an increase in red cell mass by 20%. As the plasma volume increases much more than the red cell mass, there is usually a drop in the haemoglobin levels around 34th week of gestation.
- **Proteins:** Total serum protein gradually decreases, along with a sharp decline in albumin. There is reduction in serum albumin along with the expanded plasma volume. Serum levels of vitamin C, folic acid, vitamin B6 and vitamin BE follow the decline of serum albumin levels.
- **Other Nutrients:** Fat-soluble vitamin concentrations, especially carotene and vitamin E are increased by nearly 50%. Vitamin A levels, however, remain unchanged. Progressive increase is seen in serum triglycerides, cholesterol and free fatty acids. These are brought about by increased concentrations of oestrogens, progesterone and placental hormones.

Interpretation of blood/serum nutrient values in pregnancy is therefore complex compared to the non-pregnant state, as they depend on a number of factors including the stage of gestation. It is necessary to conduct biochemical tests at suitable intervals such as in the first, second and third trimesters, to follow these changes and determine if there is a deviation that calls for an intervention. The most common measurement of nutritional importance done routinely in India is haemoglobin in the second and third trimesters. Measurement of blood pressure and fundal height are other two measurements done routinely to determine high risk pregnancies and development of the foetus.

13.4.2 Hormonal Profile in Pregnancy

Hormonal changes characteristic of pregnancy include the following:

Human chorionic gonadotropin (HCG) begins to increase immediately on implantation of the ovum and reaches a peak at around 8 weeks of gestation. It then declines to a stable value until birth. In the first 8-10 weeks, HCG maintains the corpus luteum, which is the main source of oestrogens and progesterone in the early weeks of pregnancy. These hormones play an essential role in the development of the placenta. Human placental lactogen, with a structure similar to the growth hormone, increases throughout pregnancy. Its rate of production parallels the rate of placental growth and is a good indicator of placental function. At the peak rate of secretion, the amount produced is 1-2 g per day, much higher than any other hormone. Placental lactogen stimulates lipolysis and is important in maintaining

a flow of substrates to the foetus. Placental lactogen along with prolactin also promotes the development of mammary glands. After delivery, placental lactogen disappears from the maternal circulation. Oestrogens and progesterone are secreted by the placenta from 8-10 weeks of gestation. Progesterone increases throughout pregnancy. It stimulates maternal respiration ensuring an adequate supply of oxygen to the foetus. In addition, it relaxes smooth muscle in the uterus to accommodate the growing foetus and allow for child birth. Progesterone, while stimulating lobular development in the breast, inhibits milk secretion during pregnancy.

Placental secretion of oestrogens increase with progression of pregnancy. Oestrogens perform many functions. They stimulate uterine growth, increase blood flow to the uterus and promote breast development. Oestrogens also induce prolactin secretion by the maternal pituitary. Prolactin secretion helps in mammary gland development. After delivery, oestrogen induced mammotrophs (prolactin secreting cells) in the pituitary secrete large amounts of prolactin to initiate and maintain milk production. Another hormone that is increased in maternal plasma during pregnancy is Cortisol enhances production of glucose from amino acids (gluconeogenesis) and also antagonizes the action of insulin. This way it increases the availability of glucose to the foetus which relies solely on glucose for its energy needs. In the marginally glucose intolerant women, these changes as a result of pregnancy may predispose them to frank impaired glucose intolerance.

13.4.3 Organ Functions

Dramatic changes occur in renal functions to eliminate the nitrogenous and other waste products of maternal and foetal metabolism. Effective renal plasma flow, (volume of plasma filtered by the renal tubules), increases by 75%. This is one of the earliest physiological adjustments in pregnancy. The glomerulai filtration rate increases by 50% in early pregnancy. These changes in renal functions while helping to clear waste products on one hand are also associated with increased excretion of glucose and amino acids but unrelated to the plasma levels of these constituents.

In addition, the heart and the lungs respond suitably to the increased blood flow to the placenta and to the increased demand for oxygen to the foetus. The intestinal absorption of all nutrients is enhanced to take care of the increased requirements. The amount absorbed depends on the amount ingested, maternal stores and progressively increasing requirements of the foetus.

13.4.4 Placental Transfer of Nutrients

The placenta is a transitory structure developing during pregnancy and lies implanted on the uterine wall. It is connected with the foetus through the umbilical cord. The foetus derives all its nutrition from the mother across the placental barrier. If the consumption, absorption and utilization of the nutrients by the

mother and the transport of nutrients across the placental barrier are inadequate, then foetal malnutrition develops. Dietary inadequacies are a major cause of foetal undernutrition in developing countries. Maternal diseases such as diabetes and hypertension compromise the delivery of nutrients across the placenta to the foetus. The transfer of nutrients also depends on their concentrations in maternal plasma and blood flow to the placenta.

The mechanisms for transfer of nutrients across the placental barrier are either simple or facilitated diffusion or active transport, as in the case of transfer across the intestinal brush border. Fat-soluble vitamins and electrolytes are transferred by simple diffusion; glucose is transferred by facilitated diffusion; while amino acids, water- soluble vitamins and minerals like calcium and iron are transferred by active transport. The role of placenta in promoting foetal nutrition is shown in the Table 13.1.

Nourishes the foetus	• facilitates transfer of oxygen and nutrients from mother to foetus.
Removes wastes	• picks up foetal waste products such as CO_2, urea, bilirubin.
Foetal lung	• performs the respiratory, absorptive and excretory functions that the foetus lungs, digestive system and kidneys will provide after birth.
Protective barrier	• protects the foetus from harmful agents, which are of high molecular weight including proteins except maternal immuoglobulin G conferring immunity to the foetus.
	• transports nutrients and in some cases can store them.
Endocrine gland	• produces several hormones that maintain pregnancy and prepare the mother's breasts for lactation.

Table 13.1: Role of the placenta in foetal nutrition

13.4.5 Maternal Weight Gain

The often quoted figures for weight gain during pregnancy are from the study of Hytten and Leitch reported from UK in 1971. In this study, average weight gain by primigravidae eating without any restriction was 12.5 kg. This weight gain represents two major components.

1) The products of conception, the foetus, amniotic fluid and the placenta

2) maternal tissues gained, expansion of blood and extracellular fluid, enlargement of uterus and mammary glands and maternal stores (adipose tissue). In India, several studies have examined the weight gain during pregnancy by women from upper and lower socio-economic groups. While in the upper economic group, the

average weight gain 11 kg, the lower economic group women gain only 6-7 kg during pregnancy. Lower weight gain is associated with increased risk of intra uterine growth retardation and prenatal mortality. It is useful to define certain terms here. When a baby is born full term, 39-40 weeks of gestation but has a weight less than 2.5 kg, the baby is referred as a low birth weight (LBW) baby or as a small for date baby. These babies have suffered intra uterine growth retardation, i.e. retardation in growth in utero. If a baby is born prior to full term and weighs less than 2.5 kg, it is not to be classified as low birth weight or small for date. Such babies are pre maturely born. However, in many developing countries, obtaining correct information on gestational duration is difficult and therefore quite often the babies born before full term and weighing less than 2.5 kg are classified as LBW. The developmental projectile of a pre term baby is quite different from that of a low birth weight baby and therefore it is important to distinguish between these two. The rate of weight gain is as important as the total weight gain. The rate of weight gain as pregnancy progresses for three categories of women, under weight, normal and overweight prior to pregnancy is shown in the graph in Figure 13.1.

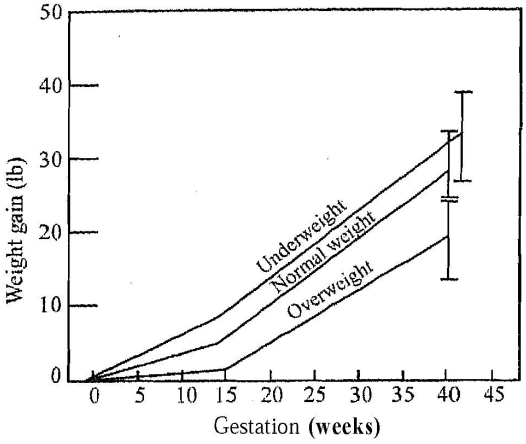

Figure 13.1: Recommended pattern of weight gain

As you may have noticed in Figure 13.1, little gain occurs during the first trimester (approx. 1 kg). In the second and third trimesters, when the foetus grows from less than 500 g to about 3 kg, the weight gain should be approximately 3 kg (l kg/ month) in the 2nd trimester and 6 kg i.e. 2 kg/month in the last trimester. This translates to approximately 0.5 kg per week. Although the total recommended weight gain is different for underweight and overweight women, it should be at a slow and steady rate (See Figure 13.1).

