NUTRITION-HEALTH AND DISEASE

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Nutrition:

- Science that deals with food and nutrients and the way the body uses them.
- Deals with interaction of nutrients and their balance in relation to health and disease.
- Nutrient: certain parts of food that the body uses for energy, growth and replacement of worn out structures.
- Nutrition: Process of utilization of food by living organisms

Human nutrition:

- Undernutrition
- Overnutrition
- Ideal nutrition

- A balanced intake of nutrients in quantities required by the body is essential to maintain good health.

Ensures adequate growth and development as well.

- Carbohydrates, fats, proteins, vitamins and minerals - some nutrients present in diet.

Carbohydrates and fats-Energy.

Dietary proteins-Growth

Proteins provide amino acids

- Serve as precursors for a number of specialized products.

Example: Histamine from decarboxylation of histidine

Carbohydrates, fats and proteins

Collectively referred to as **macronutrients-**required in relatively larger quantities- to the extent of several grams per day.

Vitamins and minerals

-Required in much smaller quantities: few micrograms to few milligrams per day.

Accordingly, referred to as **micronutrients.**

After attending lectures on this topic, you should be able to understand:

- Calorific values of food materials, components of energy requirements of the body; basal metabolic rate, specific dynamic action and physical activity; recommended dietary intake of nutrients: and proximate principles of food.
- Nutritional importance of carbohydrates, dietary fibres, fats and proteins; parameters defining protein quality such as biological value, chemical score, protein efficiency ratio and net protein utilization; nitrogen balance; and protein sparing action of carbohydrates and fats.
- Disorders related to undernutrition and overnutrition

I. Calorific Values

Chemical energy in food-released in the body by oxidation to provide for the human energy requirements.

Calorific value: Energy content of a food material

Estimation of value:

- Measurement of the energy produced by the combustion of foodstuffs in a calorimeter
- Based on Hess' law:

Energy given off in a chemical reaction is the same, no mater by which intermediate steps it is carried out

$$(C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O)$$

- Energy liberated in the combustion of glucose is the same whether it is carried out in the laboratory or in the body, so long as the end products in each case are carbon dioxide and water
- Measuring the heat released in a calorimeter on burning a given quantity of fat, carbohydrate or protein
- Possible to say what must be the energy liberated by the body consuming known quantities of the three foodstuffs

In nutritional studies

- Unit of energy- the calorie.
- One calorie- Thermal energy required to raise the temperature of 1 gm of water by 1^0C (15^0–16^0C).
- Energy is generally expressed in terms of kilocalories (kcal)

1 kcal=1000 cal. International system of units, the unit of energy is kilo-joule (kJ);

1 kJ-energy required to move a mass of 1 kg by 1 meter distance by a force of one Newton. It is related to kcal as below:

$$1 \text{ kcal} = 4.128 \text{ kJ}$$

$$1\text{kJ} = 0.24 \text{ kcal}$$

Macronutrient	Calorific value in kcal/g	
	In body	In bomb calorimeter
Carbohydrates	4	4.1
Fats	9	9.4
Proteins	4	5.4

Table: Energy yield from various macronutrients during body metabolism

Note: Vitamins and minerals have no calorific values

Respiratory Quotient (RQ)

- Molar ratio of carbon dioxide produced per unit of oxygen consumed during combustion of a foodstuff.
- For the combustion of **glucose** RQ is 6/6 =1. Assumed to be the case for all carbohydrates.

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + H_2O$$

- The RQ for **fats** is lower because of their lower oxygen content
- Palmitic acid the RQ is 16/23 0.71

$$C_{16}H_{32}O_2 + 23O_2 \rightarrow 16CO_2 + 16H_2O$$

- **Proteins** (sums of their component amino acids that may show considerable variants)
- RQ also varies accordingly; its value is generally taken as 0.8.

RQ may be used to measure energy expenditure of an organism. This method may be referred to as *indirect calorimetry* (because it does not involve direct measurement of heat evolved by burning of the foodstuff).

It is important to remember that average kcal yield per liter oxygen consumed is 4.65 when fats are metabolized (RQ = 0.71), and 5.11 per liter oxygen when carbohydrates are burnt (RQ = 1).

Determination of Energy expenditure

- Direct calorimetry (heat generated)
- Indirect calorimetry (from measurement of oxygen consumption and carbon dioxide production)

II. Components of energy requirements

Total energy required by an average normal person is the sum of three energy-requiring body processes.

- The basal requirement (the basal metabolic rate)
- The requirement for diet-induced thermo-genesis (specific dynamic action of food)
- The requirement for physical activity.

Extra provision of energy has to be made for growth, pregnancy and lactation

A. Basal Metabolic Rate (BMR): Energy expended by the body when the voluntary activity is at a minimum.

Subject should be awake, at complete physical and mental rest, 12-hour after the last meal, and at an equable temperature (about 25^0C). The metabolic rate during sleep is less than BMR.

Expenditure of energy in the absence of Physical activity?

- Functions such as pumping of blood by heart
- Conduction of nerve impulses
- Gastrointestinal motility
- Work of breathing.

- BMR also accounts for such processes as protein turnover, glycoside bond biosynthesis and maintenance of cation differences across membrane, especially the sodium-potassium gradient. A large proportion of the BMR is ascribable to the need to maintain this gradient

Normal Values

Order of *1 kcal/kg body weight/h* for human beings.

- Higher in children than in adults
- Little higher in younger adults than in the elderly
- Little higher in males than in females.
- BMR takes into account the body surface area as well, and therefore, expressed as kcal expended per square meter body surface area per hour (kcal/sqm/h respectively).
- Variations to the extent of 15% of these are considered normal.

Measurement of BMR

Measured after some 12 hours of fasting in the post-absorptive state to avoid the so-called specific dynamic action: a surge of heat production after eating.

- The subject should be at complete rest, but awake, and in comfortable surroundings (at about 25^0C).

Any deviations from these conditions may alter the measured BMR to a significant extent.

The **Benedict-Roth apparatus** is used for the measurement of BMR. Subject asked to breathe into the mouth piece of the apparatus and the volume of oxygen consumed over a 6-minute period is determined. This is multiplied by 10 to obtain the oxygen consumption in one hour.

FACTORS AFFECTING BMR

A number of physiological and pathological conditions.

- ***Body size and weight:*** Shows wide variations, taking into account individual size and weight variations.

For instance, BMR in *humans* is about **32 kcal/kg/day**, whereas in a *mouse* it is **212 kcal/kg/day**.

- Among humans, BMR varies with body weight, but the rise is not proportional. For instance, in males with body weight 60 kg, 70 kg, and 80 kg, the BMR is 2590, 3010, and 3710 kcal/day, respectively. This is because adipose tissue is not as metabolically active as lean body mass.

In fact, *BMR is more appropriately expressed per kilogram of lean body mass or fat-free mass.*

- **Surface area**, which is related to body weight and height, also affects BMR, as mentioned earlier. Person of lean built of a given body weight has a greater surface area compared to an obese subject of the same body weight, and therefore, BMR is higher in the lean individual.

Age: Significantly higher in infant and growing child than in adult, and a little higher in young adult than in the elderly.

After 40 years of age, the BMR decreases at the rate of about 2% per decade of life.

- Age affects BMR, largely through a decrease in lean body mass after adulthood. The decrease in BMR with advancing years is usually not accompanied by changes in eating habits, which is partly the reason for overweight and hypothermia in old age.

	Age in years						
	1	5	15	25	40	55	80
Male	53.0	49.3	41.6	37.3	35.4	35.4	33.0
Female	53.0	48.4	37.8	35.4	34.9	33.2	31.1

Table. Basal metabolic rate (in kilocalories/hour/square meter body surface area) in different age groups

Sex: The gender differences in BMR (higher in males by about 5%) usually reflect the lower proportion of lean body mass in women, when compared to men of the same body weight.

Genetic differences: The BMR may vary by up to 10% between subjects of the same sex, age, body weight and fat content.

Racial differences: The BMR in Eskimos is significantly higher compared to that in other ethnic groups. However, studies to find differences between various ethnic groups, such as Asians, Africans and Caucasians have so far proved *conflicting and inconclusive*.

Nutritional status: In starvation, there is an adaptive decrease in the BMR, over and above that which results from the decrease in lean body mass. The converse is true when energy intake is increased.

Endocrinal state: BMR is increased in hyperthyroidism because thyroid hormones have a stimulatory effect on metabolism. In hypothyroidism, BMR may decrease by up to 40%, leading to weight gain. Other hormones, such as epinephrine and growth hormones, tend to raise BMR.

Climate: BMR increases in cold climate. In the persons living in tropical climate, BMR is about 10% less than those living in temperate zones.

Drugs: Smoking (nicotine) and coffee (caffeine and theophylline) increase the BMR, whereas β-blockers tend to decrease it.

Lifestyle: In physically active individuals, notably the athletes, BMR shows substantial increase. Stress and anxiety also tend to elevate BMR, which is mainly due to increased secretion of epinephrine.

Disease states: The BMR increases in infections, burns and cancer. In fever, the BMR rises by about **11%** for every **1^0C** rise in body temperature.

B. Specific Dynamic Action (SDA)

Another component of energy expenditure is specific dynamic action of food.

