Uttar Pradesh Rajarshi Tandon
Open University

UGBCH-102

Nutritional Biochemistry

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BLOCK

1

NUTRITION AND OXIDATION OF FOODSTUFF

UNIT-1

Elements of Nutrition

UNIT-2

Basal Metabolic Rate (BMR)

UNIT-3

Biological oxidation of foodstuff

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COURSE INTRODUCTION

This is the first block of nutritional biochemistry. This consists of three units.

Unit-1 : In the first unit elements of nutrition has been described as under. Dietary requirements of carbohydrates, lipids and proteins are discuss briefly. The role of essential amino acids and their adverse effect has mentioned here in this unit.

Unit-2 : Basal metabolic rate or BMR is the measurement of an organism's energy expenditure when at rest.BMR is the amount of energy it takes for your body to maintain life. The basic concept of BMR, resting metabolism, physical activity and energy balance are discussed in this unit.

Unit-3 : This unit covers the biological oxidation of foodstuff through the measurement of energy content of food. The physical energy value of food, and factors affecting thermogenesis is are discussed in this unit.

UNIT-1 ELEMENTS OF NUTRITION

Structure

1.1. INTRODUCTION

Nutrition is essential for growth and development, health and well being. Eating a healthy diet contributes to prevent of future illness and improving quality and length of life. Your nutritional status is the state of your health as determined by what you eat. There are several ways of

assessing nutritional status, including anthropometry (i.e. physical body measurement), food intake and biochemical measurement. Essential nutrients include protein, carbohydrate, fat, vitamins, minerals and electrolytes. Normally, 85% of daily energy use is from fat and carbohydrates and 15% from protein.

Basal metabolic rate (BMR) is the rate of energy expenditure per unit time by endothermic animals at rest. Metabolism comprises the processes that the body needs to function. Basal metabolic rate is the amount of energy per unit time that a person needs to keep the body functioning at rest. Lipids form one of the major bulk constituents in food and other biological systems. This group of organic biomolecules can be classified into three groups: simple lipids (triglycerides, steryl esters, and wax esters), compound lipids (phospholipids, glycolipids, sphingolipids, and lipoproteins), and derived lipids (fatty acids, fat-soluble vitamins and provitamins, sterols, terpenoids, and ethers). Lipids occur in animals and plants either as storage lipids, which are potential sources of energy by beta oxidation, or as membrane lipids. Storage lipids are triglycerides, whereas membrane lipids include phospholipids, sterols, sphingolipids, and glycolipids. Many foods of plant origin contain highly unsaturated lipids. Lipids of animal origin have lower levels of unsaturated lipids, but they contain certain amounts of the higher unsaturated fatty acids.

Objective

- An overview on nutrition, nutrients and its types.
- To know the functions of nutrients (micro and macronutrients).
- To explain vitamins and their types.
- To define carbohydrates and their types.
- Brief description of carbohydrates, lipids and proteins.

1.2. NUTRIENT OVERVIEW

A nutrient is a substance used by an organism to survive, grow, and reproduce. The requirement for dietary nutrient intake applies to animals, plants, fungi, and protists. Nutrients can be incorporated into cells for metabolic purposes or excreted by cells to create non-cellular structures, such as hairs, scales, feathers, or exoskeletons. Some nutrients can be metabolically converted to smaller molecules in the process of releasing energy, such as for carbohydrates, lipids, proteins, and fermentation products (ethanol or vinegar), leading to end-products of water and carbon dioxide. All organisms require water. Essential nutrients for animals are the energy sources e.g. some of the amino acids that are combined to create proteins, a subset of fatty acids, vitamins and certain minerals. Plants require more diverse minerals absorbed through roots, plus carbon dioxide and oxygen absorbed through leaves. Fungi live on dead or living organic matter and meet nutrient needs from their host.

Different types of organism have different essential nutrients. For example, Ascorbic acid (vitamin C) is essential, meaning it must be consumed in sufficient amounts of to humans and some other animal species, but not to all animals and not to plants, which are able to synthesize it. Nutrients may be organic or inorganic. Organic compounds include most compounds containing carbon, while all other chemicals are inorganic. Inorganic nutrients include nutrients such as iron, selenium, and zinc, while organic nutrients include, among many others, energy-providing compounds and vitamins.

Plants absorb carbon, hydrogen and oxygen from air of in the form of water and carbon dioxide. Other nutrients are absorbed from soil (exceptions include some parasitic or carnivorous plants). There are 17 important nutrients for plants. The macronutrients are nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), sulfur (S), magnesium (Mg), carbon (C), oxygen(O) and hydrogen (H), and the micronutrients are iron (Fe), boron (B), chlorine (Cl), manganese (Mn), zinc (Zn), copper (Cu), molybdenum (Mo) and nickel (Ni). In addition to carbon, hydrogen and oxygen, nitrogen, phosphorus, and sulfur are also needed in relatively large quantities. Together, the big six are the elemental macronutrients for all organisms. They are sourced from inorganic matter (for example, carbondioxide, water, nitrates, phosphates, sulfates, and diatomic molecules of nitrogen and, especially, oxygen) and organic matter (carbohydrates, lipids, proteins).

1.3. TYPES OF NUTRIENTS

1.3.1. MACRONUTRIENTS

Macronutrients are defined in several ways.

- The chemical elements humans consume in the largest quantities are carbon, hydrogen, nitrogen, oxygen, phosphorus, and sulphur, summarized as CHNOPS.
- The chemical compounds that humans consume in the largest quantities and provide bulk energy are classified as carbohydrates, proteins, and fats. Water must be also consumed in large quantities.
- Calcium, sodium, potassium, magnesium, and chloride ions, along with phosphorus and sulfur, are listed with macronutrients because they are required in large quantities compared to micronutrients, i.e., vitamins and other minerals, the latter often described as trace or ultratrace minerals.

Macronutrients provide energy:

- Carbohydrates are compounds made up of types of sugar. They are classified according to their number of sugar units i.e. saccharide like monosaccharides (such as glucose and fructose), disaccharides (suchas sucrose and lactose),

oligosaccharides,and polysaccharides (suchas raffinose starch, glycogen, and cellulose).

- Proteins are organic compounds that consist of amino acids joined by peptide bonds. Since the body cannot manufacture some of the amino acids (termed essential amino acids), the diet must supply them. Through digestion, proteins are broken down by proteases back into free amino acids.
- Fats consist of a glycerol molecule with three fatty acids attached. Fatty acid molecules contain a -COOH group attached to unbranched hydrocarbon chains connected by single bonds alone (saturated fatty acids) or by both double and single bonds (unsaturated fatty acids).
- Fats are needed for construction and maintenance of cell membranes, to maintain a stable body temperature, and to sustain the health of skin and hair. Because the body does not manufacture certain fatty acids (termed essential fatty acids), they must be obtained through one's diet.
- Fat has an energy content of 9 kcal/g (~37.7 kJ/g) and proteins and carbohydrates 4 kcal/g (~16.7 kJ/g).

1.3.2. MICRONUTRIENTS

Micronutrients include vitamins and minerals. Your body needs smaller amounts of micronutrients relative to macronutrients. That's why they're labeled "micro." Humans must obtain micronutrients from food since your body cannot produce vitamins and minerals- for the most part. That's why they're also referred to as essential nutrients. Vitamins are organic compounds made by plants and animals which can be broken down by heat, acid or air. On the other hand, minerals are inorganic, exist in soil or water and cannot be broken down. When you eat, you consume the vitamins that plants and animals created and the minerals that plants absorbed from soil or water.

The micronutrient content of each food is different, so it's best to eat a variety of foods to get enough vitamins and minerals. An adequate intake of all micronutrients is necessary for optimal health, as each vitamin and mineral has a specific role in your body. Vitamins and minerals are vital for growth, immune function, brain development and many other important functions. Depending on their function, certain micronutrients also play a role in preventing and fighting disease.

1.4. TYPES AND FUNCTIONS OF MICRONUTRIENTS

Vitamins and minerals can be divided into four categories: water-soluble vitamins, fat-soluble vitamins of macrominerals and trace

minerals. Vitamins and minerals are absorbed in similar ways in your body and interact in many processes. Micronutrients act as cofactors and/or coenzymes in the liberation of energy from food. A unlimited intake can disturb energy balance and can lead to numerous side effects. Some factors that have been associated with attaining a negative energy balance include:

- Regular nut consumption
- Meal replacement supplements/super shakes
- Green tea
- Low energy density foods (veggies, fruits, lean proteins, whole grains, etc.)
- Dietary protein
- Avoidance of refined carbohydrates
- Adequate hydration
- Dietary fiber
- Fruits
- Vegetables
- Regular exercise
- Adequate sleep
- Positive social support

1.4.1. WATER-SOLUBLE VITAMINS

Most vitamins dissolve in water and are therefore known as water-soluble. They're not easily stored in your body and get flushed out with urine when consumed in excess. While each water-soluble vitamin has a unique role, their functions are related. For example, most B vitamins act as coenzymes that help trigger important chemical reactions. A lot of these reactions are necessary for energy production. The water-soluble vitamins with some of their functions are:

- **Vitamin B1 (thiamine):** It helps to convert nutrients into energy.
- **Vitamin B2 (riboflavin): It is** necessary for energy production, cell function and fat **metabolism.**
- **Vitamin B3 (niacin):** Drives the production of energy from food.
- **Vitamin B5 (pantothenic acid):** It is necessary for fatty acid synthesis.