The recommended weight gain on the basis of pre pregnancy weight for height in the case of undernourished women is almost unattainable in India. For example, for women with pre pregnancy BMI of less than 19.8, the total recommended weight gain is 12.5 to 18 kg, an impossible target for the Indian women, one-third or more of whom have a pre pregnancy BMI of less than 18. This brings out explicitly the need to address undernutrition in the early years and

during adolescence so that realistic targets can be set for weight gain in pregnancy. For women with normal BMI of 19.8 to 26, the recommended weight gain is 11.5 to 16, while for the obese with BMI of greater than 26, the recommended gain is 7-11.5. In the Indian setting, a total weight gain of 10-12 kg appears reasonable.

13.5 NUTRITIONAL NEEDS DURING PREGNANCY

It must be evident by now that several physiological changes occur in the body of an expectant mother and that malnutrition can adversely affect the health of the mother, as well as, that of the infant. In this section, we shall study about the nutrient requirements during pregnancy.

For most women, nutrient needs during pregnancy are higher than at any other time of life cycle. Let us get to know about the energy and other nutrient requirements during pregnancy. We shall begin with the calorie requirements and proceed to the need for various macro- and micro-nutrients.

- **Energy:** Two factors determine energy requirements: increase in mother's basal metabolism to support the work required for foetal growth and accessory tissues and changes in the mother's usual physical activity. The estimated total (cumulative) additional cost Of energy is 55,000 Kcal. It works out to be an additional 300 Kcal per day in the last two trimesters. Refer to Table 13.2 for Recommended Nutrient Intakes for pregnancy. Note: During the first trimester the additional energy required is small, hence the RDA is not increased

Nutrient	Pregnant **Woman**
Energy (Kcal/day)	+300
Protein (g/day)	+25
Fat (g/day)	30
Calcium (mglday)	1000
Iron (mg/day)	38
Vitamin **A** (RE) (mcg/day)	600
β-carotene	2400
Thiamin (mg/day)	4.2
Riboflavin (mg/day)	4.2
Nicotinic acid (mg/day)	+2
Pyridoxine (mg/day)	25
Ascorbic acid (mg/day)	40
Folic acid (mcg/day)	400
Vitamin B_{12} (mcg/day)	1

Table 13.2: Recommended dietary intakes during pregnancy

NOTES

FAO/WHO/UNU 2004 recommendation for the extra energy cost of pregnancy is 85 Kcal/day, 285 Kcal/day and 475 Kcal/day during the first, second and third trimesters, respectively. There are many societies with a high proportion of non-obese women who do not seek prenatal advice before the second or third month of pregnancy. Under these circumstances, FAO/WHO (2004) recommends that in such societies pregnant women increase their food intake by 360 Kcal/day in the second trimester and by 475 Kcal/day in third.

The composition of the diet during pregnancy should be the same as for a non- pregnant woman; hence the contribution to calories from carbohydrate, protein and fat does not change. However, carbohydrate intake should not be <100 g per day, otherwise ketosis may occur due to excessive breakdown of fats to meet increased calorie requirements. Prolonged ketosis may be harmful to the foetus, even though some ketone production occurs normally after an overnight fast. High acetonuria may be a marker for maternal undernutrition and the associated increased risk of foetal or neonatal death. The foetus can metabolize ketones but its preferred source of energy is glucose. Also, you know adequate carbohydrates are needed to spare protein for growth.

Pregnant adolescent girls, underweight women and women who are exceptionally active (heavy physical activity) may require more energy. The details of these specific cases and increased needs are discussed later in this unit. However, here it is important to remember that requirements vary with pre-pregnancy weight, and body composition, amount and composition of weight gain, stage of pregnancy and activity level. Therefore, it would not be appropriate to make a single recommendation for all pregnant women. Energy status may be estimated by evaluating the rate of weight gain. If the rate of weight gain is appropriate for the stage of pregnancy, you can assume that energy intake is adequate. Fasting is not recommended, for it may be a special risk for women with a tendency towards early delivery. Chemical changes associated with fasting may precipitate labour pains.

Some mothers may ask you whether they can 'diet' or undenake fasting. Studies animals show that when the mother's diet was restricted, foetal body weight was significantly reduced. Data on humans is rather limited. However, among mothers experiencing food shortages, infant birth weights get reduced. This has been documented in the .studies from World War II. Optimal foetal growth occurs only when the mother is able to accumulate a critical amount of extra body stores during pregnancy.

Next, we shall discuss about one of the most critical nutrients required for tissue synthesis i.e. protein.

- **Protein:** Altogether, 925 g of protein are deposited in a normal foetus and maternal accessory tissues and considering the dietary protein quality (NPU=65), an increase of 15 g per day is recommended. This increase could be either through vegetarian sources such as pulses (soyabean), milk and milk

products (cheese) or through mote of meat/fish and eggs in the diet. This is based on the needs of the non-pregnant woman plus the extra amounts needed for growth. The physically active pregnant women and adolescent girls would however require more as compared to sedentary pregnant woman. The protein excess/supplements are not recommended as these were associated with an increased incidence of prematurity and enhanced incidence of neonatal death.

The rate at which new tissue is synthesized is not constant throughout gestation. Maternal and foetal growth accelerates in the second month and the rate progressively increases until just before term. Therefore, the need for protein follows this youth rate. It is important to ensure protein quality, as well as, quantity. Moreover, since protein utilization depends on calorie intake, it is important to ensure that calorie needs are fully met. When there is inadequate intake of energy, protein will be catabolized to meet energy need. Under such circumstances, it has been shown that extra 100 Kcal will have the same effect on nitrogen retention as an additional 0.28 g of nitrogen itself.

- **Protein deficiency** The effects of protein deficiency during pregnancy are difficult to separate from the effects of caloric deficit, since in almost all cases, limited protein intake is accompanied by limited energy intakes. Under such circumstances, decreased birth weight and greater incidence of pre-eclampsia have been reported.
- **Protein excess:** It is not advisable to recommend protein supplements. Reports in the literature indicate that high-protein supplements were associated with increased incidence of prematurity and excessive neonatal deaths. Analysis of supplementation studies in human populations suggests that supplements providing more than 20% of the calories from protein are associated with retarded foetal growth.

Apart from proteins and non-nitrogenous sources of energy, several vitamins, minerals and trace elements have been found to play a critical role in the progression and outcome of pregnancy. We will now review some of these in detail.

- **Micronutrients:** The need for many vitamins and minerals is increased during pregnancy. Since energy intake increases, the requirements for few micronutrients needed for energy utilization i.e. thiamin, niacin, riboflavin and magnesium also increase. Since protein needs are higher, the requirements for vitamin B6 and zinc also increase. Micronutrients involved in the growth and development of bone and connective tissue and the synthesis of new cells are needed in greater amounts.

Let us review the requirements for these nutrients.

- **Folic acid and vitamin B_{12}:** Folic acid and vitamin B_{12} are important for production of new cells. DNA must replicate and transmit its genetic information to RNA intermediates. As mentioned previously, folic acid has a role in prevention of neural tube defects. However, we need to bear in mind that effects of high intakes of folic acid are not well known, but it can complicate

the diagnosis of B_{12} deficiency.

Therefore, care should be taken to keep total folate consumption under 1 mg/ day except under the supervision of a physician, for normal, healthy 'individuals, the amount of folate present in a multivitamin form containing 1312 should be sufficient.

- **Vitamins A, C E and K :** All four vitamins have specific functions and a common role for all of them is to preserve the structural and functional properties of cells. Excessive consumption of vitamin A is known to be teratogenic. Hence, it is not advisable to use supplements. Vitamin A requirements should be met through diet. Also if women of child — bearing age intend using products containing high amounts of vitamin A, they should be advised to consult their' physicians before doing so.

Vitamin C deficiency has not been shown to affect the course or outcome of pregnancy in humans, although low plasma levels have been associated with the premature rupture of the membranes and pre-eclampsia. Mega doses may adversely influence foetal metabolism. Metabolic dependency on high doses may develop in the infant such that scurvy may arise in the neonatal period.

Vitamin E needs are believed to increase during pregnancy but deficiency in humans rarely occurs. Vitamin E in the infant was correlated directly with maternal concentration.

Maternal dietary deficiency of vitamin K is almost unheard of but transport across the placenta is low. Newborns often have low body levels of vitamin K.

Although the need for vitamins A, C, E and K increase during pregnancy, symptoms of deficiency of C, E and K are seldom seen. You should advise mothers to include adequate amounts of these foods in the diet.

With the exception of iron and folic acid, routine dietary supplementation with other vitamin and mineral preparations is not necessary. You should encourage pregnant women to disregard vitamin and mineral preparations as corrective measures for inadequate dietary habits and consider food as the optimal vehicle for delivery of nutrients. For women who need supplementation e.g. those in high-risk category, a vitamin-mineral supplement is recommended from the beginning of the 2nd trimester. See Table 13.3 for amounts recommended,

Nutrient	Amount	Nutrient	Amount
Vitamin B_6	2 mg	Iron	30 mg
Folate	300 mcg	Zinc	15 mg
Vitamin C	50 mg	Copper	2 mg
Vitamin D	5 mcg	Calcium	2 mg

Table 13.3: Daily vitamin/mineral supplementation for pregnancy for those with inadequate diets or in high categories (more than one foetus, heavy smokers, alcohol and drug abusers)

Mineral Requirements

- **Iron:** While B_{12} and folic acid are needed for the normal erythropoiesis, they must be accompanied by adequate amounts of other nutrients. Iron is needed for synthesis of haemoglobin in both maternal and foetal red blood cells. At term, a normal weight infant has about 246 mg of iron in blood and body stores. An additional 134 mg is stored in the placenla and about 290 mg is used to expand the volume of mother's blood.