Refers to increased heat production after eating.

Diet-induced thermogenesis or post-prandial thermogenesis.

- SDA: Due to the *energy expended in digestion, absorption, transport and subsequent processing of food.* SDA was originally attributed solely to the metabolic handling of proteins, but it is now recognized as an effect produced by the consumption of all dietary fuels. The consumption of protein does, however, produce the greatest loss of energy (20-30% of intake), compared to fats (11- 13%) or carbohydrates (5-6%).
- Relatively higher SDA of proteins is primarily to meet the energy requirements for oxidative-deamination, synthesis of urea and biosynthesis of proteins

- **SDA is a wasteful expenditure from viewpoint of cellular energetics.** Out of every 100 g of proteins consumed, the energy available for doing useful work is 20-30% less than the calculated value.
- For instance, assume a person taking 250 g of protein, which should produce 250 x 4 = 1000 kcal. But the body must spend some energy (about 20% = 200 kcal) to extract this 1000 kcal. So the net value of 250 g protein is 800 kcal (1000 minus 200).

- **On mixed diet, value of SDA is around 10%**.

The percentage of energy lost being 10% a person must take food worth 110 kcal to obtain 100 kcal. Thus, additional calories must be added during diet planning to account for SDA. Finally, SDA shows considerable individual variation and this has been implicated as an important factor, which allows some persons to maintain their normal body weight after overeating.

C. Physical Activity

- Third important factor that must be taken into account while calculating the energy requirements. Its value varies from one individual to another, and even in the same individual from time to time. It depends on the *occupation*, *physical activity* and *lifestyle* of the individual. For convenience, the activity level may be divided into three groups: sedentary, moderate and heavy.
- To calculate total amount of energy for carrying out the muscular activities in 24 hours, the type and duration of all activities are carefully recorded. Table (next slide) shows energy expenditure for some of the common body activities. In general, a sedentary person requires about 30-50% more energy than the BMR requirement, whereas a highly active person may require 100% or more calories above the BMR.

Activity	kcal/kg body wt/hour
Fast running or dancing	9.7
Bicycling (13 miles/hour)	9.4
Swimming	8.7
Chopping wood	6.1
Walking	1.98
Brisk walk (4.5 miles/hour)	5.8
Mopping floors	3.9
Gardening, digging	3.1
Dressing	0.8
Eating	0.5
Standing	0.5
Reading/Writing	0.5
Sitting	0.4
Lying quietly	0.1

Table: Energy expenditure in some common physical activities (over and above BMR)

	ICMR recommendation
Man (55 kg)	
Sedentary work	2400
Moderate work	2800
Heavy work	4000
Women (45 kg)	
Sedentary work	1900
Moderate work	2200
Heavy work	2600
Later half of pregnancy	+300
Lactation	+700
Infants	
0–6 months	120/kg body wt
7–12 months	100/kg body wt
Children	
1–3 years	1200
4–6 years	1500
7–9 years	1800
10–12 years	2100
13–15 years	
Boys	2500
Girls	2300

Table: Recommended kcal allowances per day

D. Total Energy Requirement of an Average Normal Person

Total energy requirement of a person is calculated by adding the above three components of energy requirement:

Physical activity + BMR + SDA

- **Physical activity:** Energy required for different grades of physical activities carried out in last 24 hours, is calculated. Consider energy requirement of an 80 kg man with the following daily activities: sitting, 8 h; lying down, 4 h; walking, 1 h, standing, 0.5 h driving, 1 h; reading/writing, 1 h; gardening, 0.5 h; cycling, 0.2 h.

These activities account for 828 kcal in 24 hours (refer to table and calculate).

(Class to calculate)

- **BMR:** The energy requirement for physical activity is added to BMR. The BMR may be calculated from the approximation:
- **BMR = 1 kcal/kg/h**
- This equals 1 x 80 x 24 = 1920 kcal. Adding the two numbers, 828 and 1920=2748.
- **SDA:** The above value of 2748 equals calorie requirement excluding the SDA. A 10% surcharge is added to take into account the SDA. This amounts to about 274 kcal to give a **grand total** calorie requirement of 274 + 2748 = **3022 kcal/day**.

- Daily energy demands of most adult men vary between 2400 kcal (in sedentary workers) to 4000 kcal (in heavy workers). The corresponding figures in women are 1900-2600 kcal per day. Table shows recommended kcal allowances for individuals of different age groups and body weights.

An extra provision of energy must be made during **infancy, childhood** and pre-pubertal growth spurts (during 10-15 years of age). This is because biosynthesis of new tissues occurs during these stages of life, which requires input of considerable chemical energy. It has been estimated that laying down of 1 kg of new tissue in a year requires about 81 kcal/day extra energy. Likewise, an extra provision must be made during **pregnancy** to meet the requirements of the growing fetus. During **lactation**, an extra provision for synthesizing milk is needed; elaboration of one liter of milk (containing 642.8 kcal) requires at least 1285 kcal of energy.

III. Recommendations for Dietary Nutrients

Amount of nutrients required to meet the physiological needs of an individual is termed recommended dietary allowance (RDA).

Nutrient	Requirement per day per kg body weight
Proteins	
Males	1 g
Females	1 g
Children	
Infants	2.4 g
Up to 10 years	1.75 g
Boys (> 10 years)	1.6 g
Girls (> 10 years)	1.4 g
Pregnancy and lactation	
Pregnancy	2 g
Lactation	2.5 g

Table: Recommended daily allowance (RDA) of proteins in different age groups

- RDA of a given nutrient must be differentiated from the amount that must be consumed merely to avoid deficiency disease.
- RDA: Amount that is required for optimizing health, and not the amount merely to avoid the disease. For example, RDA for vitamin C is about 60 mg, but the amount required for preventing scurvy is only about 10 mg/ day. Intake of a nutrient at or near RDA provides considerable safety margin against the development of deficiency disorders.
- RDA for proteins is 70 g for a 70 kg adult man. The same individual would require about 80 g fats and 365 g carbohydrates each day. RDA for the micronutrients is much smaller, for example, RDA for vitamin E is 10 mg/day of α-tocopherol equivalents

Factors Affecting RDA

- Age, sex and several other factors determine RDA. For example, infants require about 2.4 times as much proteins per day as required by adults to support growth; males require greater amount of a given nutrient since their body mass is more; and RDA is enhanced in physiologically stressful states such as *pregnancy* and *lactation* and in patients with *injury* or *illness.* However, certain exceptions do occur; for example, RDA for iron in women is more than in men since women must replace the amount lost during menstruation.
- Recent studies have indicated that for optimal health, it is sometimes necessary to consume certain nutrients in amounts larger than RDA. For example, daily intake of vitamin E in amounts three times the RDA significantly reduces risk of coronary artery disease. Conversely, excessive intake of certain nutrients is hazardous, for example risk of coronary artery disease is enhanced if fats are taken in excessive amounts

IV. Proximate Principles of Food

Food plays a much wider role than merely providing energy and biochemical needs of life. In fact, culture, availability, economics, religion and several other factors play an important role in determining the type of food consumed in a given society.

In non-agricultural societies like Eskimos of Greenland and hunters of Africa, meat is the major food.

In such foods, nearly one-third of the total energy is provided by proteins and a major contribution for the rest comes from animal oils and fats. This is in sharp contrast with the average **diet in most communities,** where carbohydrates, proteins and fats account for about 75-80%, 10-12% and 10-15%, respectively, of the total energy provided. In between these two extremes lies the continental diet of the affluent Western societies. In a typical **continental diet**, contribution by carbohydrates is much less (*40-45%*), whereas fats and proteins account for more energy

V. Nutritional Importance of Carbohydrates

Regarded as a relatively cheap source of energy: the carbohydrate-rich foods cost less. Two groups of carbohydrates in the diet: **available carbohydrates-**can be assimilated and utilized for energy production: and dietary fibres-are indigestible, and therefore constitute **unavailable carbohydrates** in the diet.

A. Available Carbohydrates

- Some important available carbohydrates present in diet are *starch, sucrose, lactose, fructose* and *glucose*.

Starch-most abundant and cheapest source of energy, being present in most commonly available foods such as cereals, pulses, tubers, etc. On cooking it becomes more soluble and accessible to digestive enzymes. *Amylase* hydrolyzes the α(1-4) linkages of starch to form maltose, and oligosaccharide units.

Brush-border enzymes hydrolyse.

Glucose-major source of energy for most organs and tissues; erythrocytes, brain and other parts of central nervous system depend almost exclusively on glucose as a fuel.

- **Lactose-**present in milk (major carbohydrate for the breast-fed infants.
- **Sucrose** imparts sweetness to the diet because of its excessive sweetening property. However, the same property restricts its consumption; the daily intake may be as low as 4 g/day. It has been observed in experimental animals that feeding of excess sucrose results in hypercholesterolaemia and hypertriglyceridaemia.
- In humans, it predisposes to the development of dental caries. In view of these observations, only a limited intake of sucrose has been suggested; and avoided altogether in diabetic individuals and in those attempting weight reduction. *Rates of assimilation of different saccharides differ to a significant extent*. This is indicated by the observation that following consumption of these saccharides different responses are obtained.