- **Vitamin B6 (pyridoxine):** It helps in release sugar from stored carbohydrates for energy and incretion red blood cells in the body.
- **Vitamin B7 (biotin):** It plays a role in the metabolism of fatty acids, amino acids and glucose.
- **Vitamin B9 (folate):** It is important for proper cell division.
- **Vitamin B12 (cobalamin):** It is necessary for red blood cell formation and proper nervous system and brain function.
- **Vitamin C (ascorbic acid):** It will be required for the creation of neurotransmitters and collagen, the main protein in your skin.

1.4.2. FAT-SOLUBLE VITAMINS

Fat-soluble vitamins do not dissolve in water. They're best absorbed when consumed alongside a source of fat. After consumption, fat-soluble vitamins are stored in your liver and fatty tissues for future use. The names and functions of fat-soluble vitamins are:

- **Vitamin A:** Necessary for proper vision and organ function.
- **Vitamin D:** Promotes proper immune function and assists in calcium absorption and bone growth.
- **Vitamin E:** Assists immune function and acts as an antioxidant that protects cells from damage.
- **Vitamin K:** Required for blood clotting and proper bone development.

CHECK YOUR PROGRESS

- ✓ What do you mean by elements of nutrition?
- ✓ Define macronutrients with examples.
- ✓ Define micronutrients with examples.
- ✓ Explain functions of micronutrients.
- ✓ Explain water soluble vitamins with examples.

1.5. MACROMINERALS

Macrominerals are needed in larger amounts than trace minerals in order to perform their specific roles in your body. The macrominerals and some of their functions are:

- **Calcium :** Necessary for proper structure and function of bones and teeth. Assists in muscle function and blood vessel contraction.
- **Phosphorus :** Part of bone and cell membrane structure.
- **Magnesium :** Assists with over 300 enzyme reactions, including regulation of blood pressure.
- **Sodium :** Electrolyte that aids fluid balance and maintenance of blood pressure.
- **Chloride :** Often found in combination with sodium. Helps maintain fluid balance and is used to make digestive juices.
- **Potassium :** Electrolyte that maintains fluid status in cells and helps with nerve transmission and muscle function.
- **Sulfur :** Part of every living tissue and contained in the amino acids methionine and cysteine.

Trace Minerals

Trace minerals are needed in smaller amounts than macrominerals but still enable important functions in your body. The trace minerals and some of their functions are:

- **Iron :** Helps provide oxygen to muscles and assists in the creation of certain hormones.
- **Manganese :** Assists in carbohydrate, amino acid and cholesterol metabolism.
- **Copper :** Required for connective tissue formation, as well as normal brain and nervous system function.
- **Zinc :** Necessary for normal growth, immune function and wound healing.
- **Iodine :** Assists in thyroid regulation.
- **Fluoride :** Necessary for the development of bones and teeth.
- **Cobalt :** Assist in manufacture of blood cells and nervous systems.
- **Selenium :** Important for thyroid health, reproduction and defense against oxidative damage.

1.6. DIETARY REQUIREMENTS OF CARBOHYDRATES

Carbohydrate is the only macronutrient with no established minimum requirement. Although many populations have thrived with carbohydrate as their main source of energy, others have done so with few if any carbohydrate containing foods throughout much of the year (eg.

traditional diets of the inuit, laplanders, and some native Americans). If carbohydrate is not necessary for survival, it raises questions about the amount and type of this macronutrient needed for optimal health, longevity, and sustainability.

Carbohydrates are found in a wide array of both healthy and unhealthy foods such as breads, beans, milk, popcorn, potatoes, cookies, spaghetti, soft drinks, corn, and cherry pie. They also come in a variety of forms. The most common and abundant forms are sugars, fibers, and starches. Foods rich high in carbohydrates are an important part of a healthy diet. Carbohydrates provide the body with glucose, which is converted to energy used to support bodily functions and physical activity. But carbohydrate quality is important; some types of carbohydrate-rich foods are better than others**.**

Carbohydrates are subdivided into several categories on the basis of the number of sugar units and how the sugar units are chemically bonded to each other. Categories include sugars, starches, and fibers. Sugars are intrinsic in fruits and milk products. Sugars also are added to foods during processing and preparation or at the table. These added sugars (or extrinsic sugars) sweeten the flavor of foods and beverages and improve their palatability. Sugars are also used in food preservation and for functional properties such as viscosity, texture, body, and browning capacity. They provide calories but insignificant amounts of vitamins, minerals, or other essential nutrients. The nutrition facts label provides information on total sugars per serving but does not currently distinguish between sugars naturally present in foods and added sugars.

1.6.1. TYPES OF CARBOHYDRATES

Carbohydrates are among the most abundant compounds on earth. They are normally classified broken down into five major classes of carbohydrates:

- Monosaccharides
- Disaccharides
- Oligosaccharides
- Polysaccharides
- Nucleotides

1.6.1.1. MONOSACCHARIDES

The word monosaccharide is derived from mono, meaning one, and saccharide, meaning sugar. The common monosaccharides are glucose, fructose, and galactose. Each simple sugar has a cyclic structure and is composed of carbon, hydrogen and oxygen in ratios of 1:2:1 respectively. Although each sugar mainly exists as a cyclic compound, it

is important to note that they are all in equilibrium to a small extent with their linear forms.

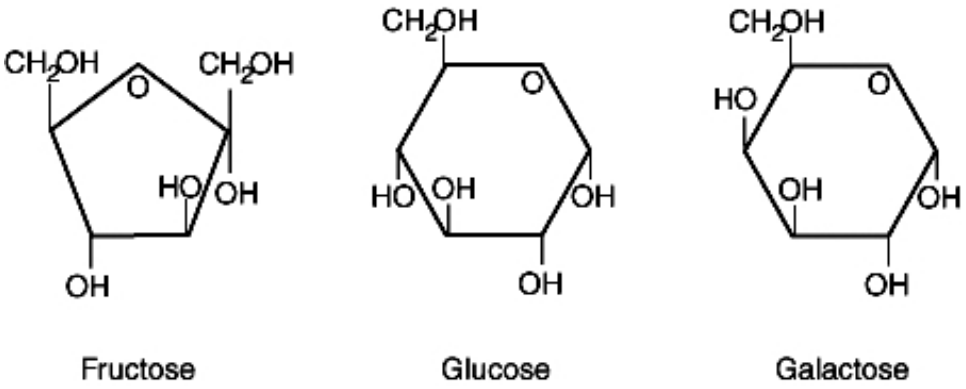

Fig. 1.1: Different types of monosaccharides

While galactose and glucose are composed of six-membered rings, fructose has five membered ring structures**.**

Glucose

Glucose is the main sugar metabolized by the body for energy. The D-isomer of glucose predominates in nature and it is for this reason that the enzymes in our body have adapted to binding this form only. Since it is an important energy source, the concentration of glucose in the bloodstream usually falls within a narrow range of 70 to 115mg/100 ml of blood. Sources of glucose include starch, the major storage form of carbohydrate in plants.

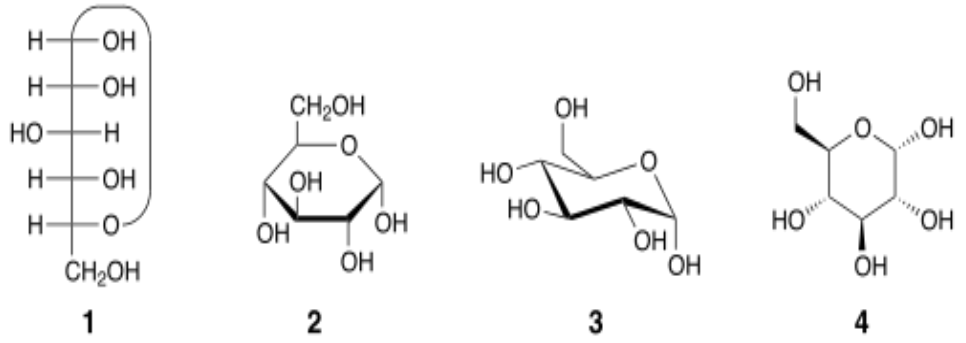

Fig. 1.2: Different structures of glucose

Galactose

Galactose is nearly identical to glucose in structure except in the position of one hydroxyl group on carbon atom number four of the six-sided sugar. Since it differs in only one position about all six asymmetric centers in the linear form of the sugar, galactose is known as an epimer of glucose. Galactose is not normally found in nature in large quantities; however it combines with glucose to form lactose in milk. After being

absorbed by the body, galactose is converted into glucose by the liver so that it can be used to provide energy for the body. Both galactose and glucose are very stable in solution because they are able to adopt chair and boat conformations.