Maintenance of erythropoiesis is one of the few instances during pregnancy when the foetus acts as a true parasite. It ensures its own production of haemoglobin by drawing iron from the mother.

We should be concerned about the mother's iron nutriture, because maternal iron deficiency may adversely affect obstetric performance. A reduction in haemoglobin concentration means that the mother must increase her cardiac output to maintain adequate oxygen supply to the placenta and the foetus. This extra work fatigues the mother and makes her more susceptible to other physiologic stress. A very low haemoglobin level places the mother at risk of cardiac arrest, and should she haemonhage on delivery, the prognosis would be poor. The most significant known consequence of maternal iron deficiency is reduced foetal iron stores, followed by increased risk of anaemia during infancy. Moderate to severe anaemia is associated with increased risk of spontaneous abortion, premature delivery, low birth weight, still birth and perinatal death. In some cases, pica has been associated with iron deficiency. Inadequate weight gain during pregnancy has been found to be more prevalent among mothers with iron deficiency anaemia and in those with anaemias of other etiologies.

If sufficient iron is available, the mother's hemoglobin level should be at 11.5 g/100 ml by term. Most women are not able to meet the additional requirement for iron, from diet alone (since the quantity ingested is less especially in lower income settings, and the bioavailability /efficiency of absorption is very low). Thus, it is recommended that pregnant women receive an oral iron supplement. 60-100 mg of iron should maintain haelnoglobin levels in normal pregnant women, but those who are anaemic will require larger doses.

Another important nutrient of physiological significance is calcium. How does calcium intake influence the health status of mother and the foetus? Let us read and find out,

- **Calcium:** The foetus retains about 25-30 g of calcium, over the course of gestation, most of which is deposited in the last trimester when the foetal skeleton is growing rapidly and the teeth are forming. On an average, the foetus draws 250-300 mg Ca per day from maternal blood supply. Additional calcium is believed to be stored in the maternal skeleton as a reserve for lactation. So an intake of additional 500 mg Ca is recommended during both pregnancy and lactation. Extensive adjustments in calcium metabolism occur. Efficiency of calcium absorption is better and urinary losses are lower in

pregnancy compared to the non-pregnant state. Hormonal factors play a role. Human chorionic somatomarnmotropin (produced by placenta) enhances the rate of bone turnover throughout pregnancy. Oestrogen largely from placenta inhibits bone resorption, thus provoking a compensatory release of parathyroid hormone. PTH maintains the serum calcium level while enhancing intestinal calcium absorption and decreasing its urinary excretion. Along with calcium and phosphorus, adequate vitamin D is required.

Other micronutrients of physiological relevance include zinc, iodine and sodium.

- **Zinc:** Zinc, as a mineral, was found to be associated with foetal growth and birth weight. Low plasma zinc was associated with more complications in the antenatal and intrapartum periods, including pregnancy-induced hypertension. Subnormal tissue zinc in pregnancy may play a role in premature rupture of membranes at term. A point of caution is the interaction between zinc and iron. Zinc absorption is inhibited by high iron intakes, thus iron supplements may compromise zinc status. Box 13.1 gives details regarding the daily intake suggested for Indian adults.

- **Iodine:** You would be already aware that maternal iodine deficiency leads to cretinism in the off spring. Hence, the maternal diet must consist of enough iodine so as to prevent the consequences of foetal damage.

Box 13.1	Suggested Daily Intake of Trace Elements for an Indian Adult	
	Chromium	67 mcg
	Copper	2.2 mg
	Manganese	5.5 mg
	Zinc	15.5 mcg
	Iodine	150 mcg

- **Sodium:** As you know, sodium plays a role in fluid balance. Sodium metabolism is altered during pregnancy under the stimulus of a modified hormonal milieu. Restriction of sodium is not recommended to combat oedema. In animals it has been shown that rigorous sodium restriction stresses the rennin - angiotensin - aldosterone system to the point of breakdown. Such animals show reduced weight gain, altered fluid consumption patterns and they tend to develop water intoxication along with renal and adrenal tissue degeneration. Neonatal hyponatremia has been observed in offspring of women who unduly restricted

their sodium intake before delivery. Although moderation in use of salt and sodium-rich foods may be appropriate, aggressive restriction is not warranted. Not less than 2-3 g of sodium should be consumed daily.

NOTES

So far we have discussed about the nutrient requirements during pregnancy. Let us now read in detail the effects of malnutrition on the health and nutritional status of the mother and the foetus/newborn.

13.6 MATERNAL NUTRITION AND FOETAL OUTCOME

Maternal malnutrition has deleterious effects on both the mother and the offspring. Inadequate energy intakes, iron deficiency and strenuous physical work all contribute to poor weight gain in the mother, increased morbidities, and in severe cases, resulting in increased maternal mortality. The effects of malnutrition in women including during pregnancy have been covered in the previous unit on women and nutrition. The focus in this section is on the foetal outcome in terms of birth weight.

A large number of studies done specially in the developing countries have shown that maternal malnutrition seriously impairs foetal outcome. The birth weight and gestational duration are adversely affected while pregnancy complications such as still birth are increased in maternal malnutrition. Therefore, it is crucial to improve maternal nutrition status in order to improve the foetal outcome. In this section, the relationship between several parameters of maternal nutrition and foetal outcome are discussed, so that we have a good knowledge of the priority actions at the individual and at a public health level to improve the foetal outcomes.

The World Health Organization, on the basis of world wide data, has recommended that a full term baby with birth weight less than 2.5 kg may be considered a low birth weight (LBW) infant carrying relatively higher risks of sub standard growth and development and higher risk of perinatal and neonatal mortality. Low birth weight in full term infants is chiefly attributable to poor maternal nutrition and health. The postnatal growth and development of the LBW infants is poorer than normal weight infants. More recently, the concern has been raised that the LBW infants may become more prone to chronic degenerative diseases later as adults.

In the subsequent discussions, the effect of maternal anthropometric measurements on the foetal outcome shall be reviewed in detail. We shall begin with the weight of the mother prior to conception.

13.6.1 Pre Pregnancy Weight and Foetal Outcome

Several studies from around the world from developing and developed countries

have demonstrated an association between pre-conception body weight of the mother and LBW. The ICMR study in urban and rural India showed that pre-conception weight of less than 40 kg was a strong determinant of LBW. Another study conducted by the Nutrition Foundation of India (NFI) showed that body weight less than 45 kg was an influencing factor. The incidence of LBW in women with pre pregnancy weight of 45 kg or more was 17% as against 30-33% in the poor communities in general. The ICMR study also demonstrated increased perinatal mortality of the infant if the mother's pre-conception weight was less than 40 kg. A favourable pre- conception weight in rural and urban Indian women would appear to be 45 kg or more within acceptable limits of body mass index (BMI). In any case, it should not be less than 40 kg, as this is associated with a high risk of delivering a LBW infant. Distressingly, according to data gathered by National Nutrition Monitoring Bureau (NNMB), 15-29% of adult women in different states have body weights less than 38 kg. This situation can only be remedied by addressing malnutrition in the girl child. Next, we will learn about the association of maternal height with the foetal growth.

13.6.2 Pre Pregnancy Height and Foetal Outcome

Maternal height prior to conception, determined by heredity, socio-economic environment and maternal nutritional status, is a strong independent determinant of birth weight and mortality. The ICMR multicentre study in India found that incidence of LBW rose sharply when maternal height was less than 140 cm. Another study found a 2.5 times higher incidence of LBW in mothers with height less than 147 cm compared to mothers with height above 147 cm. Since the cut off heights vary, it would seem again that preferably the pre pregnancy height should be above 147 cm but in any case less than 140 cm should be considered as high risk for LBW. Unlike weight which can be increased at any time during the reproductive period, adult height once reached cannot be changed.

The NNMB data from different states show that 12-25% of adult women have heights less than 145 cm. Therefore, all efforts must be done to prevent stunting in the girl child, This aspect will be discussed in further detail in Unit 14 on pre school children.

Another important aspect which is gaining importance is the extent of adiposity or the optimal weight for a given height i.e. the body mass index of the mother and is being briefly discussed below.

13.6.3 Body Mass Index (BMI)

Weight for height as a marker of nutritional status has the advantage that it is independent of other factors that affect foetal outcome such as maternal age and parity. BMI is useful in predicting LBW or small or large for gestational babies. Refer to Table 13.4 to understand the relationship between increasing body mass index and reducing incidence of low birth weight babies.