Responses:

(a) post-prandial blood glucose elevation

(b) insulin release

- The above responses are lower with the complex carbohydrates (for example starch) than with the simple carbohydrates (glucose or fructose).
- The elevation of blood glucose level following fructose intake is less than the elevation seen after intake of an isocaloric amounts of glucose. Lactose is least effective in this regard, causing the least elevation of the glucose response curve.

Functions

- Carbohydrates play a major role in body's energy balance and are involved in a number of other vital functions.

Required for the synthesis of fats and non-essential amino acids, for oxidation of fats (acetyl CoA, a product of fatty acid oxidation combines with oxaloacetate, a product of carbohydrate metabolism), and have protein sparing action.

B. Dietary Fibres

- Fibres-important component of the diet, comprise plant cell components that cannot be broken down by human digestive enzymes. It is, however, incorrect to assume that fibres are completely indigestible, since some of them are at least partially broken down by intestinal bacteria.
- Fibres-complex carbohydrates having varying degrees of solubility. The more **insoluble fibres** include *cellulose* and *lignin*; **soluble** ones include pectins and gums; and **partly soluble** ones are *arabinoglycans* (mucilage).

Physiological Significance

Being largely indigestible, the dietary fibres do not provide any energy. Yet, certain invaluable health benefits are provided:

- ***Increased bowel motility:*** Absorb significant amount of water because of their predominantly hydrophilic nature. Thus, the ingested fibres attract large quantity of water into intestinal lumen, which results in increased bowel motility.
- ***Elimination of toxic compounds:*** Bind various toxic compounds, including certain carcinogens and bacterial toxins, and eliminate them through fecal route.
- ***Cholesterol lowering effect:*** The binding properties of fibres enable them to absorb organic substances such as cholesterol and eliminate them in faeces, so as to lower plasma cholesterol concentration.

- Fibres bind bile salts and reduce their enterohepatic circulation. This in turn enhances cholesterol to bile salts conversion and promotes its disposal from the body.
- Water-soluble fibres act by additional mechanisms: they lower serum cholesterol levels either due to their effect on insulin levels (insulin stimulates cholesterol synthesis and export), or other metabolic effects (perhaps caused by end products of partial bacterial digestion)

High fibre diet recommended in patients with hypercholesterolaemia.

4. ***Anti-hyperglycaemic effect:*** Fibres form a vicious gel in stomach and intestine to slow the rate at which various nutrients, most importantly carbohydrates, are digested and absorbed from intestine. Thus, the rise in blood glucose as also the subsequent rise in insulin levels are significantly impaired if fibres are ingested along with carbohydrate-containing foods.

This accounts for their utility in diabetes mellitus

5. ***Satiety effect:*** Fibres significantly increase bulk of the diet, so that one gets a feeling of fullness after ingestion.

- This bulk-enhancing property gives a feeling of satiety even without consumption of excess calories.

Fibre	Chemical nature	Physiological effect
Cellulose	Polymer of glucose	Increases weight and bulk of faeces, promotes colonic peristalsis, decreases fecal transit time
Hemi-cellulose	Polymer of pentoses, hexoses and uronic acid	Retains water to increase bulk of faeces, increases bile acid excretion
Lignin	Aromatic alcohol	Antioxidant, hypocholesterolaemic
Pectin	Polymers of galactose, galacturonic acid, rhamnose and arabinose	Improves glucose tolerance in diabetes, increases bile acid excretion
Mucilage	Branched arabinoglycan	Increases bile acid excretion, hypocholesterolaemic

Table: Chemical nature and physiological effects of some dietary fibres

Adverse Effects

- Excess fibre ingestion is not unproblematic as it may lead to several complications:

1. Fibres provide binding sites for **divalent metals**, calcium, iron and zinc, making these metals less bio-available.

2. They decrease intestinal protein absorption.

3. Some fibres are degraded by intestinal bacteria, causing flatulence and abdominal discomfort.

VI. Nutritional Importance of Fats

- Fats are considered as richer source of energy compared to carbohydrates and protein since they provide more energy per unit mass. From energy perspective, the most important dietary fat is triacylglycerol (TAG) since it constitutes more than 90% of the total dietary lipids

TAG may contain saturated, monounsaturated and polyunsaturated fatty acids (PUFA). Smaller amounts of other lipids, e.g. phospholipids, glycolipids, cholesterol, etc. may also be present in foods.

- In Western countries, the percentage of calories derived from fats is high (about 40%) compared to developing countries (about 15%). Current recommendations are-a maximum of 35% of the energy intake as fats.
- Recommendations, which aimed primarily at influencing cholesterol metabolism, further suggest intake of less than 300 mg/day of cholesterol; 30 gm/day of PUFAs, and only 10% of the total energy intake as saturated fatty acids.

- Dietary fat content of some common food items are shown in the table.
- Divided into two types: visible fats and invisible fats.
- Visible fats are oils, butter etc. which are pure lipid forms.
- Invisible fats are part of other food items, e.g. egg, fish, meat, cereals and oil seeds.

(Recommended daily intake of visible fats is 10% of total calorie intake or about 20 g/day).

Food Item	Carbohydrate (g/100 g)	Fat (g/100 g)	Protein (g/100 g)	Energy (kcal/100 g)
Rice	78.25	0.50	6.9	345
Wheat	71.2	1.70	12.10	351
Maize	66.2	3.60	11.10	341
Bengal gram	60.9	5.30	17.10	350
Soya bean	20.9	19.50	43.20	430
Dry peas	56.5	1.10	19.70	315
Groundnut	20.3	40.1	26.70	548
Egg (hen)	2.0	13.3	13.3	177
Fish	0.2	0.6	22.6	91
Mutton (muscle)	Traces	13	18.5	196
Chicken (roasted)	1.25	8.7	25.8	182
Milk (cow)	4.40	4.10	3.20	69
Milk (buffalo)	5.10	8.80	4.30	117
Milk (human)	7.50	3.40	1.10	66
Cheese	6.1	25.1	20.50	332
Potato	22.6	0.1	1.60	98
Sweet potato	28.2	0.3	1.20	123
Tapioca	38.7	0.20	0.70	161
Banana	37.0	0.50	1.10	156
Mango	11.8	0.50	0.70	52
Papaya	9.2	0.10	0.60	42
Apple	13.3	0.10	0.30	55
Cabbage	4.6	0.10	1.80	22
Carrot	10.6	0.20	0.96	49
Cucumber	2.5	0.10	0.40	13
Mushroom	5.1	0.70	3.80	41

Table:. Macronutrient content of some common food items and their calorific values

Functions

- In addition to providing energy, fats increase the palatability of food and are mainly responsible for the feeling of satiety after meals. Constitute the favoured, cooking medium all over the world.
- Dietary fats also required for the intestinal absorption of fat-soluble vitamins (A, D, E and K).

Dietary fats provide the polyunsaturated fatty acids (PUFAs) that are required for various body functions.

Role of PUFAs

1. Components of phospholipids and form biomembranes.

2. Required for esterification of cholesterol.

3. Serve as precursors of prostaglandins and leukotrienes.

4. Have hypocholesterolaemic effect and, therefore, offer protection against atherogenesis.

- The ω-6 bring down the plasma LDL level. However, they lower plasma levels of HDL as well, thus reducing the cardioprotective effect. The ω-3 PUFAs reduce serum triglyceride levels. Moreover, they increase production of TXA_3, which is less thrombogenic than TXA_2. Thus, consumption of the ω-3 PUFAs decreases platelet aggregation, which accounts for their anti-thrombogenic properties.
- The monounsaturated fatty acids also lower the serum cholesterol levels when substituted for the saturated fatty acids. An additional advantage is that they do not lower HDL levels

In recent times various hazardous effects following over-consumption of PUFAs have been reported.

- Excess PUFA may lead to production of free radicals that may be injurious to the cell unless antioxidants are available.
- Advisable to consume a proper mixture of fats, containing a balanced proportion of saturated and unsaturated fatty acids. The present recommendation is that not more than 30% of the total fats should be in the form of PUFA.

There has been considerable debate regarding utility of fats from plant sources vis-à-vis those from animal sources.

Animal fats generally contain a higher proportion of saturated fatty acids (with the exception of fish which contains mostly unsaturated fatty acids), whereas the fatty acids from plants are mostly unsaturated (with the exception of coconut oil which contains mostly saturated fatty acids).

Though vegetable oils are rich in PUFA, they are mostly unpalatable because of unpleasant odour and unpleasant taste.

Free fatty acids and substances responsible for bad odour, taste and rancidity are, therefore, removed to yield refined oils. Vegetable oils are refined by treating them with steam, alkali, etc.

VII. Nutritional Importance of Proteins

Recommended daily intake of proteins is 1.0 g/kg body weight.

Dietary protein intake considered adequate if it supplies up to 12% of body's energy needs.

- In children, protein requirement is higher because of a higher growth rate.
- Protein requirement is higher in both, pregnancy and lactation

Dietary proteins:

- Body growth, repair and maintenance of tissues
- Replenishing amino acids lost in urine, faeces, saliva, skin, hair and nails.
- Replenishing amino acids in the (amino acids) pool, after these amino acids are used up for the synthesis of non-protein nitrogenous compounds and for other bodily activities.

Note: Excess dietary intake of proteins or low intake of carbohydrates and fats results in protein degradation for obtaining energy.