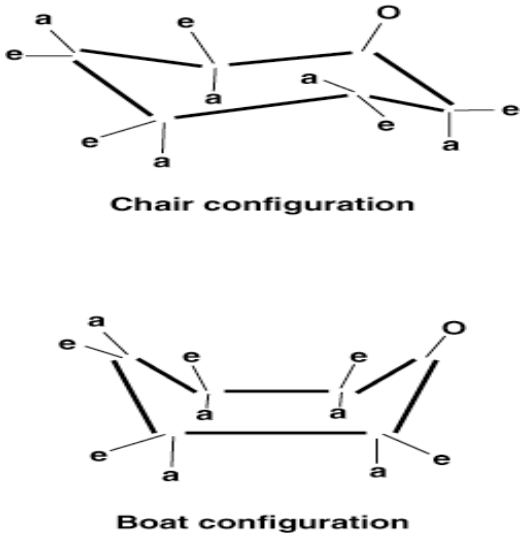

Fig. 1.3 : Chair and Boat Conformations of Galactose

These conformations are most stable because their OH groups are pointed away from the structure, preventing steric hindrance.

Fructose

Fructose is a structural isomer of glucose, meaning it has the same chemical formula but a completely different three-dimensional structure. The main difference is that fructose is a ketone in its linear form while glucose is an aldehyde. Through an intramolecular addition reaction with the C-5 OH group, glucose forms a six-membered ring while fructose forms a five-membered ring as seen in Figure 1. Upon consumption, fructose is absorbed and converted into glucose by the liver in the same manner as lactose. Sources of fructose include fruit, honey and high-fructose corn syrup that is why fructose is also known as fruit sugar.

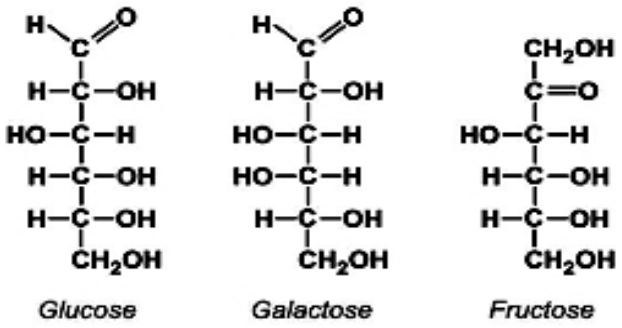

Fig. 1.4 : Structures of Glucose, Galactose and Fructose

1.6.1.2. DISACCHARIDES

Disaccharides, meaning two sugars, are commonly found in nature as sucrose, lactose and maltose. They are formed by a condensation reaction where one molecule of water condenses or is released during the joining of two monosaccharides. The type of bond that is formed between the two sugars is called a glycosidic bond.

1.7. LIPIDS

In biology and biochemistry, a lipid is a biomolecules that is solublein nonpolar solvents. Non-polar solvents are typically hydrocarbons used to dissolve other naturally occurring hydrocarbon lipid molecules that do not (or do not easily) dissolve in water, including fatty acids, waxes, sterols, fat-soluble vitamins (such as vitamins A, D, E, and K), monoglycerides, diglycerides, triglycerides, and phospholipids. The functions of lipids include storing energy, signaling, and acting as structural components of cell membranes. Lipids have applications in the cosmetic and food industries as well as in nanotechnology.

Scientists sometimes broadly define lipids as amphipathic or amphiphilic small molecules. The amphiphilic nature of some lipids allows them to form structures such as vesicles, multilamellar/unilamellar liposomes, or membranes in an aqueous environment. Biological lipids originate entirely or in part from two distinct types of biochemical subunits or building-blocks: ketoacyl and isoprene groups.

Using this approach, lipids may be divided into eight categories: fatty acids, glycerolipids, glycerophospholipids, sphingolipids, saccharolipids,a nd polyketides (derived from condensation of ketoacyl subunits); and sterol lipids and prenol lipids (derived from condensation of isoprene subunits). Although the term lipid is sometimes used as a synonym for fats, fats are a subgroup of lipids called triglycerides. Lipids also encompass molecules such as fatty acids and their derivatives (including tri-, di-, monoglycerides, and phospholipids), as well as other sterol-containing metabolites such as cholesterol. Although humans and other mammals use various biosynthetic pathways both to break down and to synthesize lipids, some essential lipids can't be made this way and must be obtained from the diet.

Fatty acids

Fatty acids, or fatty acid residues when they are part of a lipid, are a diverse group of molecules synthesized by chain-elongation of an acetyl-CoA primer with malonyl-CoA or methylmalonyl-CoA groups in a process called fatty acid synthesis. They are made of a hydrocarbon chain that terminates with a carboxylic acid group; this arrangement confers the molecule with a polar, hydrophilic end, and a

nonpolar, hydrophobic end that is insoluble in water. The fatty acid structure is one of the most fundamental categories of biological lipids, and is commonly used as a building-block of more structurally complex lipids.

The carbon chain, typically between four and 24 carbons long, may be saturated or unsaturated, and may be attached to functional groups containing oxygen, halogens, nitrogen, and sulfur. If a fatty acid contains a double bond, there is the possibility of either a cis or trans geometric isomerism, which significantly affects the molecule's configuration. Cis-double bonds cause the fatty acid chain to bend, an effect that is compounded with more double bonds in the chain. Three double bonds are present in 18-carbon linolenic acid.

Glycerolipids

Glycerolipids are composed of mono-, di-, and tri-substituted glycerols,[28] the best-known being the fatty acid triesters of glycerol, called triglycerides. The word "triacylglycerol" is sometimes used synonymously with "triglyceride". In these compounds, the three hydroxyl groups of glycerol are each esterified, typically by different fatty acids. Because they function as an energy store, these lipids comprise the bulk of storage fat in animal tissues. The hydrolysis of the ester bonds of triglycerides and the release of glycerol and fatty acids from adipose tissue are the initial steps in metabolizing fat. Additional subclasses of glycerolipids are represented by glycosylglycerols, which are characterized by the presence of one or more sugar residues attached to glycerol via a glycosidic linkage. Examples of structures in this category are the digalactosyl and diacylglycerols found in plant membrane and seminolipid from mammalian sperm cells.

Glycerophospholipids

Glycerophospholipids, usually referred to as phospholipids (though sphingomyelins are also classified as phospholipids), are ubiquitous in nature and are key components of the lipid bilayer of cells, as well as being involved in metabolism and cell signaling. Neural tissue (including the brain) contains relatively high amounts of glycerophospholipids, and alterations in their composition has been implicated in various neurological disorders. Glycerophospholipids may be subdivided into distinct classes, based on the nature of the polar head group at the sn-3 position of the glycerol backbone in eukaryotes and eubacteria, or the sn-1 position in the case of archaebacteria. Examples of glycerophospholipids found in biological membranes are phosphatidylchloric, phosphatidylethanolamine and phosphatidylserine.

Sphingolipids

Sphingolipids are a complicated family of compounds that share a common structural feature, a sphingoid base backbone that is synthesized *de novo* from the amino acid serine and a long-chain fatty acyl

CoA, then converted into ceramides, phosphosphingolipids, glycosphingolipids and other compounds. The major sphingoid base of mammals is commonly referred to as sphingosine. Ceramides (N-acyl-sphingoid bases) are a major subclass of sphingoid base derivatives with an amide-linked fatty acid. The fatty acids are typically saturated or mono-unsaturated with chain lengths from 16 to 26 carbon atoms. The major sphingolipids of mammals are sphingomyleins.

1.8. PROTEINS

Proteins are large biomolecules, or macromolecules, consisting of one or more long chains of amino acid residues. Proteins perform a vast array of functions within organisms, including catalysing metabolic reactions, DNA replication, responding to stimuli, providing structure to cells and organisms, and transporting molecules from one location to another. Proteins differ from one another primarily in their sequence of amino acids, which is dictated by the nucleotide sequence of their genes, and which usually results in protein folding into a specific three-dimensional structure that determines its activity.

They are biological polymers composed of amino acids. Amino acids, linked together by peptide bonds, form a polypeptide chain. One or more polypeptide chains twisted into a 3-D shape form a protein. Proteins have complex shapes that include various folds, loops, and curves. Folding in proteins happens spontaneously. Chemical bonding between portions of the polypeptide chain aid in holding the protein together and giving it its shape.

There are two general classes of protein molecules: globular proteins and fibrous proteins. Globular proteins are generally compact, soluble, and spherical in shape. Fibrous proteins are typically elongated and insoluble. Globular and fibrous proteins may exhibit one or more of four types of protein structure.

A linear chain of amino acid residues is called a polypeptide. A protein contains at least one long polypeptide. Short polypeptides of containing less than 20-30 residues, are rarely considered to be proteins and are commonly called peptides, or sometimes oligopeptides. The individual amino acid residues are bonded together by peptide bonds and adjacent amino acid residues. The sequence of amino acid residues in a protein is defined by the sequence of a gene, which is encoded in the genetic code.