BMI	LBW %
< 16	53
16 - 17	41
17 - 18.5	36
18.5 - 25	27
25 - 30	15
> 30	20

Table 13.4: Prediction of low birth weight on the basis of BMI

It is well known now that the health status both before and after conception hold great significance for both the mother and the child. Remember, we read about maternal weight gain during pregnancy in the sub-section 13.3.5. Let us now learn about weight gain during pregnancy and its impact on foetal outcome.

13.6.4 Weight Gain during Pregnancy and Foetal Outcome

Weight gain and birth weight are indisputably related to each other. Several studies have shown a higher occurrence of LBW with inadequate maternal weight gain. It is suggested that a low weight gain after 20 weeks of gestation may result in pre term birth and low weight gain throughout pregnancy in LBW. A weight gain of 7-11 kg appears to be a measure of adequate foetal growth although preferably it should be closer to 10 kg rather than 7 kg.

Yet another significant factor is the food intake and dietary choices of the mother, which is being discussed next.

13.6.5 Maternal Dietary Intake and Foetal Outcome

Among the various nutrients, energy intake appears to be the most crucial, for ' developing countries. Studies from India have reported lower mean birth weight for lower income urban and rural mothers who had an energy intake of 1200-1600 Kcals, pre pregnancy weight of 43 kg and a weight gain during pregnancy of only 5-6 kg. The mean birth weight of the infants was 2.7 kg. As against this women from upper socio-economic groups with energy intake of 2000-2500 Kcal, pre pregnancy weight of 45-55 kg, and a weight gain of 11 kg, had babies with a mean birth weight of 3.1 Kg. It is not only the energy intake during pregnancy but chronic energy deficiency from early childhood that is a major factor in the low body weights of the lower income women. Therefore, body weight changes must

occur much before pregnancy. Iron and folate are the other crucial nutrients that have an effect on birth weight. A recent review concluded that there was enough evidence to suggest that iron deficiency anaemia resulted in higher occurrence of LBW through pre filature deliveries. Folate supplementation of pregnant women was shown to improve birth weights. Additionally, dietary folate deficiency is implicated in neural tube defect, as you may already be aware by now.

Certain other factors which may influence the health status of the mother and/or the foetus are being elucidated next.

13.6.6 Non Nutritional Factors: Antenatal Care, Age, Heavy Physical Work and Intra Uterine Infections

The incidence of LBW is lowest and mean birth weight is highest in the state of Kerala, which is attributed to better quality of health care and higher female literacy rate in Kerala. An ICMR study in six states of India has shown that average age of marriage in girls was 13.8 years and the age at consummation of marriage was 15.3 years. It should be noted that the age of 14-18 is a period of active growth, the period of adolescence. From the average weights and heights of Indian rural girls, it is seen that 68% of the girls will be at high risk of poor pregnancy outcome at the age of 14 y and the risk reduces to 24% at the age of 18 years. Thus, early age at marriage is another high risk factor for poor foetal outcome.

Heavy physical labour even in advanced stages of pregnancy is another factor to contend with in the settings of developing countries like India. It is suggested that under warm environmental temperatures and in an upright posture, increased sympathetic activity could result in poor utero placental blood flow affecting the foetus adversely. The average gestational duration of full term deliveries in poor communities in India is about a week shorter than in the well off sections. This is attributed to the increased sympathetic via the heavy physical labour.

Pre natal intra uterine infections could be another factor contributing to LBW. It has been reported that infants born in poor environmental backgrounds have increased IgM (immunoglobin M, an antibody), which is a reflection of the high exposure to intra uterine infections.

A WHO review has identified 43 factors that influen ed birth weight and gestational duration. They are grouped into seven categories for convenience. These include:

1) Genetics and constitution (e.g. sex of the baby)

2) Demographic and psycho social factors (e.g. age of the mother)

3) Obstetric Parity)

4) Nutritional factors

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5) Maternal morbidity during pregnancy

6) Toxic exposures (e.g. cigarette smoking)

7) Antenatal care (Number of visits and quality of care)

The following are the salient modifiable factors which affect birth weight and gestation adversely: Iron deficiency anaemia, folic acid deficiency, inadequate pre/ antenatal care. These are the factors that must be addressed as a top priority from public health point of view to improve foetal outcomes and reduce the high incidence of LBW in India.

We will now learn about the significance and various aspects of nutritional care during (prenatal/prior to) pregnancy.

13.7 NUTRITIONAL ASSESSMENT AND GUIDANCE IN PRENATAL CARE

In the preceding sections, we have seen that there are unique physiologic changes in the pregnant woman's body, which has enhanced metabolic work that obviously accounts to the increased nutrient and energy needs. Thus, care during pregnancy is of special importance and the first step required for this is a comprehensive nutritional assessment. As in case of any other person, this will provide the foundation for planning personalized nutritional care, education and guidance throughout pregnancy so that we can help ensure that both mother and baby are healthy.

What should we focus on?

Our focus should be strongly on the preventive aspects of nutrition, identify women at-risk, recognize special needs for counseling, and plan an optimal follow-up nutrition care.

Although nutritional needs are increased, there are individual differences and problems that may affect the nutritional status of the mother. The factors that may influence the mother's status include physiologic, psychological, situational, cultural, social, economic or personal. Among these, socio-economically disadvantaged and adolescent mothers require more attention.

When providing advice and counseling to the mother, it is important to remember that nutrition is essential to health in 2 ways i.e. on a physiological level and on a personal level. We need to consider both of these in assessing the mother's needs and goals. Ideally, we should undertake preconception nutrition assessment and education correct any deficits and promote a planned pregnancy.

Phase		Aspects to be Focused on
Assessment	**Nutrition status**	Anthropometric data: weight, height, mid-arm circumference, focus on pre pregnant weight and serial measurements to monitor weight gain
		Laboratory data: Haemoglobin, haematocrit, blood glucose
		Clinical signs of nutrient deficiencies
	Historical data/	Age
	relevant background	Obstetrical history
	information	Medical history (including medications or supplements)
		Social history (living situation, availability & access to food)
		Personal history (substance abuse, level of physical activity)
		Nutrition history (allergies, food intolerances, cultural-ethnic food practices)
	Diet history	Use 24-h recall
		Food record
		Food frequency questionnaires
		Diet history (including activity – associated general day's intake pattern)
Analysis		Determine whether there are any nutrient deficiencies. Whether food intake is adequate and whether food habits are appropriate
		Check whether energy intake is sufficient vis-à-vis energy expenditure
		Identify areas for counseling and education and problem areas.
		Identify the reasons for deficiencies i.e. the limiting factors
Planning **care**		Based on your observations, develop a counseling plan. The focus should be on:
		Guiding her to identify for herself how her food practices are meeting nutritional needs for her pregnancy
		Reviewing the reasons for these increased needs (why it is important to get the increased nutrients needs)
		Help her to realize which nutrient needs are not met
		Guide her to identify ways in which to meet the nutritional demands
		If she is from low-income circumstances and there is an ICDS anganwadi in the area, counsel her to avail of the food supplement and the iron-folate prophylactic supplements
		Counsel her to make the requisite timely ANC visits

Table 13.5: Essentials of a prenatal care process

13.8 COMMON CONCERNS DURING PREGNANCY

Many of the physiological changes that occur during pregnancy affect the digestive tract and may cause discomfort to the mother. Most of these problems are minor,

but in some cases they may be more serious. Nausea, constipation, heartburn, pica, food cravings and aversions, as well as, food sensitivities are common nutrition-related concerns. We may need to advise, mothers about simple strategies to help avert them. In this section however, we shall elaborate upon certain clinical conditions which may arise during pregnancy that may increase the risk for the development of complications during pregnancy, delivery and post-partum and how to manage these. Let us begin with the study of these conditions.

13.8.1 High Risk Pregnancies

Until now we have considered the nutritional needs of pregnant women. In this sub-section, we will consider specific conditions that contribute high-risk pregnancies. Health care professionals favour health promotion with a preventive approach. Various factors have been identified which are associated with high risk. They are summarized in the Table 13.6. Some of these, you will realize cannot be changed as in case of personal characteristics and some can be changed, some are preventable and others can be controlled.

Some problems are directly related to the pregnancy itself such as anaemia, hyperemesis gravidarum (extreme form of morning sickness) or pregnancy-induced hypertension. For some, the normal physiological stress imposes demands on a relatively poor maternal nutritional status or maternal reserves that are not sufficie t to meet the new additional needs. Pre-existing diseases such as diabetes, chronic hypertension or phenylketonuria also pose risks. Hence, it is important to pay attention to such mothers. Adequate nutrition and consistent prenatal care can reduce the risk of premature delivery or low birth weight babies. High-risk pregnancies need special management including intervention to correct malnutrition. This aspect is discussed next.