A. Protein Quality

- Proteins from different sources differ in their ability to support growth and to maintain and repair the body tissues.

Ability-an indicator of quality of protein.

- *Protein quality depends on amino acid composition, digestibility and efficiency with which the amino acids are absorbed and subsequently incorporated in the body proteins*. Some parameters used to define protein quality are biological value, protein efficiency ratio and chemical score.

Biological Value (BV)

$$BV = \frac{\text{Nitrogen retained}}{\text{Nitrogen absorbed}} \times 100$$

Food item	Chemical score	Protein efficiency ratio	Biological value
Egg	100	4.5	96
Cow milk	65	3.0	84
Meat	70	2.8	80
Fish	60	3.0	85
Rice	60	2.0	64
Wheat	42	1.7	58
Bengal gram	44	1.7	58
Ground nut	44	1.7	54
Soya bean	57	1.7	64
Biological value is most commonly used parameter for assessing protein quality.			

Table: Protein quality of some food items

- BV-Empirical measure of the efficiency of protein as a supply of essential amino acids. Biological value of egg protein is very high (96) because it contains an adequate quantity of all essential amino acids and more importantly, it supplies these amino acids in the needed proportions.
- Generally, *animal proteins have higher biological value*. Gelatin, prepared from animal collagen, is an exception since it lacks several essential amino acids. Consequently its biological value is low.

- Proteins obtained from plant sources have lower biological value

Lack one or other essential amino acid.

Missing amino acids are called the limiting amino acids. Limitation of plant foods is overcome when these foods are consumed in combinations. For example, wheat is deficient in lysine but contains other essential amino acids in adequate amounts. Kidney beans contain lysine in adequate amounts, though deficient in methionine.

- When these two food items are combined, the body gets the required supply of both methionine and lysine
- Thus, dietary combinations of higher biological value are designed by appropriate combination of foodstuffs

Referred to as the mutual supplementation of proteins

- To improve biological value-addition of the limiting amino acid to a foodstuff, e.g. lysine can be added to wheat flour.
- Process is fortification with (limiting) amino acid.
- Vegetable proteins can be fortified with their limiting amino acids: lysine, methionine, threonine and tryptophan.

Protein Efficiency Ratio (PER)

- Less commonly used parameter for assessing the protein quality. Defined as gain in body weight for each unit weight of protein ingested. Apparently, the amount of dietary protein used for maintenance is ignored.

$$PER = \frac{\text{Gain in body weight (g)}}{\text{Protein fed (g)}}$$

- Eggs, milk and meat have high PER (2.5) and legumes, lentils, cereals and nuts have PER between 0.5 and 2.5. PER of gelatin is less than 0.5

Chemical Score

- Essential amino acid content can also be expressed in terms of chemical score. C

Calculate:

$$\frac{\begin{array}{c}\text{mg of limiting amino acid}\\ \text{in one gram test protein}\end{array}}{\begin{array}{c}\text{mg of same amino acid}\\ \text{in one gram of reference protein}\end{array}} \times 100$$

The egg protein is taken as the reference protein- chemical score is 100.

Digestibility Coefficient (DC)

Percentage of ingested protein absorbed into the bloodstream (after digestion) in the gastrointestinal tract.

Net Protein Utilization (NPU)

A measure of utilization of dietary protein for synthesizing body proteins, calculated by the formula

$$NPU = \frac{\text{Nitrogen retained}}{\text{Intake of nitrogen}} \times 100$$

NPU-better index than biological value since it takes into account the digestibility factor, also

Depends on both digestibility coefficient and biological value.

$$PU = DC \times BV/100$$

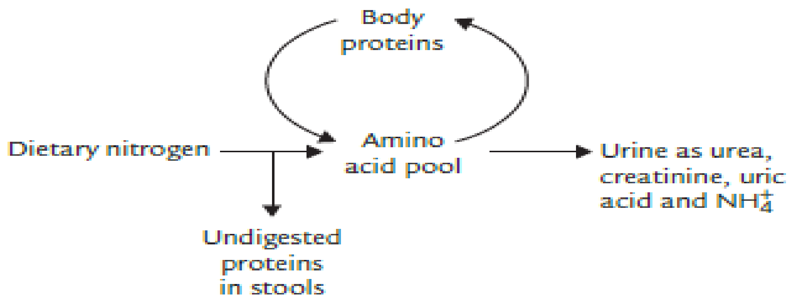
B. Nitrogen Balance

Comparative amounts of the nitrogen entering the body and that leaving it.

A normal adult with adequate protein intake should be in nitrogen equilibrium: Amounts of incoming and outgoing nitrogen are equal.

Since the exclusive source of nitrogen in the body are dietary proteins (16% of which is nitrogen), the nitrogen balance studies are used for assessing utilization of dietary amino acids for synthesis and for studying the balance between anabolic and catabolic processes.

- A 100 g sample of dietary protein contains approximately 16 g nitrogen, of which, approximately 83% leaves the body as urea, 7% as ammonium ion, and 10% as organic waste products such as uric acid and creatinine.
- Most of this nitrogen is eliminated via urine but 1-2 g of nitrogen from undigested protein are excreted in stool also.



- In addition to the state of nitrogen balance in a normal healthy body, two abnormal states, positive and negative-nitrogen balance.
- A positive nitrogen balance-nitrogen intake exceeds nitrogen excretion-implies that amount of body protein increases. Seen in situations where tissue growth occurs; for example, in *growing children, convalescing adults and in pregnant women*.
- Negative nitrogen balance-reflects nitrogen excretion exceeding nitrogen intake. Occurs when the dietary protein intake is inadequate, or when some physiological stress is encountered, such as *trauma, burns,* or *emaciating illness*

C. Protein Sparing Action

- Dietary intake of carbohydrates and fats indirectly influences protein requirement of an adult. If dietary consumption of carbohydrates and fats is inadequate, some dietary protein must be used for energy generation. Thus, protein becomes unavailable for building and replacing tissues; consequently, dietary requirement of protein increases to make up this loss. Conversely, when sufficient calories are obtained from carbohydrates and fats, protein is no longer required for providing energy, and therefore it can be used for building up body proteins.
- Proteins are thus spared by carbohydrates and fats-action referred to as protein sparing action. Carbohydrates are more efficient in sparing proteins than fats, probably because carbohydrates can be used by almost all tissues.

D. Reasons for Increase in Protein Requirement

- **In active growth**, more dietary proteins are required to supply amino acids to the growing tissue. Pregnancy, infancy, childhood and adolescence are some examples.
- Prolonged illness, trauma and surgery cause a major **catabolic response** to meet increased energy needs of the body.

Response mediated by epinephrine, glucocorticoids, glucagon and certain cytokines secreted in increased amounts. Breakdown of body proteins occurs, which must be replaced by dietary intake so as to prevent negative nitrogen balance.

In **old age-** increased dietary protein intake is required. This appears paradoxical as the requirement should fall since there is little growth. However, older people need and generally consume fewer calories.

Proteins should provide a larger percentage of total calories.

Absorption of dietary proteins may be less due to digestion and absorption problems, common in old age.

	Sedentary	Moderate	Heavy
Cereals	290	340	450
Pulses	100	120	120
Leafy and other vegetables	200	200	200
Roots and tubers	200	225	250
Fruits	40	4040	
Milk	200	200	200
Fats and oils	35	3540	
Sugar and jaggery	35	3545	
Ground nut	10	1040	
Sprouts	50	5030	
All values in grams.			

Table: Balanced vegetarian diet for an adult male

VIII. Balanced Diet

Has all the macronutrients and micronutrients recommended for individual's age, sex, occupation and lifestyle.

- Supplies all the nutrients in amounts slightly more than the minimum requirement to withstand any stressful state.
- Composition of balanced diet differs depending on socio-cultural background, economic status, availability of foods, etc.
- **Special allowances** should be made in the formulation of balanced diet during physiologically stressful states, such as *pregnancy* and *lactation*.
- ***Pregnancy:*** Fetal growth, tissue differentiation, and organogenesis require energy, which is met by mother's nutritional resources. Hence, marked increase in requirement of energy and protein, in addition to calcium, iron, folate and iodine is recommended.
- ***Lactation:*** Like pregnancy, requirement of various nutrients increases during lactation. However, vitamins A and C are required additionally, but requirement of iron reverts to normal.

	Deficiency in weight for height	% of body weight compared to standard weight	Oedema
Kwashiorkor	+	60–80	+
Marasmus	+	< 60	Nil
Marasmic kwashiorkor	+	< 60	+

Table: WHO classification of protein-energy malnutrition

IX. Nutritional Implications of Diseases

Nutritional disorders classified into two broad categories:

- Arising due to undernutrition
- Arising due to overnutrition

A. Undernutrition: Protein Energy Malnutrition (PEM)

- Dietary resources in the developing countries limited
- Protein energy malnutrition a common problem.
- Infants and children are the worst sufferers.
- Signs and symptoms of PEM vary from case to case depending on the degree of inadequacy.
- Two major categories: **Marasmus** and **Kwashiorkor**.

*Marasmus: A*n inadequate intake of both proteins and energy (under a year of age).

Kwashiorkor: An inadequate intake of proteins with relatively adequate energy intake (between 1 and 4 years of age).