In general, the genetic code specifies 20 standard amino acids; however, in certain organisms the genetic code can include selenocysteine and-in certain archaea-pyrrolysine. Shortly after or even during synthesis, the residues in a protein are often chemically modified by post-translational modification, which alters the physical and chemical properties, folding, stability, activity, and ultimately, the function of the proteins. Sometimes proteins have non-peptide groups

attached, which can be called prosthetic groups or cofactors. Proteins can also work together to achieve a particular function, and they often associate to form stable protein complexes.

Structure of Proteins

The four levels of protein structure are distinguished from one another by the degree of complexity in the polypeptide chain. A single protein molecule may contain one or more of the protein structure types: primary, secondary, tertiary, and quaternary structure.

1. Primary Structure

Primary Structure describes the unique order in which amino acids are linked together to form a protein. Proteins are constructed from a set of 20 amino acids. Generally, amino acids have the following structural properties.

- **A carbon (the alpha carbon) bonded to the four groups below:**
- **A hydrogen atom (H)**
- **A Carboxyl group (-COOH)**
- **An Amino group ($-NH_2$)**
- **A variable group or R group**

All amino acids have the alpha carbon bonded to a hydrogen atom, carboxyl group, and an amino group. The **R group** varies among amino acids and determines the differences between these protein monomers. The amino acid sequence of a protein is determined by the information found in the cellular genetic code. The order of amino acids in a polypeptide chain is unique and specific to a particular protein. Altering a single amino acid causes a gene mutation, which most often results in a non-functioning protein.

2. Secondary Structure

Secondary Structure refers to the coiling or folding of a polypeptide chain that gives the protein its 3-D shape. There are two types of secondary structures observed in proteins. One type is the **alpha (α) helix** structure. This structure resembles a coiled spring and is secured by hydrogen bonding in the polypeptide chain. The second type of secondary structure in proteins is the **beta (β) pleated sheet.** This structure appears to be folded or pleated and is held together by hydrogen bonding between polypeptide units of the folded chain that lie adjacent to one another.

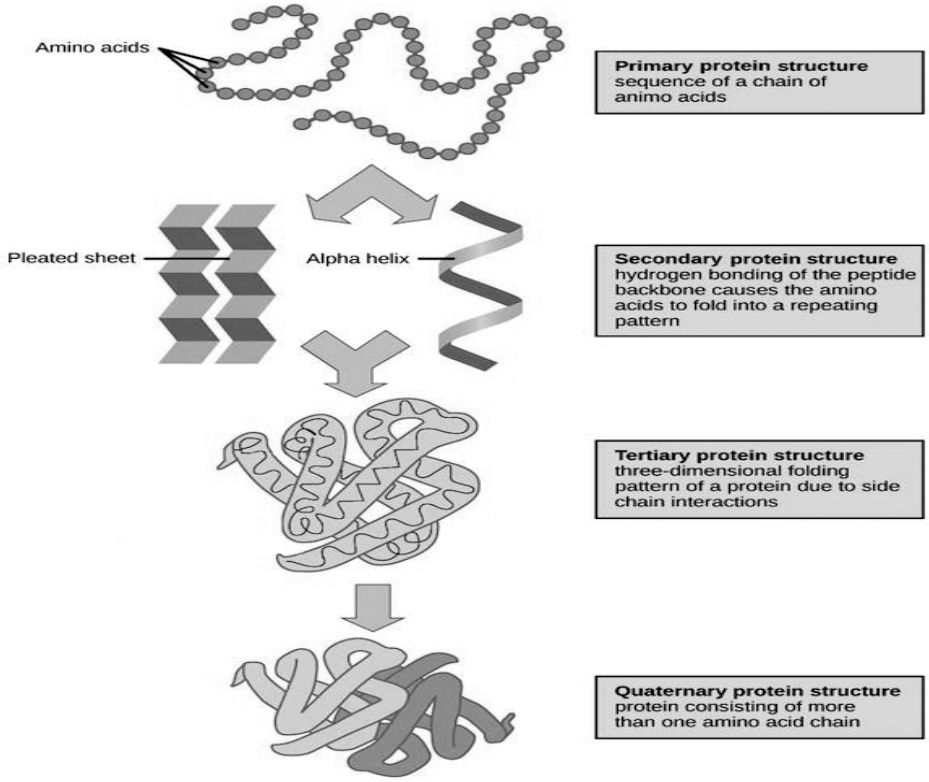

Fig.1.5 : Structure of proteins

3. Tertiary Structure

Tertiary Structure refers to the comprehensive 3-D structure of the polypeptide chain of a protein. There are several types of bonds and forces that hold a protein in its tertiary structure.

- **Hydrophobic interactions** greatly contribute to the folding and shaping of a protein. The R group of the amino acid is either hydrophobic or hydrophilic. The amino acids with hydrophilic "R" groups will seek contact with their aqueous environment, while amino acids with hydrophobic R groups will seek to avoid water and position themselves towards the center of the protein.
- **Hydrogen bonding** in the polypeptide chain and between amino acid R groups helps to stabilize protein structure by holding the protein in the shape established by the hydrophobic interactions.
- Due to protein folding, **ionic bonding** can occur between the positively and negatively charged "R" groups that come in close contact with one another.
- Folding can also result in covalent bonding between the R groups of cysteine amino acids. This type of bonding forms

of is called a **disulfide bridge.** Interactions called van der Waals forces also assist in the stabilization of protein structure. These interactions pertain to the attractive and repulsive forces that occur between molecules that become polarized. These forces contribute to the bonding that occurs between molecules.

4. **Quaternary Structure**

Quaternary Structure refers to the structure of a protein macromolecule formed by interactions between multiple polypeptide chains. Each polypeptide chain is referred to as a subunit. Proteins with quaternary structure may consist of more than one of the same type of protein subunit. They may also be composed of different subunits. Hemoglobin is an example of a protein with quaternary structure. Hemoglobin, found in the blood, is an iron-containing protein that binds oxygen molecules. It contains four subunits: two alpha subunits and two beta subunits.

Biochemistry of Proteins

Most proteins consist of linear polymers built from series of up to 20 different L-α- amino acids. All proteinogenic amino acids possess common structural features, including an α-carbon to which an amino group, a carboxyl group, and a variable side chain are bonded. Only proline differs from this basic structure as it contains an unusual ring to the N-end amine group, which forces the CO–NH amide moiety into a fixed conformation. The side chains of the standard amino acids. They have a great variety of chemical structures and properties. It is the combined effect of all of the amino acid side chains in a protein that ultimately determines its three-dimensional structure and its chemical reactivity.

The amino acids in a polypeptide chain are linked by peptide bonds. Once linked in the protein chain, an individual amino acid is called a residue, and the linked series of carbon, nitrogen, and oxygen atoms are known as the main chain or protein backbone. The peptide bond has two resonance forms that contribute some double-bond character and inhibit rotation around its axis, so that the alpha carbons are roughly coplanar.

The other two dihedral angles in the peptide bond determine the local shape assumed by the protein backbone. The end with a free amino group is known as the N-terminus or amino terminus, whereas the end of the protein with a free carboxyl group is known as the C-terminus or carboxy terminus (the sequence of the protein is written from N-terminus to C-terminus, from left to right).

The words protein, polypeptide, and peptide are a little ambiguous and can overlap in meaning. Protein is generally used to refer to the complete biological molecule in a stable conformation, whereas peptide is

generally reserved for short amino acid oligomers often lacking a stable three-dimensional structure. However, the boundary between the two is not well defined and usually lies near 20–30 residues. Polypeptide can refer to any single linear chain of amino acids, usually regardless of length, but often implies an absence of a defined conformation

Proteomics

The total complement of proteins present at a time in a cell or cell type is known as its proteome, and the study of such large-scale data sets defines the field of proteomics, named by analogy to the related field of genomics. Key experimental techniques in proteomics include 2D electrophoresis, which allows the separation of a; large number of proteins. Mass spectrometry, which allows rapid high-throughput identification of proteins and sequencing of peptides (most often after in-gel; digestion); protein microarrays, which allow the detection of the relative levels of a large number of proteins present in a cell, and two-hybrid screening, which allows the systematic exploration of protein-protein interactions. The total complement of biologically possible such interaction is known as the interactome. A systematic attempt to determine the structures of proteins representing every possible fold is known as structural proteomics.

Bioinformatics

Vast arrays of computational methods have been developed to analyze the structure, function, and evolution of proteins. The development of such tools has been driven by the large amount of genomic and proteomic data available for a variety of organisms, including the human genome. It is simply impossible to study all proteins experimentally, hence only a few are subjected to laboratory experiments while computational tools are used to extrapolate to similar proteins. Such homologous proteins can be efficiently identified in distantly related organisms by sequence alignment.

Genome and gene sequences can be searched by a variety of tools for certain properties. Sequence profiling tools can find restriction enzyme sites, open reading frames in nucleotide sequences, and predict secondary structures. Phylogenetic trees can be constructed and evolutionary hypotheses developed using special software like Clustal W regarding the ancestry of modern organisms and the genes they express. The field of bioinformatics is now indispensable for the analysis of genes and proteins.