Personal Characteristics (Cannot change)	Personal Habits Living Situation (Seek to change)	Chronic Preexisting Maternal Problems (Screen, Treat)	Obstetric History (Screen, Prevent)	Current/ Potential Pregnancy-Induced Problems (Screen, Prevent Treat)
- Sex - Age - Adolescent - Older woman - Family history - Diabetes - Heart disease - Hypertension - Phenylketonuria	- Smoking - Alcohol/drug-use - Poor diet - Malnutrition - Obesity - Underweight - Sedentary-lifestyle	- Hypertension - Insulin-dependent diabetes mellitus - Non-insulin dependent DM - Heart disease - Pulmonary disease - Renal disease - Maternal phenylketonuria	- Low birth weight - Stillbirth - Abortion - Foetal anomalies - High parity	- Anaemia - Iron deficiency - Folate deficiency - Pregnancy-induced hypertension - Gestational diabetes

Table 13.6: High-risk pregnancies: risk faetors for poor pregnancy outcome and pregnancy.

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13.8.2 Management of High Risk Pregnancies

Although the risk factors are many, we will consider some selected factors, especially the nutrition related ones. Let us have a look at these one by one.

A) Anaemia in Pregnancy

Anaemia is the most common complication and is often compounded by low socio-economic status. However, it is seen frequently in upper income women too in the absence of poverty. In majority of cases, the anaemia is of nutritional origin, the main cause being dietary iron deficiency which may date back to pre pregnancy years. Acute blood loss caused by haemorrhage is a related cause. Folate deficiency, which is less common, results in megaloblastic anaemia. Although it can exist singly, it usually occurs with iron deficiency. Anaemia caused by other factors is less common. Iron deficiency anaemia (microcytic hypochromic anaemia) is widespread among adolescents and young women during their reproductive years. They become highly vulnerable when greater physiological demands are imposed by pregnancy. Since the iron cost of pregnancy as shown in Table 13.7 is high (1200 mg), negative iron balance tends to occur. Iron deficiency anaemia accounts for approximately 3/41h or more of the non-physiologic anaemia in pregnancy. Physiologic anaemia is a term used to indicate anaemia due to haemodilution in normal pregnancy.

Based on blood volume changes during pregnancy and the iron content of foetuses at different gestational ages, the iron requirements for pregnancy in an iron replete non anaemic woman has been computed as shown in Table 13.7.

Requirement	Iron (mg)
Foetus at term	280
Expansion of red call mass	450
Placenta and umbilical cord	90
Maternal blood loss during delivery	150
Obligatory loss in the mother - day to day	230
Total iron cost of a pregnancy	1200

Table 13.7: Iron requirement for pregnancy

The increase in iron requirements during the first trimester is minimal as menstruation losses are nil and transfer to the foetus has not begun but the increase during the second and third trimester is quite large. The absorbable iron requirements are worked out to be 0.8 mg per day in the first trimester, which

increases to 6.3 mg during the second and third trimesters. Assuming a 5-8% absorption of iron in Indian pregnant women, the dietary iron requirement in the first trimester is 10-16 mg per day that can be easily met through existing diets. However, in the second and third trimesters, the iron need simply cannot be met through the diet as it rises to a phenomenal 80-120 mg per day. If a woman begins her pregnancy with normal iron stores of 500 mg, then the amount to be provided will reduce to 30-40 mg per day. This is the basis on which pregnant women in developed countries are recommended supplemental iron of 30 mg per day. However, among the Indian pregnant women, stores of iron are likely to be negligent. Further, most women in India are already anaemia even before the pregnancy commences. Computation of iron requirements for correction of anaemia and pregnancy needs in Indian women have been worked out and these estimates indicate that 60-100 mg elemental iron will be needed as supplements for pregnant women. On this basis the nutritional anaemia control programme in India provides 100 mg elemental iron. One tablet daily for pregnant women in the second and third trimesters to be continued for three more months postpartum.

The mother may not have adequate iron stores and dietary intakes may not fulfill the increased need for iron during the second half of pregnancy. Iron is required not only for haemoglobin synthesis but also to ensure adequate foetal stores that will last in the infant for the first 6 months of postnatal life.

Upto 2 years of pregnancy, iron rich diets are required to replace the iron lost during pregnancy and delivery. If there is a shorter interval between pregnancies, the drain on the mother's depleted iron reserves will be even greater. Hence, it is necessary to ensure adequate iron intake. In addition to dietary intake, an iron supplement is routinely prescribed. We will need to be alert that routine iron supplements may have unpleasant gastrointestinal side effects or imbalances with other trace elements of zinc. Also excess iron intake may potentially mask inadequate pregnancy-induced haemodilution. While supplementation is needed, it is important to emphasize food sources of iron in the mother's daily diet.

Certain degenerative diseases may also arise during pregnancy. The most common ones being, hypertension and gestational diabetes. These may regress after pregnancy or continue to progress throughout life.

B) Hypertensive Disorders of Pregnancy

Hypertension may have been existing before pregnancy. Alternatively, a mother may develop hypertension during pregnancy, a pregnancy-induced hypertension (PIH) which presents a serious complication. The cardinal symptoms are: hypertension, proteinuria and oedema, which usually occur after the 20d1 week of pregnancy. The onset of PIH may be signaled by unusual weight gain within a few days. Studies show that PIH incidence is higher in very young mothers (< 20 years) or older mothers (>35 years), mothers who are underweight and whose nutritional status is poor (including deficits in energy, protein, vitamins and minerals), in those who have pre-existing vascular disease e.g. essential hypertension, Type I

diabetes mellitus or a familial predisposition. Several nutrients have been studied for their role in PIH. These include protein, sodium, calcium and zinc. Incidence of PIH is greater among underweight women who fail to gain weight normally during pregnancy. Research evidence therefore indicates that an optimal and regular pattern of weight gain is vital to support the pregnancy.

Of course, prevention is best. However, if PIH develops, we need to advise the mother to have a well-balanced nutritious diet with sufficient energy and protein. Sodium intake can be 2-3 g since dietary sodium intake should be moderate but sodium restriction does not cure the syndrome. Maintenance of good nutritional status is important. Mothers should be aware and careful since severe PIH can cause convulsions and can prove to be life-threatening.

D) Pregnancy and Diabetes Mellitus

During pregnancy, a woman who has pre-existing chronic disease requires special care, especially in case of mother's suffering from diabetes. Diabetes developed during pregnancy is termed as gestational diabetes. Studies have clearly shown that patient education and intensive management for glycemic control can help the mother to have a healthy pregnancy, a healthy baby and reduce the risk of complications. We need to emphasize to the mother that self-monitoring plays a very important role in maintaining a 'tight' control on the blood glucose levels. For more details on control of diabetes, you may refer to Unit 12 in the Clinical and Therapeutic Nutrition Course (MFN-005).

another important factor which poses increased risk during pregnancy and delivery is excess body weight, whether it is prior to or during pregnancy. Let us read about the consequences and management of overweight obesity with regards to pregnancy.

E) Pregnancy and Obesity

Obesity is associated with increased risk for gestational diabetes, hypertension, pre- eclampsia, perinatal mortality and the need for induced labour or caesarian section. Lower weight gains are acceptable for overweight women because the foetus can receive a part of its energy requirements from the maternal stores. Studies have shown that obese mothers have the best pregnancy outcomes when they gain approximately 6-7 kg during pregnancy.

Each obese pregnant woman should receive individual assessment and be given nutrition counseling at the beginning and throughout the course of pregnancy. Weight management should be directed towards a slower rate of gain rather than weight loss at any time during gestation.

Besides this, a carefully supervised exercise programme should be recommended as adjuncts for cardiovascular fitness, maintaining a sense of well-being and normal blood sugar levels.

F) Adolescent Pregnancy

The pregnant adolescent is viewed as a high-risk patient, highly susceptible to suboptimal pregnancy outcome. Even when not pregnant, a teenage girl has difficulty meeting her nutrient needs. Nourishing a growing foetus adds to her burden, The competition between maternal and foetal needs places both mother and infant at a risk. The frequency of prenatal problems e.g. toxemia, anaemia, premature births, low birth weight and increased maternal/neonatal mortality is higher for adolescents than for adult women. Complications like iron deficiency anaemia reflect poor diet and inadequate prenatal care. Prolonged labour reflects the mother's physical immaturity.

Growth usually continues for 4 years post menarche, although at a much slower rate than during pre-puberty. Adolescent girls who become pregnant within 4 years of menarche/at a low gynecologic age, are generally considered biologically immature, and therefore, at a high risk.

Thus, nutritional needs for an adolescent mother must be estimated, in addition to her needs for growth. The dietary intake must meet the requirements for pregnancy, as well as, her individual needs at different stages of growth. Her nutritional requirements can be estimated by summing the RDI for the specific age and the additional recommendations. (We do not have sufficient specific information on nutritional needs of pregnant adolescents). Energy expenditure of adolescent girls is variable; hence the best assurance of an adequate intake is satisfactory weight gain. This should be accomplished by individual counseling on the basis' of estimates of body size, growth rate, and age and activity level.