Marasmus

- Likely to occur among poor families, when
- There is a rapid succession of pregnancies, and early and often abrupt weaning, followed by inadequate artificial feeding
- Diet is low in both calories and protein

- A child suffering from marasmus *looks like a little old person with skin and bone*.

Thin, wasted appearance and weight is less than the desirable weight for their age.

If the dietary deficiency continues for long, the developmental milestones get delayed and the condition ultimately leads to permanent stunting of growth and development.

Not only the physical development, but the mental development is also affected

Kwashiorkor

Child has a *plump appearance due to oedema*.

- Oedema-lack of adequate plasma proteins that normally maintain the distribution of fluids between the intra and the extra-vascular compartments.
- Protuberant abdomen (due to oedema) is often seen, which is a deceptive presenting feature in view of muscle wasting and stunted growth of the child.
- Other symptoms associated with kwashiorkor are brittle hair, diarrhoea, dermatitis of various forms, and retarded growth.
- ***In contrast to early weaning in marasmus, late weaning, often extending over 2 years, is characteristic of kwashiorkor.***

	Marasmus	Kwashiorkor
1.	Diet with inadequate calories	Diet **insufficient in proteins and calories**
2.	Usually seen in early weaning, or infants never breast-fed (under an year of age)	Usually seen in late weaning (1–4 years of age)
3.	Oedema not present	Oedema characteristically present
4.	Severe cachexia is seen	Body weight decreased or normal
5.	Serum albumin normal or slightly decreased	Hypoalbuminaemia present
6.	Somatic protein compartment depleted	Visceral protein compartment depleted
7.	**Face shrivelled** and monkey-like	**Face puffy,** protuberant abdomen
8.	Voracious appetite	Impaired appetite (anorexia)

Table: Comparative features of marasmus and kwashiorkor

- **Both marasmus and kwashiorkor have similar devastating results**. Reduced ability of the afflicted individuals, to fight off infection in both conditions.
- Mortality is very high, the underlying cause of death is mostly some infection rather than starvation itself.
- Increased susceptibility to infection is due to decreased immunological response; reflected by: Various components of immune system affected are as follows:

✓ The number of T lymphocytes is decreased, resulting in decreased cell-mediated immune response.

✓ Generation of phagocytic cells, immunoglobulins, interferons and other components of immune response is diminished.

Biochemical Changes in PEM

A number of biochemical parameters are altered in the following conditions:

- Decreased plasma levels of **serum albumin** and **other serum proteins** are most commonly seen.
- In kwashiorkor, the serum albumin may fall to a value as low as 2 g/dl, whereas in marasmus it need not be so low.
- The level of **retinol-binding protein** (RBP) is also characteristically lowered.
- **Glucose tolerance** is often normal in both conditions, but hypoglycaemia is often seen in a marasmic child. In kwashiorkor, blood urea may decrease and excretion of creatinine in urine is reduced due to loss of muscle mass.
- The cellular immunity tests are also affected.
- Features of associated deficiency of vitamins and minerals (mostly iron) are commonly seen.
- Hypokalaemia and dehydration occur when there is diarrhoea.

Treatment

Treatment of PEM comprises three components:

- Administration of adequate calories (and proteins in kwashiorkor).
- Control of infections.
- Treatment of associated disorders mentioned above.

B. Overnutrition

Diseases due to overnutrition are becoming more prevalent all over the world, especially among city dwellers.

Diseases influenced by dietary excess and dietary imbalances.

- High calorific and high fat diet is associated with ischaemic heart disease-the biggest killer in urban settings. High fibre diet is beneficial for such individuals.
- Saturated fatty acids consumption is associated with increased risk of certain cancers, especially cancer of colon, breast and prostate.

Obesity

State in which excess fats (triacylglycerols) accumulate in the body. Increased number and/or size of adipocytes occurs in obesity.

Common Causes

- One of the most serious problems among the urban affluent populations is consumption of excessive calories with inadequate exercise, of which obesity is the natural consequence.
- Obesity is not a simple problem of excessive calorie consumption; several other factors contribute to its development.

Genetic predisposition plays an important role.

- Genetic predisposition has been suggested based on the familial incidence of obesity. If one parent is obese, 40-50% chances are there that the children would also suffer from obesity. No single gene is responsible for obesity.
- Leptin-a 16-kD polypeptide, encoded by the *obese* genes in adipocytes, influences appetite control system in the brain. These proteins cause decreased food intake, thus representing “satiety signal” in the body.
- Certain metabolic aberrations-commonly associated with obesity. *Hypothyroidism*, *hypogonadism, Cushing’s syndrome* and *hypopituitarism* may lead to obesity. Women are more prone to become obese during puberty, pregnancy, and after menopause.

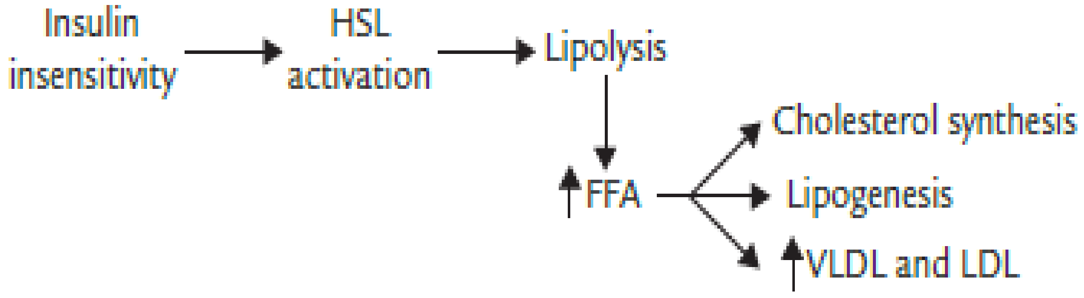
Biochemical Profile

Most commonly affected parameters are the **lipid parameters**. Elevation of serum concentration of free fatty acids, cholesterol and triacylglycerol commonly occur.

- Parameters poorly respond to dietary restrictions.

- Underlying cause of the altered lipid profile traced to decreased sensitivity of peripheral tissues (including adipocytes) to insulin. Number of insulin receptors on cell surface is decreased (e.g. down-regulation) so that these tissues respond poorly to insulin, even though plasma insulin level is elevated. Since insulin inhibits activity of the *hormone-sensitive lipase* within adipocytes, this inhibition is impaired in obesity. Consequently, activity of the *hormone-sensitive lipase* increases, resulting in mobilization of fatty acids from adipocytes. This leads to increase in circulating free fatty acid levels.

Excess fatty acids are carried to the liver and degraded to acetyl CoA through β-oxidation. Since acetyl CoA is a precursor for cholesterol and fatty acids (and hence triacylglycerols), increased generation of these molecules results. The excess cholesterol and triacylglycerols are released (after incorporation in very low density lipoprotein particles) leading to high circulating levels of these lipid components.



Major ill-effects of obesity are reduced lifespan and *coronary artery disease* due to the prevailing alterations of lipid profile.

Obese individuals are at higher risk of developing *diabetes*; *nearly 80% of the adult onset diabetic individuals are obese*. Underlying cause of diabetes in obese people is decrease in number of insulin receptors and decreased sensitivity to insulin.

Decreased sensitivity to insulin results in hyperglycaemia and hence a persistent stimulus for the pancreatic β-cells.

- Hyperinsulinaemia is the natural consequence.
- Hyperinsulinaemia causes stimulation of sympathetic nervous system, which results in vasoconstriction and retention of sodium and water.

Both these changes lead to *hypertension*.

Only effective mode of treatment- **reduction of body weight**.

All the aforementioned metabolic changes get significantly reversed if the ideal body weight is attained.

- Goal can be accomplished by reducing the intake of calories and performing controlled exercise.
- Frequent small meals with lots of vegetables have been found especially effective.
- Fat restricted diet may retard the ageing process also and thus prolong the lifespan

Diet and Coronary Heart Disease (CHD)

- Coronary heart disease-potentially lethal condition; mortality is very high if timely diagnosis is not made and proper treatment is not initiated.
- Underlying defect in CHD is deposition of **atherosclerotic plaques** on the inner surface of the small and medium-sized arteries.
- A plaque consists of *deposits of cholesterol, cholesterol esters and cellular debris*. As the disease progresses, these deposits reduce or even block the blood flow. The blood supply to the peripheral tissues is impaired resulting in inadequate supply of oxygen and nutrients to these tissues. The consequences depend on the blood vessel that is affected:
- When the blockage occurs in the coronary vessels, damage to myocardium results. The cardiac tissue may become non-functional, and the condition is termed *myocardial infarction* (MI), commonly referred to as heart attack.
- Blockage in cerebral blood vessels may result in stroke.
- Risk of developing *thrombosis* is also greatly enhanced in atherosclerosis.

Several dietary factors are thought to influence the incidence of coronary artery disease, most notably cholesterol.

LDL cholesterol is bad cholesterol, whereas HDL cholesterol is cardio-protective.

- Relatively higher HDL levels are seen in women before **menopause**, which may account, in part, for lower incidence of CHD in them.

Measures recommended in the susceptible individuals.