1.9. AMINO ACIDS

Amino acids are organic compounds that contain amine (-NH_2) and carboxyl (-COOH) functional groups, along with a side chain (R group) specific to each amino acid. The key elements of an amino acid are carbon (C), hydrogen (H), oxygen (O), and nitrogen (N), although

other elements are found in the side chains of certain amino acids. About 500 naturally occurring amino acids are known (though only 20 appear in the genetic code) and can be classified in many ways.

They can be classified according to the core structural functional groups' locations as alpha (α-), beta (β-), gamma (γ-) or delta- (δ-) amino acids; other categories relate to polarity, pH level, and side chain group type (aliphatic, acyclic, aromatic, containing hydroxyl or sulfur, etc.). In the form of proteins, amino acid residues form the second-largest component (water is the largest) of human muscles and other tissues. Beyond their role as residues in proteins, amino acids participate in a number of processes such as neurotransmitter transport and biosynthesis.

In biochemistry, amino acids having both the amine and the carboxylic acid groups attached to the first (alpha-) carbon atom have particular importance. They are known as 2-, alpha-, or α-amino acids (generic formula $H_2NCHRCOOH$ in most cases, where R is an organic substituent known as a "side chain"); often the term "amino acid" is used to refer specifically to these. They include the 22 proteinogenic (protein-building) amino acids, which combine into peptide chains (polypeptides) to form the building-blocks of a vast array of proteins. These are all L-stereoisomers (left-handed isomers), although a few D-amino acids (right-handed) occur in bacterial envelopes, as a neuromodulator (D-serine), and in some antibiotics. An essential amino acid, or indispensable amino acid, is an amino acid that cannot be synthesized de novo (from scratch) by the organism at a rate commensurate with its demand, and thus must be supplied in its diet. Of the 21 amino acids common to all life forms, the nine amino acids humans can not synthesize are phenylalanine, valine, threonine, tryptophan, methionine, leucine, isole ucine, lysine and histidine.

Six other amino acids are considered conditionally essential in the human diet, meaning their synthesis can be limited under special pathophysiological conditions, such as prematurity in the infant or individuals in severe catabolic distress. These six are arginine, cysteine, glycine, glutamine, proline, and tyrosine. Six amino acids are non-essential (dispensable) in humans, meaning they can be synthesized in sufficient quantities in the body. These six are alanine, aspartic acid, asparagine, glutamic acid, serine, and selenocysteine (considered the 21st amino acid). Pyrrolysine (considered the 22nd amino acid) is not used by humans; thus, it is non-essential.

Various attempts have been made to express the "quality" or "value" of various kinds of protein. Measures include the biological value, net protein utilization, protein efficiency ratio, protein digestibility-corrected amino acid score and complete proteins concept. These concepts are important in the livestock industry, because the relative lack of one or

more of the essential amino acids in animal feeds would have a limiting effect on growth and thus on feed conversion ratio. Thus, various feedstuffs may be fed in combination to increase net protein utilization, or a supplement of an individual amino acid (methionine, lysine, threonine, or tryptophan) can be added to the feed.

Although plants tend to have less protein per weight than animal sources such as eggs or milk, they are nevertheless "complete" in that, as a whole, they contain all of the amino acids essential in human nutrition. The same is true for algae and marine phytoplankton. Eating various plant foods over an extended period of time can provide a protein of higher biological value. Certain native combinations of foods, such as corn and beans, soybeans and rice, or red beans and rice, contain the essential amino acids necessary for humans in adequate amounts.

However, the idea that plant-based foods must be combined to provide humans all of the essential amino acids is outdated. The official position of the academy of nutrition and dietetics is that protein from a variety of plant foods eaten during the course of a day supplies enough of all essential amino acids when caloric requirements are met.

1.10. ESSENTIALITY IN HUMANS

Table.1.1 : Essential and nonessential elements

Essential amino acids amino acids	Conditionally essential amino acids	Non-essential amino acids
Histidine (H)	Arginine (R)	Alanine (A)
Isoleucine (I)	Cysteine (C)	Aspartic acid (D)
Leucine (L)	Glutamine (Q)	Aspargine (N)
Lysine (K)	Glycine (G)	Glutamic acid (E)
Methionine (M)	Proline (P)	Serine (S)
Phenylalanine (F)	Tyrosine (Y)	Selenocysteine (U)
Threonine (T)		Pyrrolysine (O)
Tryptophan (W)		
Valine (V)		

Effects of deficiency

If one of the essential amino acids is less than needed for an individual the utilization of other amino acids will be hindered and thus protein synthesis will be less than adequate. Protein deficiency has been shown to affect all of the body's organs and many of its systems, including the brain and brain function of infants and young children; the immune system, thus elevating risk of infection; gut mucosal function and permeability, which affects absorption and vulnerability to systemic disease; and kidney function. The physical signs of protein deficiency include edema, failure to thrive in infants and children, poor musculature, dull skin, and thin and fragile hair. Biochemical changes reflecting protein deficiency include low serum albumin and low serum transferrin.

The amino acids that are essential in the human diet were established in a series of experiments led by William Cumming Rose. The experiments involved elemental diets to healthy male graduate students. These diets consisted of corn starch, sucrose, butterfat without protein, corn oil, inorganic salts, the known vitamins, a large brown candy made of liver extract flavored with peppermint oil (to supply any unknown vitamins), and mixtures of highly purified individual amino acids. The main outcome measure was nitrogen balance. Rose noted that the symptoms of nervousness, exhaustion, and dizziness were encountered to a greater or lesser extent whenever human subjects were deprived of an essential amino acid.

Essential amino acid deficiency should be distinguished from protein-energy malnutrition, which can manifest as marasmus or kwashiorkor. Kwashiorkor was once attributed to pure protein deficiency in individuals who were consuming enough calories (sugar baby syndrome). However, this theory has been challenged by the finding that there is no difference in the diets of children developing marasmus as opposed to kwashiorkor. Still, for instance in dietary reference intakes (DRI) maintained by the USDA, lack of one or more of the essential amino acids is described as protein-energy malnutrition.

1.10.1. MALNUTRITION

Malnutrition is a condition that results from eating a diet in which one or more nutrients are either not enough or are too much such that the diet causes health problems. It may involve calories, protein, carbohydrates, vitamins or minerals. Less enough nutrients is called undernutrition orundernourishment while too much is called over nutrition.

Malnutrition is often used to specifically refer to undernutrition where an individual is not getting enough calories, protein, or micronutrients. If undernutrition occurs during pregnancy, or before two years of age, it may result in permanent problems with physical and

mental development. Extreme undernourishment, known as starvation, may have symptoms that include: a short height, thin body, very poor energy levels, and swollen legs and abdomen. The symptoms of micronutrient deficiencies depend on the micronutrient that is lacking. Undernourishment is most often due to not enough high-quality food being available to eat. This is often related to high food prices and poverty. A lack of breastfeeding may contribute, as may a number of infectious diseases such as: gastroenteritis, pneumonia, malaria, and measles, which increase nutrient requirements.

There are two main types of undernutrition: protein-energy malnutrition and dietary deficiencies. Protein-energy malnutrition has two severe forms: marasmus (a lack of protein and calories) and kwashiorkor (a lack of just protein). Common micronutrient deficiencies include: a lack of iron, iodine, and vitamin A. During pregnancy, due to the body's increased need, deficiencies may become more common. In some developing countries, overnutrition in the form of obesity is beginning to present within the same communities as undernutrition. Other causes of malnutrition include anorexia nervosa and bariatric surgery

Undernutrition and over nutrition

Malnutrition is caused by eating a diet in which nutrients are not enough or is too much such that it causes health problems. It is a category of diseases that includes undernutrition and over nutrition. Over nutrition can result in obesity and being overweight. In some developing countries, over nutrition in the form of obesity is beginning to present within the same communities as undernutrition. However, the term malnutrition is commonly used to refer to undernutrition only. This applies particularly to the context of development cooperation. Therefore, malnutrition in documents by the World Health Organization, UNICEF, save the children or other international non-governmental organizations (NGOs) usually is equated to undernutrition.

Protein-energy malnutrition (PEM)

Undernutrition is sometimes used as a synonym of protein–energy malnutrition (PEM). While other include both micronutrient deficiencies and protein energy malnutrition in its definition. It differs from calorie restriction in that calorie restriction may not result in negative health effects. The term hypo alimentation means underfeeding. The term severe malnutrition or severe undernutrition is often used to refer specifically to PEM. PEM is often associated with micronutrient deficiency. Two forms of PEM are kwashiorkor and marasmus, and they commonly coexist.

Kwashiorkor

Kwashiorkor is mainly caused by inadequate protein intake.The main symptoms are edema, wasting, liver enlargement, hypoalbuminaemia, steatosis, and possibly depigmentation of skin and

hair. Kwashiorkor is further identified by swelling of the belly, which is deceiving of actual nutritional status. The term means 'displaced child' and is derived from a Ghana language of West Africa, means the sickness the older one gets when the next baby is born, as this is when the older child is deprived of breast feeding and weaned to a diet composed largely of carbohydrates.

Marasmus

Marasmus is caused by an inadequate intake of protein and energy. The main symptoms are severe muscular wasting, leaving little or no edema, loss of subcutaneous fat, of and non-normal serum albumin levels. Marasmus can result from a sustained diet of inadequate energy and protein, and the metabolism adapts to prolong survival. It is traditionally seen in famine, significant food restriction, or more severe cases of anorexia. Conditions are characterized by extreme wasting of the muscles and a gaunt expression.