Special attention needs to be paid to the calcium and iron needs. Nutritional assessment should include pre-pregnancy weight, the gynecological age (the chronological age minus the age at menarche), and the dietary intake history and activity patterns. Attention should be given to the pre-pregnancy nutrient intakes and nutritional status, low intakes of nutrient-dense foods during pregnancy and restricted food intakes. Weight gain is another aspect deserving attention. 'Allowable' or recommended weight gain could be higher than for adults. The weight gain required can be calculated by adding the following:

- Expected weight increase as a result of normal growth (non-pregnant) during the 9 months of pregnancy. (The increase in weight may be much higher for a girl during the first year after menarche to almost 10 kg, 4 years after menarche).
- Increase is required to support pregnancy.
- If underweight, the increase that is needed to achieve average weight for height.

13.9 LACTATION

Lactation is a physiologic process which has profound relevance for both the mother

and the newborn. It is the period following pregnancy when the woman nourishes a fully developed and a rapidly growing baby with breast milk.

A lactating woman secretes about 500 ml milk/day in the first month which increases to about 850 ml/day by the fifth month. On an average, a well-nourished lactating woman secretes about 850 ml/day.

We need to understand the establishment and maintenance of lactation, if we want to help mothers with proper and effective lactation management and prevent lactation failure especially in case of inexperienced mothers.

During pregnancy, changes occur in the mother's breasts to prepare for milk production and as you have seen, body fat are deposited to ensure that energy is available for lactation.

The establishment and maintenance of lactation are determined by several factors including the anatomical structure of the mammary gland and adequate development of the alveoli, ducts and nipples, initiation and maintenance of milk secretion and the ejection of milk from the alveoli to the nipple.

This information will help you in grasping the concepts explained here better. The major physiological features of lactation are being discussed next.

13.9.1 Physiology of Lactation

Lactogenesis is the onset of copious milk secretion around parturition, triggered by a fall in plasma progesterone levels. Although some colostrum is secreted after delivery (2-3 days), full lactation begins later. The first 2-3 days after delivery is a period of rapid lactation initiation, followed by the longer period of maintenance of lactation. This complex neuroendocrine process is facilitated by interplay of various hormones. Oxytocin and prolactin instigate the lactation process. Prolactin is responsible for milk production and oxytocin is involved in milk ejection from the breast.

A cyclic process of secretory activity, luminal distention and expulsion of milk into the duct system continues throughout lactation as directed by the suckling of the infant and the let-down reflex. Regular sucking stimulates the continuation of milk secretion. Milk removal from the breast is a product of coordinated interaction between suckling of the infant and let-down reflex of the mother, as depicted in the Figure 13.2. As the infant commences suckling, afferent impulses generated in the receptors in areola travel to the brain where they stimulate the release of oxytocin from the posterior pituitary. Oxytocin travels through the blood stream to the breast where it combines with specific receptors on the myoepithelial cells, stimulating them to contract and force milk from the alveoli into the mammary ducts and sinuses.

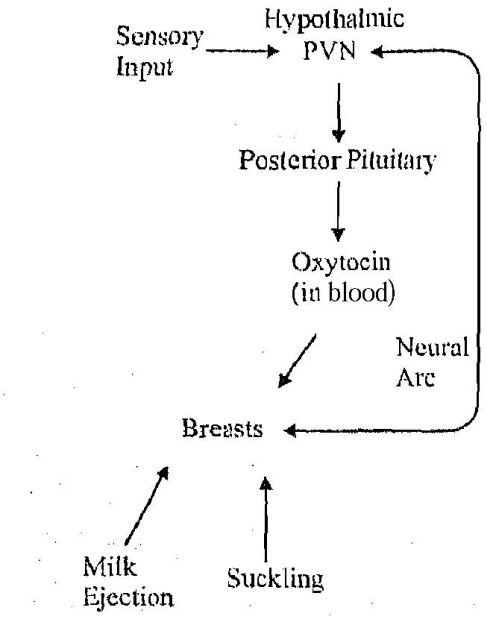

Figure 13.2; Basic features of 'let-down reflex'

We all know that human milk contains several nutrients and that it is tailor made to meet the requirements of the growing infant. The subsequent text will dwell upon the composition Of milk with special reference to its influence on the health of the infant.

13.9.2 Human Milk Composition and Infant Growth and Development

This sub-section deals with composition of human milk, compares human milk with cow's milk and why human milk is preferred and recommended for infants. We will also examine the impact of mother's diet and nutritional status on the quantity (volume) and quality (composition) of human milk.

Nature has designed milk to be species-specific. Thus, human milk is unique to the needs of the young homosapiens. The value of human milk for the health and growth of the baby is undisputed and rarely does breastfeeding need to be discouraged. The composition of the breast milk is described next.

A) Composition of Human Milk

Research clearly shows that each type of mammalian milk is unique and consists of a highly complex mixture of organic and inorganic compounds. Human milk is a solution of proteins, sugar and inorganic compounds in which a variety of fatty acids are suspended. Its nutritional composition is presented in Table 13.8.

Nutrients	Amount (per 100 ml)
Energy (Kcal)	65
Protein (g)	1.1
Carbohydrates (g)	7.4
Fats (g)	3.4
Calcium (mg)	28
Iron (mg)	-
β-carotene (mcg)	137
Thiamine (mg)	2
Riboflavin (mg)	2
Niacin (mg)	
Vitamin C (mg)	3

Source: Nutritive Value of Indian Foods, NIN (1989).

Table 13.8: Nutrient composition of human milk

Milk composition varies between mothers (inter-individual variation) from one period of lactation to the next (intra-individual variation) and even within a single 24-hour period (diurnal variation) and the time during the feed, as well as, the breast. The composition of milk is also related to the amount secreted, timing of withdrawal and individual variations, which includes maternal age, parity, health and socio-economic status. Gestational age of the infant also affects, since milk from mothers of premature infants has higher concentrations of some nutrients as compared to milk from mothers of term infants. Similarly, diet and use of oral contraceptives may also influence composition.

The concentrations of most nutrients fall between certain limits in the milk of healthy well-nourished mothers. The caloric value of human milk depends mainly on the fat content. Even after prolonged lactation for 2 years or more, the quality of milk produced by Indian and African women appears to be relatively well-maintained, although the quantity may be small.

Special characteristics of colostrum, beneficial to the infant are summarized herein:

- **Volume of colostrum:** 2-10 ml/feeding/day — related in part to the parity of the mother
- Typically yellow, due to a relatively high carotene content

- Transparent, contains more protein, less sugar and much less fat
- Lower in calories than mature milk (58 vs. 70 Kcal/100 ml)
- Concentration of sodium, potassium, and chloride greater than in mature milk
- Facilitates establishment of 'bifid bacteria' in the gastrointestinal tract of newborn
- Facilitates passage of meconium in the newborn's intestines
- Abundant content of antibodies — passive immunity for infant.

Colostrums changes to transitional milk between the 3rd and 61b day at which time the protein content is still quite high. By the 10th day, major changes have been completed. By the end of the 1st month, the protein content reaches a consistent level. As the content of protein falls, the content of lactose and fat progressively rise, as lactation becomes more firmly established.

The energy density of human milk depends on the relative proportions of protein, fat and the principal carbohydrate, lactose. Lactose content is ~7 g/dl and protein 0.9-1.0 g/dl. Lactose contributes 40-45% of the calories and protein 5-6%. Fat concentration and energy density may not affect total energy intake of breastfed infants since those who nurse on demand apparently compensate for a lower milk energy density by consuming higher volume of milk. Triglycerides constitute 98%of milk lipid with wide diversity in the fatty acid composition. Medium chain fatty acids are synthesized only in mammary alveolar cells while both saturated and unsaturated acids C atoms) are derived either from diet or fat stores.

Having studied the composition of breast milk, let us next get to know about importance of human milk.

B) Importance of Human Milk for Infant Growth and Development

Let us now look at the value of human milk in promoting infant growth and development. Success of lactation must be judged ultimately by its adequacy for growth and health of the breast fed infant. Lactation performance can be evaluated from the weight gain of the infant, in everyday life, although researchers have used a variety of methods.

We have listed some characteristics that make breastfeeding beneficial to the infant:

Mature milk contains about 1/3'd the protein found in cow's milk — more than 25% of its nitrogen is non-protein nitrogen. The concentration of casein to protein is lower; 1.5 for breast milk and 0.2 for cow's milk. Thus human milk with its low casein content forms a flocculent suspension with a curd tension of 0. These curds are easily digested and hence better tolerated by the infant.

- Lactoferrin in human milk inhibits the growth of certain iron-dependent

bacteria in the GI tract and therefore affords protection against gastrointestinal infections.

- Presence of phagocytes, lysozymes and lactoperoxidases, afford immunity against harmful microorganisms such as, S.aureus, Candida sp.; Salmonella sp.
- Protection from respiratory tract allergy and eczema.
- Immunoglobulins provide passive immunity and protect against infection by retarding viral and bacterial invasion of the mucosa.
- Brotective effects have been substantiated for necrotizing enterocolitis, acrodermatitis enteropathica, intractable diarrhoea, pathogenic E.coli infection.
- Relatively low in amino acids that are detrimental at high levels. High in amino acids that infant cannot synthesize e.g. cystine and taurine.
- **Lipids:** lower in foremilk-hind milk has a threefold higher fat content. Higher content of linoleic and oleic acid, cholesterol, the latter being needed for myelin synthesis.
- Contains lipase which helps in digestion of milk triglycerides and partly accounts for a greater ease in fat digestion of breastfed infants.
- Higher levels of lactose and nitrogen-containing oligosaccharides which have L.bifidus promoting activity
- **Minerals:** As compared to cow's milk, 6-times more phosphorus, 4-times more calcium — lower renal solute load — better availability.
- Lower iron content but nearly 50% of iron in human milk is absorbed.
- Levels of water-soluble vitamins likely to reflect maternal dietary or supplementary intake.
- Several hormone-like substances and growth factors in human milk.