- *Reduction of dietary intake of cholesterol*. Cholesterol, being a product of animal metabolism, is found only in foods of animal origin; egg yolk and organ meats are extremely rich sources. In contrast, the plant products- even vegetable oils contain no cholesterol. In view of these facts, necessary dietary modifications must be made in diet so that intake of cholesterol rich foods is reduced.
- *Change in lifestyle* in such a way that adequate *physical exercise* becomes part of daily routine.
- *Increased dietary intake of fibres*, although exact role of high-fibre diet on coronary artery disease is still controversial.
- *Increased intake of dietary antioxidants*, such as vitamins C, E, and β-carotene. These compounds chemically inactivate the oxidative radicals derived from molecular oxygen and hence protect LDL against oxidation

Protection against heart diseases confirmed by certain studies: Daily intake of 100 International Units of vitamin E (RDA 15 IU) may reduce death from coronary artery disease by approximately 40%.

- *Hypocholesterolaemic drugs*-usually recommended in middle-aged men with very high plasma cholesterol levels.

Note: Type of fatty acids consumed have a significant bearing on serum cholesterol levels.

Saturated fatty acids are harmful-tend to elevate serum cholesterol levels, especially the LDL fraction.

Foods rich in these fatty acids, such as meat products and some vegetable oils like coconut and palm oil, must be avoided.

Interesting to note that all saturated fatty acids do not have cholesterol raising effects: stearic acid(18-C) and short-chain saturated fatty acids (10-C) tend to raise serum cholesterol to a lesser extent than the 12-C to 16-C saturated fatty acids.

DIGESTION AND ABSORPTION

- Most nutrients are large polymers.
- Disintegration requires coordinated action of a number of enzymes and associated cofactors.
- Approximately 30 g of digestive enzymes are secreted per day.
- Whole process of digestion consists of hydrolytic cleavage reactions catalyzed by these enzymes
- Macromolecular nutrients are hydrolyzed to their monomeric building blocks.

Extent to which various nutrients are hydrolyzed, and then utilized varies.

Utilization of starch and glycogen is nearly complete: molecules are completely degraded to their monomeric unit, glucose, which is then readily absorbed.

Indigestible compounds like dietary fibres, remain unutilized and are excreted as such.

Processes:

Mechanical homogenization of food and mixing of the ingested solids with gastrointestinal secretions

Secretion of digestive *enzymes* that hydrolyze dietary polymers to oligomers and dimers.

- *electrolytes, acids or bases* to provide an environment for optimum digestion.
- *bile acids* to emulsify lipids.

Hydrolysis of the oligomers and dimers by intestinal surface enzymes.

Carbohydrates

- Major share of the daily caloric requirement.
- Dietary carbohydrates consist of digestible compounds such as starch, glycogen, lactose and sucrose.
- Indigestible fibres of plant origin, such as *cellulose, hemi-cellulose, pentosans*, and *inulin* are present in normal diet, which cannot be degraded by digestive enzymes of non-ruminants.

Note: Starch and glycogen provide bulk of the dietary carbohydrates

- Starch: Plant polysaccharide, consisting of linear chains of glucose molecules linked by α(1-4) glycosidic linkages, and branch points linked by α(1- 6) glycosidic linkages. Glycogen is a polysaccharide of animal origin, having a similar structure as starch, but is more extensively branched.
- Digestion of these polysaccharides begins in mouth in humans by action of the *salivary* enzyme, ***α-amylase***. Hydrolyzes the α(1-4) bonds to release smaller oligosaccharide fragments.
- As soon as the food reaches the stomach, it is acidified and the acidic pH stops the action of this enzyme (optimum pH for salivary *amylase* is 6.9). No further digestion of carbohydrates occurs in the stomach.

Duodenum

Low pH stimulates release of *secretin,* an intestinal hormone, which helps elevation of pH to neutral range.

Stimulating bicarbonate release from the exocrine pancreas. Neutral pH is optimum for the action of the *pancreatic amylase*, the principal enzyme for digestion of starch (and glycogen).

A *dextrinogenic endosaccharidase*, specific for hydrolyzing the α(1-4) linkages. Hydrolyzing bonds that lie towards the core of the starch molecule. *exosaccharidases* of plant origin, which can act only on the terminal α(1-4) linkages.

- *Amylases cannot hydrolyze the branch linkages, i.e. α(1-6) linkages, being specific only for the α(1-4) linkages*

- Extensive action of *a-amylase* in intestine cleaves the starch molecule into smaller fragments such as maltose, maltriose, and short oligosaccharides.
- Oligosaccharides may be linear or α-limit dextrins (5-9 glucose units with a branch point).
- Further hydrolysis of these products carried out by surface enzymes of the small intestinal epithelium cells.
- Enzymes are also referred to as *brush border enzymes* firmly attached to the cell surfaces with their catalytic domains protruding into the intestinal lumen.

B**rush border enzymes:**

- *Maltase:* Enzyme possesses *a(1-4) glucosidase* activity which enables it to cleave maltose into two glucose residues. It can also hydrolyze short linear oligosaccharides of up to 9-carbon unit length.
- *Lactase:* It degrades lactose into glucose and galactose. Its action is slower than the other brush-border enzymes which have excess capacity to hydrolyze their substrates.

Quantity of the *lactase* is just about sufficient to degrade the lactose that is presented to it. In contrast to the other brush border enzymes, where synthesis can be induced, if required.

- *Isomaltase or sucrase:* Enzyme is initially synthesized as a single polypeptide chain, which is later cleaved into two subunits, each having a distinct enzymatic activity.
- The *isomaltase activity* accounts for cleaving the α(1-6) linkages in isomaltose and the α-limit dextrins.
- The *sucrase activity* accounts for the hydrolysis of sucrose into glucose and fructose.

Summary on the next slide.

Concerted action of various enzymes results in breakdown of dietary carbohydrates to produce monosaccharides such as D-glucose, D-galactose and D-fructose

Enzyme	Cleavage specificity
Maltase	Maltose, maltotriose; also acts as *exoglycosidase* on $\alpha(1 \rightarrow 4)$ bonds at the non-reducing end of starch and starch-derived oligosaccharides
*Lactase**	Lactose; also cellobiose#
*Cerebrosidase**	Gluco- and galactocerebroside
Sucrase	Sucrose; also maltose and maltotriose
Isomaltase	$\alpha(1 \rightarrow 6)$ bonds in isomaltose and α-limit dextrins
Trehalase	Trehalose•

* The *lactase* and *cerebrosidase* activities reside in two different globular domains of the same polypeptide.

Cellobiose is a disaccharide of two glucose residues in $\beta(1 \rightarrow 4)$ glycosidic linkage.

• Trehalose is a disaccharide with a structure of α-D-glucopyranosyl-α-D-glucopyranoside (in 1,1 glycosidic linkage); common only in mushrooms.

Table: *Disaccharidases* and *oligosaccharidases* of the intestinal brush border

Absorption by **facilitated diffusion**-mediation of the carrier proteins present in the plasma membrane.

Based on studies, carried out in rat-intestine, it has been estimated that the relative rates of absorption of the monosaccharides are as follows: glucose, 100%; galactose, 11%; fructose, 43%; mannose, 10% and xylose, 15%.

- After absorption, monosaccharides pass into portal circulation.
- Transport of glucose and galactose into the cell can be coupled with passive diffusion of sodium ions. As the sodium diffuses across the cell membrane of enterocyte along the concentration gradient, glucose and galactose are also transported along with it.

Mode of transport is referred to as the ***secondary active transport***.

SUMMARY

Final product of digestion of starch (or its animal equivalent, glycogen) is glucose through a complex series of reactions. Initial digestion involves *amylase*, which occurs free in the lumen, whereas the final processes involve brush border enzymes, which are attached to the enterocyte mucosal membrane.

- **Absorption of monosaccharides resulting from digestion of dietary carbohydrates occurs via specific carrier mediated mechanisms, which demonstrate substrate specificity and stereospecificity**.

Proteins

Digestion of Dietary Proteins Begins in the Stomach

- Gastric secretion contains ***hydrochloric acid*** and ***pepsinogen***, a zymogen. Both play important role in protein digestion. The most potent stimuli for gastric secretion are dietary proteins: partially digested proteins and amino acids are more effective stimuli than the intact food proteins.
- These compounds first stimulate release of a hormone, **gastrin**
- Gastrin in turn stimulates the gastric parietal cells (to release hydrochloric acid) and the chief cells (to release pepsinogen). Pepsinogen, an inactive precursor form, is subsequently converted to *pepsin* which is primarily responsible for the digestive activity of gastric juice.