Check your progress

- ✓ What do you mean by macro minerals?
- ✓ Define trace elements with examples.
- ✓ Define carbohydrates with examples.
- ✓ Write a short note on sphingolipids.
- ✓ Write a short note on fatty acids.

1.10.2. DIETARY PRACTICES

Undernutrition

A lack of adequate breastfeeding leads to malnutrition in infants and children, associated with the deaths of an estimated one million children annually. Illegal advertising of breast milk substitutes contributed to malnutrition and continued three decades after its 1981 prohibition under the WHO International Code of Marketing Breast Milk Substitutes. Maternal malnutrition can also factor into the poor health or death of a baby. Over 800,000 neonatal deaths have occurred because of deficient growth of the fetus in the mother's womb.

Deriving too much of one's diet from a single source, such as eating almost exclusively corn or rice, can cause malnutrition. This may either be from a lack of education about proper nutrition, or from only having access to a single food source. It is not just the total amount of calories that matters but specific nutritional deficiencies such as vitamin A

deficiency, iron deficiency or zinc deficiency can also increase risk of death.

Over nutrition

Over nutrition caused by overeating is also a form of malnutrition. In the United States, more than half of all adults are now overweight-a condition that, like hunger, increases susceptibility to disease and disability, reduces worker productivity, and lowers life expectancy. Overeating is much more common in the United States, where for the majority of people, access to food is not an issue. Many parts of the world have access to a surplus of non-nutritious food, in addition to increased sedentary lifestyles. Yale psychologist Kelly Brownell calls this a toxic food environment where fat and sugar laden foods have taken precedence over healthy nutritious foods.

The issue in these developed countries is choosing the right kind of food. More fast food is consumed per capita in the United States than in any other country. The reason for this mass consumption of fast food is its affordability and accessibility. Often fast food, low in cost and nutrition, is high in calories and heavily promoted. When these eating habits are combined with increasingly urbanized, automated, and more sedentary lifestyles, it becomes clear why weight gain is difficult to avoid.

Not only does obesity occur in developed countries, problems are also occurring in developing countries in areas where income is on the rise. Overeating is also a problem in countries where hunger and poverty persist. In China, consumption of high-fat foods has increased while consumption of rice and other goods has decreased. Overeating leads to many diseases, such as heart disease and diabetes, which may result in death.

Micronutrient-related malnutrition

Inadequacies in intake of vitamins and minerals often referred to as micronutrients, can also be grouped together. Micronutrients enable the body to produce enzymes, hormones, and other substances that are essential for proper growth and development.

Iodine, vitamin A, and iron are the most important in global public health terms; their deficiency represents a major threat to the health and development of populations worldwide, particularly children and pregnant women in low-income countries.

1.11. OVERWEIGHT AND OBESITY

Overweight and obesity, when a person is too heavy for his or her height is defined as an abnormal or excessive fat accumulation can impair health. Body mass index (BMI) is an index of weight-for-height commonly used to classify overweight and obesity. It is defined as a person's weight in kilograms divided by the square of his/her height in

meters (kg/m²). In adults, overweight is defined as a BMI of 25 or more, whereas obesity is a BMI of 30 or more. Overweight and obesity result from an imbalance between energy consumed (too much) and energy expended (too little). Globally, people are consuming foods and drinks that are more energy-dense (high in sugars and fats), and engaging in less physical activity.

Diet-related non-communicable diseases

Diet-related non-communicable diseases (NCDs) include cardiovascular diseases (such as heart attacks and stroke, and often linked with high blood pressure), certain cancers, and diabetes. Unhealthy diets and poor nutrition are among the top risk factors for these diseases globally.

Effect of Malnutrition

Malnutrition increases the risk of infection and infectious disease, and moderate malnutrition weakens every part of the immune system. For example, it is a major risk factor in the onset of active tuberculosis. Protein and energy malnutrition and deficiencies of specific micronutrients (including iron, zinc, and vitamins) increase susceptibility to infection. Malnutrition affects HIV transmission by increasing the risk of transmission from mother to child and also increasing replication of the virus. In communities or areas that lack access to safe drinking water, these additional health risks present a critical problem. Lower energy and impaired function of the brain also represent the downward spiral of malnutrition as victims are less able to perform the tasks they need to in order to acquire food, earn an income, or gain an education.

Poverty and food prices

In Bangladesh, poor socioeconomic position was associated with chronic malnutrition since it inhibits purchase of nutritious foods such as milk, meat, poultry, and fruits. As much as food shortages may be a contributing factor to malnutrition in countries with lack of technology. The FAO (Food and Agriculture Organization) has estimated that eighty percent of malnourished children living in the developing world live in countries that produce food surpluses. The economist Amartya Sen observed that, in recent decades, famine has always been a problem of food distribution and/or poverty, as there has been sufficient food to feed the whole population of the world. He states that malnutrition and famine were more related to problems of food distribution and purchasing power.

It is argued that commodity speculators are increasing the cost of food. As the real estate bubble in the United States was collapsing, it is said that trillions of dollars moved to invest in food and primary commodities, causing the 2007–2008 food price crisis. The use of biofuels as a replacement for traditional fuels raises the price of food.

1.12. SUMMARY

In this unit, we have learned……

The main classes of nutrients that the body needs of are carbohydrates, proteins, fats, vitamins, minerals, fibre and water. Nutrients can be grouped into six categories: carbohydrate, protein, lipid (fat), water, vitamins, and minerals. These six nutrients are further classified according to size and energy. Carbohydrate, protein, and fat are macronutrients because they make up the bulk of your diet. Carbohydrates are a type of macronutrient found in many foods and beverages. Most carbohydrates occur naturally in plant-based foods, such as grains. Food manufacturers also add carbohydrates to processed foods in the form of starch or added sugar. Common sources of naturally occurring carbohydrates include: fruits, vegetables, milk, nuts, grains, seeds and legumes etc. The key elements of an amino acid are carbon (C), hydrogen (H), oxygen (O), and nitrogen (N), although other elements are found in the side chains of certain amino acids. The fatty acid structure is one of the most fundamental categories of biological lipids, and is commonly used as a building-block of more structurally complex lipids. A lack of adequate breastfeeding leads to malnutrition in infants and children, associated with the deaths of an estimated one million children annually.

1.13. TERMINAL QUESTIONS

Q.1. Describe nutrition and types of nutrients with examples.

Answer:----------

Q.2. Define water soluble vitamins with examples.

Answer:----------

Q.3. Define fat soluble vitamins with examples.

Answer:----------

Q.4. Explain micronutrients and macronutrients with examples.

Answer:----------

Q.5. Write short notes on trace minerals and macro minerals.

Answer:----------

Q.6. Describe carbohydrates with their types.

Answer:----------

Q.7. Write short notes on lipids and fatty acids.

Answer:----------

1.14. FURTHER READINGS

1. Biochemistry- Lehninger A.L.
2. Biochemistry –J.H.Weil.
3. Biochemistry fourth edition-David Hames and Nigel Hooper.
4. Textbook of Biochemistry for Undergraduates - Rafi, M.D.
5. Biochemistry and molecular biology- Wilson Walker.

UNIT-2 BASAL METABOLIC RATE (BMR)

Structure

2.1 INTRODUCTION

The basal metabolic rate (BMR) is the amount of energy that is expended at rest in a neutral environment after the digestive system has been inactive for about 12 hours. It is the rate of one's metabolism when walking in the morning after fasting during sleep.

The BMR is the enough energy for the brain and central nervous system, heart, kidneys, liver, lungs, muscles, sex organs, and skin to function properly. People who are overweight or obese do not necessarily have a

slow BMR. In fact, their BMR is usually faster to accommodate for extra fat and for their body to work harder to perform normal body functions. Building lean muscle mass can increase BMR, but there is a limit for both men and women as to how much lean muscle mass can be built. Some supplements may increase BMR, but also only to a limit, and they may have serious side effects.

Expending extra calories through increased physical activity is the most sensible way to increase metabolism. When a person diets, BMR slows down to conserve energy and protect vital organs. A regimen of reasonable dieting with increased exercise maintains or increases BMR and promotes weight loss and weight maintenance. It all depends on calories and caloric balance.

The basal metabolic rate (BMR) is the rate of energy expenditure of a person at rest, to eliminate the variable effect of physical activity. The BMR accounts for approximately 60% of the daily energy expenditure. Thus, it includes energy used for normal body cellular homeostasis, cardiac function, brain and other nerve function, and so on.

Objectives

In this unit we will discuss about basal metabolic rate (BMR), its types, responsible factors, which affect it and energy balance etc. The main objectives are as given below.

- To understand the concept of respiration.
- To understand the concept of basal metabolic rate (BMR)
- To explain the process of metabolism and its types.
- Responsible factors which affect the metabolic process.
- To know energy balance and importance of energy.
- To know about negative and positive energy balance.