The significance of human milk in maintaining the health of an infant was highlighted above. However, we all know that in countries like India, the prevalence of malnutrition is widespread and it can have serious consequences on the health of the mother and the quantity/quality of milk secreted. Read the subsequent text to learn more on this aspect.

13.9.3 Malnutrition — Effects on Milk and Effects on Mothers

Milk is the sole source of nourishment for many infants for upto 6 months or a year or even more. Therefore, the relationship between .maternal nutritional status and lactation performance is important. Let us look into the effects of maternal undernutrition. Theoretically, we could expect both quantity and quality of milk to be affected:

- **Volume:** A large healthy baby who can vigorously suck will induce and obtain much more milk from its mother than a small, sickly or preterm infant. These differences in yield may not be indicative of a mother's capacity for lactation. However, studies on women from less developed countries including Ethiopia,

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Nigeria and on poor Indian women show that volume of milk produced is not adversely affected, since milk production is a function of infant demand. However, it is strongly affected by feeding other foods/fluids.

- **Energy:** In case of chronic undernutrition, an association between postpartum weight loss and lower energy transfer may occur. In dietary supplementation trials, increasing maternal energy intake did not help much in increasing energy transfer except in women whose initial fat reserves were very low. In women with adequate fat reserves, apparently a gradual weight loss up to 0.5 kg/week may not adversely affect lactation.
- **Protein:** Some studies show that the protein content of milk may be affected by chronic protein undernutrition. In some cases, the tyrosine content of milk was significantly lower. In Indian women, it was seen that the milk of malnourished mothers had more casein and less whey. By giving a high protein diet supplement, the whey: curd ratio could be increased.
- **Fat:** Fat content of milk appears to be subject to variability as compared to other constituents. The average fat content in milk from well-nourished mothers tends to be higher than milk from less well-nourished mothers. This may have implications for the caloric intake of the infant. Supplementing the mother with adequate intake of energy, protein and fat helped to increase the fat concentration in milk. Low levels of fat are apparently related to diet during lactation, inadequate energy intake in pregnancy and an inadequate amount of fat gain. The fatty acid composition of milk lipid is altered by the mother's diet, including the type and amount of dietary fat, total energy intake and carbohydrate intake.

When lactating women were fed a diet rich in PUFA, their milk also had a higher PUFA content. Providing mothers with fish oil supplements increased the 0)-3 fatty acid in milk. When caloric intake is severely restricted, fatty acid composition resembles that of the depot fat. A substantial increase in the proportion of dietary Kcals from carbohydrate results in an increase in the milk lurid and myristic acids. The proportion of medium chain fatty acids was observed to be 30-45% on a low fat diet. However, the total fat content was not significantly altered.

What would be the effect on the micronutrient content of the milk? Let us read to find out.

- **Minerals:** There appears to be no relationship between dietary intake and concentrations in milk for copper, iron or zinc. Iron supplementation did not increase milk iron levels. In case of zinc, the milk concentrations may be influenced by maternal zinc intake within a physiologic range and the effects of low maternal intakes are most apparent with prolonged nursing. Selenium content of human milk indicates that it is related to maternal selenium status.
- **Vitamins:** Although there are inter-individual variations in vitamin concentrations, diet and drug use by individual women influences vitamin composition in human milk. Vitamin D activity of human milk is influenced by maternal vitamin D intake, as well as, maternal exposure to UV light.

Concentration of vitamin A is strongly influenced by the mother's diet. Vitamin A content of breast milk has been found to be much lower in some developing countries than in Western countries.

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The levels of water-soluble vitamins are more likely to reflect maternal dietary or supplement intake than most other ingested compounds. In lactating women of low socio-economic status, supplementation with folate, vitamin B_{12} and B_6 increased the levels of each vitamin in milk. B_6 in rti.lk may be a sensitive indicator of maternal vitamin B6 status. There are reports of vitamin B_{12} deficiency in infants of vegan and malnourished mothers.

So far, we have dealt with the various aspects of lactation and the importance of maternal nutrition for ensuring infant well-being. Let us now examine the impact of lactation from the mother's perspective.

Effects on Mother

Successful breastfeeding requires adequate nutrition and rest. For adequate lactation, substrates must be available in sufficient quantities from the mother's diet or body stores laid down during pregnancy. If these are insufficient, some degree of subsidy from maternal body tissue can be expected. As you well know, the simplest evidence of tissue depletion is weight loss. In a sense, pregnancy and lactation need to be considered as a continuum.

Among well-nourished women, weight loss can occur after childbirth, although this depends on their caloric intake and their physical activity. In poorer communities, dietary intakes of breastfeeding mothers are not very different from non-lactating women. However, given the lower caloric intakes, weight loss during lactation may not always be as severe as might be theoretically expected. It is possible that changes in tissue composition may mask the changes in body weight. An increase in body water, concomitant with an increase in body fat would result in great weight loss. However, the longer the duration of lactation, the greater would be the impact on the mother's nutritional status.

Studies indicate that there are major physiological alterations in calcium and bone metabolism during lactation, independent of maternal calcium intake. Bone resorption and bone formations are high, particularly in the 1"3-6 months of lactation. Decreased urinary calcium excretion and increased absorption efficiency have been observed.

13.10 MATERNAL NUTRITION DURING LACTATION

As we have already seen, the mother's nutrient intake must support breast 1i,Jc production and can influence the nutrient composition of milk. In fact, you will find that the need for energy and many nutrients is even greater during lactation than during pregnancy. The maternal nutrient need is highlighted next.

13.10.1 Nutrient Requirements during Lactation

Maternal nutrient requirements during the period of lactation include requirements for maintenance and activity and in addition, the amount of nutrients secreted in human milk. The latter would generally be determined from the yield and composition produced by healthy women with adequate lactation. Hence, you will realize that needs of women relate to the volume of milk produced. It is important to remember however that the requirement for a nutrient will be greater than the amount secreted in milk because the transfer of energy and nutrients from diet to milk is not 100% efficient. In practice, the mother subsidizes lactation from the nutrient stores she has laid down during pregnancy and if not, by the loss of body tissues. Specific requirements during lactation for many nutrients have not been extensively investigated. The RDIs are generally based on allowances for the non-pregnant, non-lactating woman plus the amount secreted in the milk. You will need to remember that it is assumed that the mother is more than 18 years old, and she herself is no longer growing. Let us then get to know about the nutrient needs of a lactating mother.

- **Energy and Protein Needs:** Remember that during pregnancy, well-nourished women will have laid down approximately 2-4 kg of fat. This can be mobilized to supply a portion of the additional energy for lactation. It is estimated that this amount of storage fat will provide 200-300 Kcal/day for a period of three months. However, this amount represents only a part of the energy cost of milk production.

The volume of milk produced is assumed to be 750 mL based on various studies. With an average content of 70 Kcal/100ml, the daily output of energy would be approximately 520 Kcal. You must remember that the efficiency of milk production would be 80% or a maximum of 90%. Thus, an additional energy supply of approximately 600 Kcal/day should be adequate to support lactation. The intakes recommended by the ICMR are shown in Table 13.9.

Nutrients	RDIs	
	0-6 months of Lactation	6-12 months of Lactation
Energy (Kcal)	+550	+400
Proteins (g)	+25	+18
Calcium (mg)	1000	1000
Iron (mg)	30	30
Vitamin A(mcg)		
Retinol or	950	950
β-carotene	3800	3800
Thiamine (mg)	+0.3	+0.2
Riboflavin (mg)	+0.3	+0.2
Niacin (mg)	+4.0	+3.0
Ascorbic acid (mg)	80	80
Folic acid(mcg)	150	150
Vitamin B_{12} (rncg)	1.5	1.5

Source: Nutrient Requirements and Recommended Dietary Intakes for Indian, ICMR (1990).

The RDIs for all major nutrients are given for the first 6 months of lactation, as well as, the second 6 months of lactation, when the volume of milk produced has decreased. However, women who had a low pre pregnancy weight gain, who have decreased weight for height and who breastfeed more than one infant, will more likely need additional kilo calories during lactation. FAO/WHO 2004 recommends that well-nourished women with adequate gestational weight gain should increase their food intake by 505 Kcal/day for the first six months of lactation, while undernourished women and those with insufficient gestational weight gain should add to their personal energy demands 675 Kcal/day during the first six months of lactation. Energy requirements for milk production in the second six months are dependent on rates of milk production, which are highly variable among women and populations.