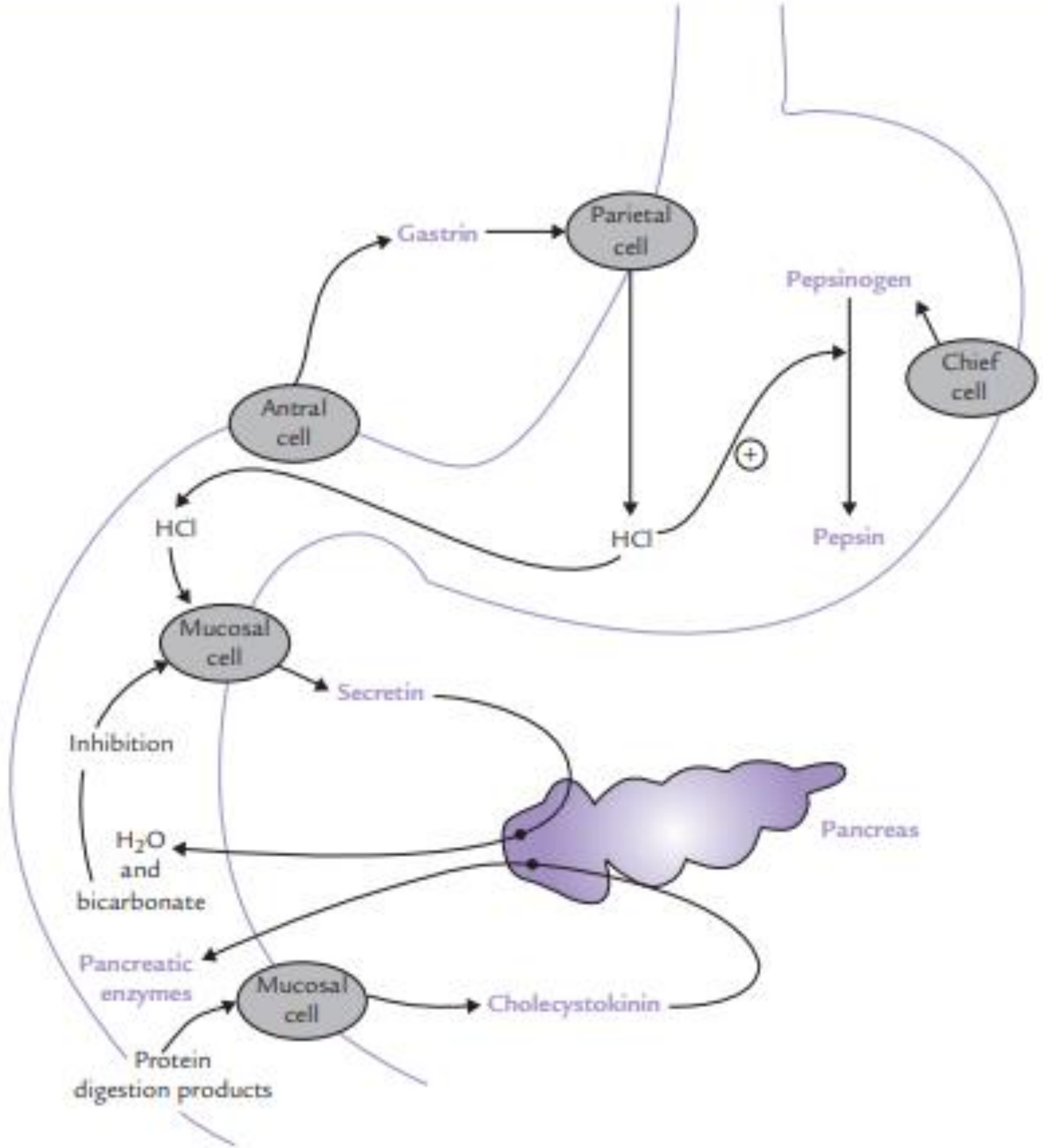


Fig. 26.1. Release and action of intestinal hormones.

Functions of Hydrochloric acid

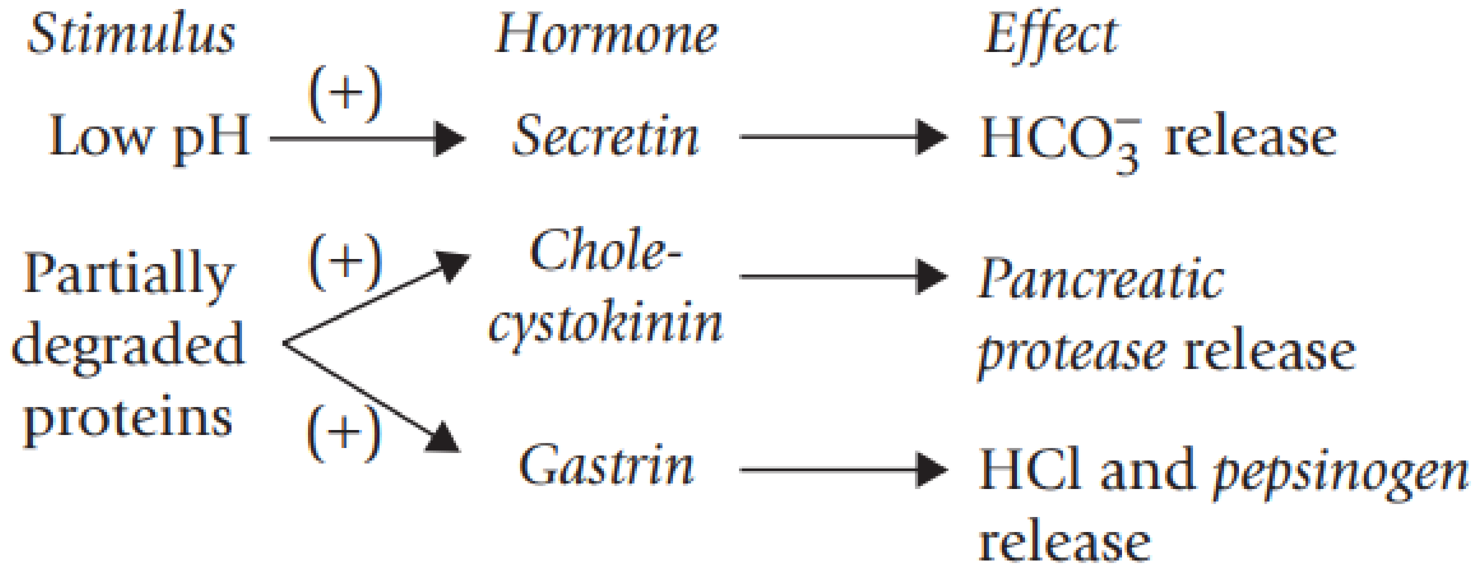
- Acts as an antiseptic and lowers the pH of the food mixture to about 1.5-2.5-pH range optimum for the action of *pepsin*.
- Hydrochloric acid brings about denaturation (unfolding) of the polypeptide chains, which exposes the peptide bonds for enzymatic action.
- Low pH (below 5) induces the conversion of *pepsinogen* to its activated form, *pepsin*, by removal of 42 amino acids from the N-terminal of the polypeptide chain.

- Further conversion proceeds autocatalytically, i.e. pepsin itself activates more of pepsinogen molecules

- *Pepsin* is an ***endopeptidase***-cleaves the peptide linkages lying towards the core of the polypeptide chain. Moreover, it is **site-specific** in action, cleaving only those peptide bonds whose carboxy terminal amino acid is an aromatic amino acid (phenylalanine, tyrosine, or tryptophan). Action yields partially disintegrated proteins.

Bulk of Protein Digestion Takes Place in Duodenum

- As the acidic gastric contents reach duodenum, their low pH acts as stimulus for duodenal mucosa, inducing it to release ***secretin*** (*Secretin was the first hormone ever to be identified*). Its predominant action is to stimulate release of water and bicarbonate ions from the exocrine pancreas. The bicarbonate ions elevate pH of the duodenal contents towards the neutral range, which is optimal for the action of *pancreatic enzymes*, including those of protein digestion. Enzymes are secreted in response to another hormone released from the duodenal mucosa, i.e. *cholecystokinin*, earlier known as *pancreozymin*. Release of this hormone is stimulated by the products of protein digestion.


Stimulus
Hormone
Effect
Low pH
(+)
Secretin
HCO_3^- release
Partially degraded proteins
(+)
Chole-cystokinin
Pancreatic protease release
(+)
Gastrin
HCl and pepsinogen release

- *The pancreatic proteases are released in the form of inactive precursors*, the form in which they are stored in the exocrine cells. Subsequently, the inactive precursors (**zymogens**) are activated in the intestinal lumen. *Arrangement acts as safeguard against autodigestion of pancreatic cells since the activated pancreatic enzymes that are capable of digesting the cellular components are generated away from the cell.*
- *Trypsinogen, chymotrypsinogen, procarboxypeptidase* and *proelastase*- some examples of inactive precursors of the pancreatic *proteases*. Trypsinogen is initially activated by a duodenal enzyme, *enterokinase* which is located in the brush border. Once trypsin has been generated in this way, it acts as a major stimulus for the activation of other zymogens: chymotrypsinogen, *procarboxypeptidase* and *proelastase*.

$$\textit{Trypsinogen} \xrightarrow{\textit{Entrokinase}} \textit{Trypsin}$$

$$\textit{chymotrypsinogen} \xrightarrow{\text{Trypsin}} \textit{Chymotrypsin}$$

$$\textit{Procarboxypeptidase} \xrightarrow{\text{Trypsin}} \textit{Carboxypeptidase}$$

$$\textit{Proelastase} \xrightarrow{\text{Trypsin}} \textit{Elastase}$$

Fig: Some inactive precursors of the pancreatic *proteases and how they are activated*.