2.2. RESPIRATION

It is the process by which the respiratory substrate is broken down to release energy. The two main operating factors of cell respiration are aerobic and anaerobic respiration, where aerobic respiration requires the presence of oxygen and anaerobic respiration does not. The most common respiratory substrate is glucose, which has a six carbon compound. The substrate is metabolized through glycolysis, TCA cycle, electron transport chain, and oxidative phosphorylation. Through these cycles, cells are able to produce and store ATP, and carbon dioxide is produced as a by-product. It is important to understand the levels of carbon dioxide produced from different substrates because toxic levels can be destructive to the body. Healthcare professionals can recommend that a patient alter his or her diet,

particularly for those with pulmonary and liver conditions, to increase the release of CO_2 and avoid respiratory fatigue and utilize it as a prognostic factor, respectively.

Definition of basal metabolic rate

Basal metabolic rate is the energy released when the subject is at complete mental and physical rest i.e. in a room with comfortable temperature and humidity, awake and sitting in a reclining position, 10-12 hours after the last meal. It is essentially the minimum energy required to maintain the heart rate, respiration, kidney function etc.

The B.M.R. of an average Indian man is 1750-1900 Kcal/day. In terms of oxygen consumption it would amount to about 15 litre/hr. Heavily built persons have higher BMRs, but the BMR per unit body weight is higher in the smaller built individuals. For example although the BMR of a man as given above is higher than that of a boy of 15 kg body weight that spends about 800 Kcal/day for its basal metabolism, the BMR per kg/day of man is about 30 Kcal, while that of the boy is about 53 Kcal/kg/day. The variable that correlates most with the BMR is the surface area of the body. Thus in case of both boy and man the BMR is around 1000 Kcal/m^2 body surface/day.

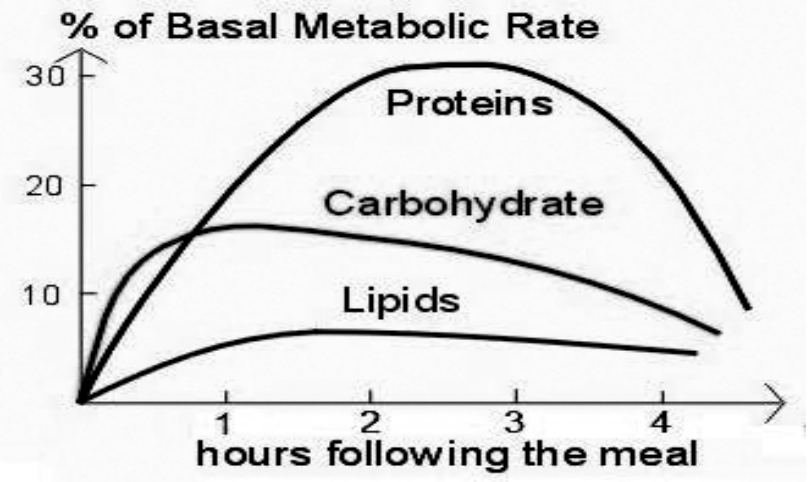

Fig.2.1 : Basal metabolic rate

2.3. CONCEPT OF BASAL METABOLIC RATE (BMR)

It is the rate of energy expenditure per unit time by endothermic animals at rest. It is reported in energy units per unit time ranging from watt (joule/second) to ml O_2/min or joule per hour per kg body mass J/(h·kg). Proper measurement requires a strict set of criteria be met. These criteria include being in a physically and psychologically undisturbed state, in a thermally neutral environment, while in the post-absorptive state (i.e., not actively digesting food). In brady metabolic animals, such

as fish and reptiles, the equivalent term standard metabolic rate (SMR) is used. It follows the same criteria as BMR, but requires the documentation of the temperature at which the metabolic rate was measured. This makes BMR a variant of standard metabolic rate measurement that excludes the temperature data, a practice that has led to problems in defining "standard" rates of metabolism for many mammals.

Metabolism comprises the processes that the body needs to function. Basal metabolic rate is the amount of energy per unit time that a person needs to keep the body functioning at rest. Some of those processes are breathing, blood circulation, controlling body temperature, cell growth, brain and nerve function, and contraction of muscles. Basal metabolic rate (BMR) affects the rate that a person burns calories and ultimately whether that individual maintains, gains, or loses weight. The basal metabolic rate accounts for about 60 to 75% of the daily calorie expenditure by individuals. It is influenced by several factors. BMR typically declines by 1-2% per decade after age 20, mostly due to loss of fat-free mass, although the variability between individuals is high.

The body's generation of heat is known as thermogenesis and it can be measured to determine the amount of energy expended. BMR generally decreases with age, and with the decrease in lean body mass (as may happen with aging). Increasing muscle mass has the effect of increasing BMR. Aerobic (resistance) fitness level, a product of cardiovascular exercise, while previously thought to have effect on BMR, has been shown in the 1990s not to correlate with BMR when adjusted for fat-free body mass. But anaerobic exercise does increase resting energy consumption (aerobic vs. anaerobic exercise). Illness, previously consumed food and beverages, environmental temperature, and stress levels can affect one's overall energy expenditure as well as one's BMR.

BMR is measured under very restrictive circumstances when a person is awake. An accurate BMR measurement requires that the person's sympathetic nervous system not be stimulated, a condition which requires complete rest. A more common measurement, which uses less strict criteria, is resting metabolic rate (RMR). BMR may be measured by gas analysis through either direct or indirect calorimetry, though a rough estimation can be acquired through an equation using age, sex, height, and weight. Studies of energy metabolism using both methods provide convincing evidence for the validity of the respiratory quotient (RQ), which measures the inherent composition and utilization of carbohydrates, fats and proteins as they are converted to energy substrate units that can be used by the body as energy.

2.3.1. GLUCOSE

Because the ratio of hydrogen to oxygen atoms in all carbohydrates is always the same as that in water-that is, 2 to 1- all of the oxygen consumed by the cells is used to oxidize the carbon in the carbohydrate molecule to form carbon dioxide. Consequently, during the

complete oxidation of a glucose molecule, six molecules of carbon dioxide and six molecules of water are produced and six molecules of oxygen are consumed. The overall equation for this reaction is:

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

(38 ATP molecules)

Because the gas exchange in this reaction is equal, the respiratory quotient (R.Q.) for carbohydrate is unity or 1.0:

$$R.Q. = 6\ CO_2 / 6\ O_2 = 1.0$$

2.3.2. FATS

The chemical composition for fats differs from that of carbohydrates in that fats contain considerably fewer oxygen atoms in proportion to atoms of carbon and hydrogen. When listed on nutritional information tables, fats are generally divided into six categories: total fats, saturated fatty acid, polyunsaturated fatty acid, monounsaturated fatty acid, dietary cholesterol, and trans fatty acid. From a basal metabolic or resting metabolic perspective, more energy is needed to burn a saturated fatty acid than an unsaturated fatty acid.

The fatty acid molecule is broken down and categorized based on the number of carbon atoms in its molecular structure. The chemical equation for metabolism of the twelve to sixteen carbon atoms in a saturated fatty acid molecule shows the difference between metabolism of carbohydrates and fatty acids. Palmitic acid is a commonly studied example of the saturated fatty acid molecule. The overall equation for the substrate utilization of palmitic acid is:

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

Thus the R.Q. for palmitic acid is 0.696:

$$R.Q. = 16\ CO_2 / 23\ O_2 = 0.696$$

2.3.3. PROTEINS

Proteins are composed of carbon, hydrogen, oxygen, and nitrogen arranged in a variety of ways to form a large combination of amino acids. Unlike fat the body has no storage deposits of protein. All of it is contained in the body as important parts of tissues, blood hormones, and enzymes. The structural components of the body that contain these amino acids are continually undergoing a process of breakdown and replacement. The respiratory quotient for protein metabolism can be demonstrated by the chemical equation for oxidation of albumin:

$$C_{72}H_{112}N_{18}O_{22}S + 77\ O_2 \rightarrow 63\ CO_2 + 38\ H_2O + SO_3 + 9\ CO(NH_2)_2$$

The R.Q. for albumin is $63\ CO_2 / 77\ O_2 = 0.818$

The reason this is important in the process of understanding protein metabolism is that the body can blend the three macronutrients and based on the mitochondrial density, a preferred ratio can be established which determines how much fuel is utilized in which packets for work accomplished by the muscles. Protein catabolism (breakdown) has been estimated to supply 10% to 15% of the total energy requirement during a two-hour aerobic training session. This process could severely degrade the protein structures needed to maintain survival such as contractile properties of proteins in the heart, cellular mitochondria, myoglobin storage, and metabolic enzymes within muscles.

The oxidative system (aerobic) is the primary source of ATP supplied to the body at rest and during low intensity activities and uses primarily carbohydrates and fats as substrates. Protein is not normally metabolized significantly, except during long term starvation and long bouts of exercise (greater than 90 minutes.) At rest approximately 70% of the ATP produced is derived from fats and 30% from carbohydrates. Following the onset of activity, as the intensity of the exercise increases, there is a shift in substrate preference from fats to carbohydrates. During high intensity aerobic exercise, almost 100% of the energy is derived from carbohydrates, if an adequate supply is available.