The additional protein intake suggested in Table 13.9 not only takes into account the additional protein needs but also the net protein utilization of Indian diets,

The requirement of several micronutrients also increases and is summarized herewith.

- **Micronutrient:** Vitamin and mineral deficiencies can have profound influenc on the composition of milk. Calcium is a nutrient of special concern, since there are some reports in the literature that if the mother's diet is not adequate, it will be mobilized from her bones. This is especially of concern in case of prolonged lactation. Hence, the RDI for calcium is high for lactating mothers.

The requirements for other nutrients are all increased, reflecting the need for milk production and the need to replenish maternal stores. Folate needs are increased above non-pregnant levels but are not as high as during pregnancy. Iron needs are not increased during lactation because little iron is lost in milk, and in most women, losses are decreased because menstruation is absent. However, if the mother's iron status is poor, supplements of 30 mg of elemental iron per day may be recommended for the first 2 to 3 months of lactation to replete iron stores.

Besides these, water needs during lactation should be paid attention to. An increase in fluid intake does not increase milk volume, however, additional fluid is needed to maintain a normal maternal fluid balance. When fluid intake is low, the mother's urine will become more concentrated to conserve water for milk production. To avoid dehydration and ensure adequate milk production, fluid intake should be increased by about IL per day.

Now that we are aware of the nutrient needs, let us next study how to meet these needs of the lactating women.

13.10.2 Dietary Management

Meeting the needs of lactation requires a varied nutrient-dense diet. Generally, a well balanced diet will meet nutrient needs of the mother. Whenever feasible, food should be the source of nutrients and self-initiated vitamin and mineral

supplements should be avoided. The dietary intake of caffeine, artificial sweeteners and alcohol must be totally avoided. This is because most chemicals ingested by the lactating mother cross into the milk. Therefore, the mother should seek the advice of her physician before taking any dietary supplement, any medication or drugs such as caffeine and alcohol, which also pass into the milk and consequently 'affects infant. Excess caffeine may make the infant irritable and wakeful, but the research indicates that moderate amounts of caffeine (1-2 cups of coffee per day) will not harm or upset the infant. Large doses of coffee may interfere with availability of iron from milk. Ethanol appears in human milk in a similar concentration to the maternal blood, although acetaldehyde, which is the major toxic breakdown product of ethanol, does not appear in the milk. Alcohol may impair the milk ejection reflex, therefore, it is prudent to avoid alcohol intake when lactating.

Further, infants metabolize alcohol inefficiently. Smoking also reduces milk volume. Infant exposure to passive smoke negates the protective effect of breastfeeding and offers against sudden infant death syndrome.

Foods with a strong flavour may alter the flavour of milk. A few infants may be sensitive to particular foods e.g. cow's milk protein. Hence, when the mother's diet includes such foods, the infants may experience discomfort. However, this may not happen to most of the infants.

In general, the mother can eat whatever she likes. However, if she suspects that a particular food is causing the infant discomfort, she should consult the physician. If the food is eliminated for an extended time, appropriate foods should be substituted to ensure nutrient adequacy.

13.10.3 Other Concerns during Breastfeeding

Let us look into some special concerns during breastfeeding that might be useful to you as a dietitian.

- **Medical Considerate :** This is an area, which needs consideration. If a mother has a communicable disease like tuberculosis or hepatitis that could threaten the infant's health, then the mother and baby have to be separated. The mother can express her milk several times a day and feed the infant. In case of a mother with HIV infections, though the virus can be transmitted to the baby through milk, breast feeding the baby yet protects the infant.

Women with chronic diseases such as Type 1 diabetes continue to need careful monitoring and counseling to ensure successful lactation. They need to adjust their energy intakes and insulin doses to meet the heightened needs of lactation. Maintaining good glucose control helps to initiate lactation and support milk production.

Many drugs are compatible with breastfeeding, but some medications are contraindicated either because they suppress lactation or can be secreted into

breast milk and thus harm the infant, As a precaution, therefore, the mother should consult her physician before taking any drug.

- **Weight Loss :** Some women may want to return quickly to their pre-pregnancy weight. It is important to remember that some women will lose more, whereas others may maintain or even gain weight. Moderate to severe ca101iC restriction and rapid weight loss is not recommended because it can decrease milk production. This is especially important in the early weeks of lactation before the process is firmly established. Therefore, a gradual rate of weight loss in the first 6 months and that exercise is die best way to reduce excess weight. However, intense exercise can raise the lactic acid concentration of breast milk which influences the taste of milk. A study has shown that infants appear to prefer milk produced prior to exercise.

Among well-nourished mothers, those who exercised demonstrated a higher level of fitness, a lower percentage of body fat and higher level of energy expenditure as compared to sedentary women. There was no difference between the groups in plasma hormones or milk energy, lipid, protein or lactose content. Exercising women tended to have a higher milk volume. It has been recommended that energy intakes should not fall below 1500 Kcal/day at any time during lactation.

The cost of providing adequate nutritional support to the mother depends mostly on what foods she can afford and selects. The cost of providing appropriate foods for the lactating mother is cheaper than feeding the infant with animal milk, if economical food choices are made. Human milk is a vital national resource, which could markedly improve the health and nutritional status of children.

This section briefed upon the nutritional requirements of the mother during lactation and some general dietary and medical considerations to be borne in mind for maintaining a safe and healthy lactation. With this, we end our discussions on this topic and hope that the information given here would be of great help in managing diverse practical situations.

13.11 LET US SUM UP

In this unit, we studied about the most crucial periods of a woman's life, pregnancy and lactation, especially from a nutritional point of view. We got to know that good nutritional care and a well-balanced diet can help to ensure that the mother herself and the infant will be healthy. Maternal nutrition has an impact on the health and nutritional status of the infant's growth and development.

We learnt about the role of various nutrients and the corresponding increase in their RDA in order to meet the increased needs. Generally, the requirements for energy and most of the nutrients are increased during pregnancy and lactation especially for adolescents and women with multiple pregnancies. Adequate monitoring and care has a crucial role in ensuring satisfactory health of the mother. Dietary restriction for weight loss is contra indicated especially

during pregnancy, if the mother is obese. In our next section on lactation, we got to know the role of adequate nutrition during lactation. We also discussed about the composition of human milk and potential benefits of breast feeding. Finally, we learnt about the different disease conditions and their effect on the process of breastfeeding.

13.12 GLOSSARY.

Acrodermatitis enterocolitis : a rare inherited childhood disorder resulting in the inability to absorb adequate zinc from diet.

Basal Metabolic Index : a relationship between weight and height that is associated with body fat and health risk.

Basal Metabolic Rate : a measurement of energy required to keep the body functioning at rest.

Cretinism : a condition of endemic or inherited idiocy, accompanied by physical degeneracy and deformity.

External feeding : a method of providing food through a tube placed in nose, stomach or small intestine.

Oesophageal regurgitation : flow of the stomach's contents back up into the oesophagus.

Heartburn : a burning sensation experienced in the lower area of the heart.

Haemoconcentration : an increase in the proportion of red blood cells relative to the plasma, brought about by a decrease in the volume of plasma.

Human chorionic gonadotropin : a human hormone made by chorionic cells (in the foetal part of the placenta).

Homeostasis : metabolic equilibrium actively maintained by several complex biological mechanisms that operate via autonomic nervous system to offset disrupting.

Hyperemesis gravidarum : extreme, persistent nausea and vomiting during pregnancy and may lead to dehydration.

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Ketosis : a condition of having ketone bodies build up in body tissues and fluids

Macrosomia : 'Large body'; a baby that is considered larger than normal, a condition that occurs when mother's blood sugar levels have been higher.

Menarche : onset of menstruation.

Necrotizing enterocolitis : a serious intestinal illness that can cause tissue damage to the intestines.

Net Protein Utilization : the ratio of amino acids converted in to proteins compared to the ration of amino acids supplied throughout the day.

Neural tube defect : a congenital defect of the central nervous system, including spinal cord, skill and brain, resulting from failure of the neural and brain.

Parenteral feeding : a method of providing a liquid food mixture through a special tube in the chest.

Parity : the number of children borne by one woman.

Pre-eclampsia : abnormal state of pregnancy characterized by hypertension and fluid retention and albuminuria

Pregnancy induced hypertension : a complication of pregnancy marked by high blood pressure especially in the last three months of pregnancy.

Stroke volume : the amount of blood pushed into the aorta with each beat of the heart.

Teratogenic : substances such as chemicals of radiation that cause abnormal development of an embryo.

Toxemia : an abnormal condition of pregnancy characterized by hypertension, oedema and proteinuia.

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13.13 CHECK YOUR PROGRESS

1) What are the consequences of malnutrition during pregnancy?

2) Enumerate the physiological changes associated with pregnancy.

3) Describe the association between mother's weight and pregnancy outcome.

4) What modifications are made in the requirements of the following nutrients during pregnancy and why?

a) Protein

b) Folate and B_{12}

c) Iron

d) Calcium

5) Which non-nutritional factors can adversely affect the health of the pregnant mother and the foetus?