- Like pepsin, the pancreatic *proteases-trypsin, chymotrypsin* and *elastase* are also **site-specific *endopeptidases***.
- *Trypsin* cleaves those peptide bonds the carboxy terminal of which is contributed by the basic amino acid (lysine and arginine).
- *Chymotrypsin* hydrolyzes the ones in which an aromatic amino acid forms the carboxy terminal.
- *Elastase* acts on the peptide linkages at carboxy terminal of small amino acids such as valine, leucine and alanine.

Enzyme	Source	Type	Catalytic mechanism
Pepsin	Stomach	*Endopeptidase*	*Carboxyl protease*
Trypsin	Pancreas	*Endopeptidase*	*Serine protease*
Chymotrypsin	Pancreas	*Endopeptidase*	*Serine protease*
Elastase	Pancreas	*Endopeptidase*	*Serine protease*
Carboxypeptidase A	Pancreas	*Exopeptidase*	*Metalloprotease* (Zn^{2+})
Carboxypeptidase B	Pancreas	*Exopeptidase*	*Metalloprotease* (*Zn21*)

Table: Enzymes of protein digestion

- *Carboxypeptidase* is referred to as an ***exopeptidase***-because *carboxypeptidases* (both A and B type) act only on the terminal peptide bond of the polypeptide chain: their action catalyzes successive removal of a single amino acid from the carboxy terminal of the polypeptide chain.
- Cleavage specificity of **type A** is hydrophobic amino acid at carboxy terminal, and that of **type B** is basic amino acid at carboxy terminal.

Final Stages of Digestion Occur in Small Intestine

- Various *peptidases* released in small intestine act at multiple sites. Greatly enhances the overall efficiency and speed of proteolysis.
- Concerted action cleaves the polypeptide chain into multiple oligopeptide fragments.

- Final stages of protein digestion-hydrolysis of these oligopeptides into constituent amino acids occurs.
- Enzymes operating at this stage are called *peptidases* (*dipeptidase* and *aminopeptidase*). Located in the brush border membrane. *Aminopeptidase* catalyzes removal of a single amino acid from the N-terminal end of the oligopeptide fragment.
- D*ipeptidase* cleaves dipeptides to yield two amino acids.

Absorption

- Amino acids produced by the action of these enzymes are actively absorbed, being coupled with passive diffusion of sodium (i.e. **secondary active transport**).
- At least six different carrier proteins for amino acid transport across the luminal mucosa.
- Dipeptides and tripeptides can also be absorbed, although at a much slower rate. About 5% of the ingested proteins remain unabsorbed and are excreted in faeces.

SUMMARY

- Combined effect of *pancreatic peptidases*, which have different substrate specificity with respect to peptide bond cleavage, is to produce abundance of free amino acids and oligopeptide fragments.
- Protein digestion is completed by *endopeptidases: dipeptidases* and *aminopeptidases*

Lipids

- An average diet provides 90-100 g lipids, **90%** of which are **triacylglycerols**. Dietary triacylglycerols are termed saturated or unsaturated fats depending on whether the glycerol backbone is esterified with the saturated fatty acids or the unsaturated fatty acids. The other dietary lipids are **phospholipids** and **cholesterol esters**. In addition to dietary lipids, the gastrointestinal system has to handle about 1 g of cholesterol and 5g of lecithin that enter intestine through bile each day.

- *Digestion of lipids is more complex than that of proteins or carbohydrates* because the hydrophobic nature of lipids limits the digestive process to the lipid-water interphase.
- This is in contrast with the proteins and the carbohydrates, which being hydrophilic are thoroughly exposed to action of hydrolytic enzymes. For instance, the enzymes catalyzing digestion of carbohydrates and proteins, such as *endosaccharidase* and *endopeptidases* are capable of hydrolyzing the internal bonds of these molecules, including those lying near the core.

- Digestion of lipids starts in the mouth by action of the enzyme ***lingual lipase***-secreted by the sublingual glands. As the food mixes with saliva, this enzyme begins hydrolytic removal of the fatty acids esterified to the C-1 and the C-3 of the triacylglycerol molecule. Result-dietary triacylglycerol is converted to the corresponding diacylglycerol and then to monoacylglycerol.

Hydrolytic process continues in the stomach also due to action of another lipolytic enzyme, the ***gastric lipase***.

- **The partially hydrolyzed food then enters the duodenum in the form of an unstable emulsion**.

Emulsification

Emulsion is stabilized and subsequently dispersed by the action of **bile-salts**, namely *sodium taurocholate* and *sodium glycocholate*-compounds synthesized from cholesterol in hepatocytes, and secreted into the duodenum through the hepatobiliary route. Bile-salts are major constituents of bile.

- Bile salts are amphipathic in nature, i.e. they have a polar portion (termed head) and a non-polar portion (called tail). The polar heads form a hydrophilic coating on surface of the lipid particles which face the aqueous exterior. The non-polar tails, on the other hand, extend into the interior of these particles. The above-stated action of the bile salts is supplemented by phospholipids and other emulsifiers already present in food. This results in *dispersion of the lipid particles into the finer emulsion droplets*. As a result, the surface area of the lipid: water interphase, on which the digestive enzymes can act, is increased several folds.

Enzymatic Hydrolysis

- P***ancreatic lipase*** is the principal enzyme of fat digestion, carrying out bulk of the digestion in the duodenum.
- Enzyme is secreted in an inactive precursor form, *prolipase*, along with its cofactor, called *colipase*. The latter is also initially secreted in a precursor form called *procolipase*.
- *The **colipase** positions itself on the surface of a fat particle and helps in anchoring the pancreatic lipase to the fat particle*

. The enzyme then carries out fat degradation: the triacylglycerol particles are hydrolyzed to fatty acids, diacylglycerol and monoacylglycerol.

- As in case of other pancreatic enzymes, the neutral pH required for the optimum activity of *lipase* is attained by action of bicarbonate ions.
- Hydrolysis of other dietary lipids, cholesterol esters and phospholipids also occurs in the duodenum

$$\text{Cholesterol esters} \xrightarrow{\textit{Esterase}} \text{Cholesterol} + \text{Fatty acid}$$

$$\text{Lecithin} \xrightarrow{\textit{Phospholipase}} \text{Lysolecithin} + \text{Fatty acid}$$

Fig: Hydrolysis of other dietary lipids

Micelle Formation

- Fatty acids and other simple molecules formed by enzymatic hydrolysis of the dietary lipids are aggregated with bile salts to form mixed micelles. In this type of micelle, aggregation of different types of molecules occurs.
- The polar heads of the bile salts from the hydrophilic exterior that faces the aqueous medium; non-polar tails of the bile salts form the hydrophobic core, in which fatty acids and monoacylglycerols are held. A single emulsion particle can from 106 micelles, each of about 20 nm diameter. Micelles can accommodate small quantities of cholesterol, carotene and other such non-polar substances as well.

Absorption

- Absorption of the products of lipid digestion occurs by *passive diffusion*, mainly in the proximal jejunum. The micellar complex gets destabilized when it faces the relatively acidic pH prevailing at the brush border of enterocytes.
- Liberation of the monoacylglycerols, fatty acids, cholesterol and other non-polar substances, held in the hydrophobic interior, occurs as a result of the destabilization.
- This is followed by passive diffusion of these substances across the luminal cell membrane. Some fatty acids such as oleic acid and linoleic acid cross the luminal cell membrane by *facilitated diffusion* to enter the enterocyte.
- Within the enterocyte, resynthesis of triacylglycerols and cholesterol esters occurs in endoplasmic reticulum.

- Lipids, together with small quantities of phospholipids and apolipoprotein B-48 are incorporated into **chylomicrons**.
- Chylomicrons cross the cell membrane (serosal aspect) of enterocytes and pass into the lymphatic vessels. The triacylglycerols having short chain fatty acids directly enter the portal circulation.
- Some short chain fatty acids of chain length of 6-10 carbon atoms do not even need esterification in the cells and can directly enter the portal circulation.

- Prevalence of non-communicable diseases has been on an upward trajectory for some time and this puts an enormous burden on the healthcare expenditure.
- Lifestyle modifications including dietary interventions hold an immense promise to manage and prevent these diseases.
- Recent advances in genomic research provide evidence that focussing these efforts on individual variations in abilities to metabolize nutrients (nutrigenetics) and exploring the role of dietary compounds on gene expression (nutrigenomics and nutri-epigenomics) can lead to more meaningful personalized dietary strategies to promote optimal health.
- Gene-diet interactions at multiple levels to support the need of embedding targeted dietary interventions as a way forward to prevent, avoid and manage diseases

- Diet along with physical activity plays a key role in the development of non-communicable chronic diseases that are responsible for > 70% of all deaths globally (World Health Organisation, 2018).
- Diet is also one of the key modifiable factors that can reduce the risk of developing these diseases

- There are multiple interactions between food and genes and this chapter explores some examples where there is a clear evidence.
- Gene-diet interactions are bi-directional and impact the health and disease status of the individual.

- Nutrigenetics: Explores the role of our genetic makeup on the metabolic response, nutritional status, ability to respond/not-respond to nutritional interventions.
- Nutrigenomics: Involves a broader approach to understand the way nutrition influences the genome in terms of its expression and more widely the metabolism.

- Major aim of these approaches is to decipher gene-diet interactions at the cellular and molecular level and develop nutritional interventions which are personalized to an individual's genome

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