2.3.4. AEROBIC VS. ANAEROBIC EXERCISE

Studies published in 1992 and 1997 indicate that the level of aerobic fitness of an individual does not have any correlation with the level of resting metabolism. Both studies find that aerobic fitness levels do not improve the predictive power of fat free mass for resting metabolic rate. When you consider time commitments against health benefits, AT (aerobic training)is the optimal mode of exercise for reducing fat mass and body mass as a primary consideration. RT (resistance training) is good as a secondary factor when aging and lean mass are a concern. RT causes injuries at a much higher rate than AT. Compared to RT, it was found that AT of resulted in a significantly more pronounced reduction of body weight by enhancing the cardiovascular system which is what is the principle factor in metabolic utilization of fat substrates. RT if time is available is also helpful in post exercise metabolism, but it is an adjunctive factor because the body needs to heal sufficiently between RT episodes, whereas with AT, the body can accept this every day. RMR, and BMR are measurements of daily consumption of calories. The majorities of studies that are published on this topic look at aerobic exercise because of its efficacy for health and weight management.

	Anaerobic	Aerobic
Reactants	Glucose	Glucose **and** oxygen
Combustion	Incomplete	Complete
Energy Yield	Low (2 ATP)	High (36 – 38 ATP)
Products	**Animals:** Lactic acid **Yeast:** Ethanol + CO_2	CO_2 and H_2O
Location	Cytoplasm	Cytoplasm **and** mitochondrion
Stages	Glycolysis Fermentation	Glycolysis Link reaction Krebs cycle Electron transport chain

Fig. 2.2 : Aerobic and anaerobic respiration

Anaerobic exercise, such as weight lifting, builds additional muscle mass. Muscle contributes to the fat-free mass of an individual and therefore effective results from anaerobic exercise will increase BMR. However, the actual effect on BMR is controversial and difficult to enumerate. Various studies suggest that the resting metabolic rate of trained muscle is around 55kJ per kilogram, per day. Even a substantial increase in muscle mass, say 5 kg, would make only a minor impact on BMR.

2.3.5. FACTORS INFLUENCING BMR

There are many factors that affect the BMR. These include body temperature, age, sex, race, emotional state, climate and circulating levels of hormones like catecholamine's (epinephrine and norepinephrine) and those secreted by the thyroid gland.

1. **Genetics (Race)**

   Some people are born with faster metabolism and some with slower metabolism. Indians and Chinese seem to have a lower BMR than the Europeans. This may as well be due to dietary differences between these races. Higher BMR exists in individuals living in tropical climates. Eg. Singapore.

2. **Gender**

   Men have a greater muscle mass and a lower body fat percentage. Thus men have a higher basal metabolic rate than women. The BMR of females declines more rapidly between the ages of 5 and 17 than that of males.

3. Age

BMR reduces with age i.e. it is inversely proportional to age. Children have higher BMR than adults. After 20 years, it drops about 2 per cent, per decade.

4. Weight

The heavier the weight, the higher the BMR, ex. the metabolic rate of obese women is 25 percent higher than that of thin women.

5. Body surface area

This is a reflection of the height and weight. The greater the body surface area factor, the higher the BMR. Tall, thin people have higher BMRs. When a tall person is compared with a short person of equal weight, then if they both follow a diet calorie-controlled to maintain the weight of the taller person, the shorter person may gain up to 15 pounds in a year.

6. Body fat percentage

The lower the body fat percentage, the higher the BMR. The lower body fat percentage in the male body is one reason why men generally have a 10-15% higher BMR than women.

7. Diet

Starvation or serious abrupt calorie-reduction can dramatically reduce BMR by up to 30%. Restrictive low-calorie weight loss diets may cause BMR to drop as much as 20%. BMR of strict vegetarians is 11% lower than that of meat eaters.

8. Body temperature/health

For every increase of 0.5° C in internal temperature of the body, the BMR increases by about 7 percent. The chemical reactions in the body actually occur more quickly at higher temperatures. So a patient with a fever of 42° C (about 4° C above normal) would have an increase of about 50 percent in BMR. An increase in body temperature as a result of fever increases the BMR by 14-15% per degree centigrade which evidently, is due to the increased rate of metabolic reactions of the body.

9. External temperature :

Temperature outside the body also affects basal metabolic rate. Exposure to cold temperature causes an increase in the BMR, so as to create the extra heat needed to maintain the body's internal temperature. A short exposure to hot temperature has little effect on the body's metabolism as it is compensated mainly by increased heat loss. But prolonged exposure to heat can raise BMR.

10. Glands :

Thyroxine is a key BMR-regulator which speeds up the metabolic activity of the body. The more thyroxine produced, the higher the BMR. If too much thyroxine is produced (thyrotoxicosis) BMR can actually double. If too little thyroxine is produced (myxoedema) BMR may shrink to 30-40 percent of normal rate. Like thyroxine, adrenaline also increases the BMR but to a lesser extent. Anxiety and tension may not show on the face but they do produce an increased tensing of the muscles and release of norepinephrine even though the subject is seemingly quiet. Both these factors tend to increase the metabolic rate.

2.4. MEASUREMENT OF FUEL VALUE OF FOODS

The foodstuffs (carbohydrates, fats and proteins) on combustion by oxygen produce heat. This amount of heat can be measured in a bomb calorimeter. Carbohydrate and fat are completely oxidized in the body to CO_2 and water like that of bomb calorimeter. But proteins are not completely burned because urea, the end product of protein metabolism, still contains some energy which is not available to the body. Therefore, the energy value of protein in the body (4.1 kcal/gm.) is less than that obtained in the bomb calorimeter. The energy value of foods in the body is customary to express in round figures. The table below shows the energy value of foodstuffs.

2.5. THE ENERGY REQUIREMENT OF MAN

The energy requirement of man can be determined either directly by measuring his output in a calorimeter or indirectly by measuring his oxygen consumption.

Respiratory Quotients (RQ) of foodstuffs :

The respiratory quotient (RQ)

It is a dimensionless number used in calculations of basal metabolic rate (BMR) when estimated from carbon dioxide production. It is calculated from the ratio of carbon dioxide produced by the body to oxygen consumed by the body. Such measurements, like measurements of oxygen uptake, are forms of indirect calorimetry. It is measured using a respirometer. The Respiratory Quotient value indicates which macronutrients are being metabolized, as different energy pathways are used for fats, carbohydrates, and proteins. If metabolism consists solely of lipids, the Respiratory Quotient is 0.7, for proteins it is 0.8, and for carbohydrates it is 1.0. Most of the time, however, energy consumption is composed of both fats and carbohydrates. The approximate respiratory quotient of a mixed diet is 0.8. Some of the other factors that may affect the respiratory quotient are energy balance, circulating insulin, and insulin

sensitivity. It is the ratio of the volume of CO_2 eliminated to the volume of oxygen utilized in the oxidation.

The respiratory quotient (**RQ**) is the ratio:

$RQ = CO_{2\ \text{eliminated}} / O_{2\ \text{consumed}}$

Where the term eliminated refers to carbon dioxide (CO_2) removed from the body. In this calculation, the CO_2 and O_2 must be given in the same units, and in quantities proportional to the number of molecules. Acceptable inputs would be either moles, or else volumes of gas at standard temperature and pressure.

Many metabolized substances are compounds containing only the elements carbon, hydrogen, and oxygen. Examples include fatty acids, glycerol, carbohydrates, deamination products, and ethanol. For complete oxidation of such compounds, the chemical equation is

$$C_xH_yO_z + (x + y/4 - z/2)\ O_2 \rightarrow x\ CO_2 + (y/2)\ H_2O$$

And thus metabolism of this compound gives an RQ of $x/(x + y/4 - z/2)$.

For glucose, with the molecular formula, $C_6H_{12}O_6$, the complete oxidation equation is

$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$. Thus, the $RQ = 6\ CO_2 / 6\ O_2 = 1$.

Proteins

Since the chemical structure of proteins is variable their oxidation cannot be so readily expressed. The R.Q. of proteins by indirect method has been calculated to be about 0.8.

Mixed Diets

The R.Q. of mixed diets is about 0.85. The R.Q. is lowered if the carbohydrate metabolism is impaired.

Significance of R.Q.

- R.Q. helps in the determination of metabolic rate.
- It is the guide for assessing the type of food burning or the nature of synthesis taking place in the whole body or in any particular organ.
- The determination of R.Q. aids in the diagnosis of acidosis, alkalosis and diabetes mellitus, etc.
- Non-protein R.Q. is used for calculating the total energy output and the proportions of various foodstuffs being burnt.

2.6. BASAL AND RESTING METABOLISM

Metabolism comprises everything that goes on inside your body to maintain and build tissues, produce energy and ensure you stay healthy. Basal metabolism only refers to the basic, or least, amount of energy your body needs to survive when you're resting. It does not include additional energy required to support even a small amount of activity once you're awake and on-the-go. This energy is used to support life-sustaining jobs, from breathing and pumping blood to maintaining body temperature. Your body also needs constant energy to make sure you have the right amount of fluids and essential substances for metabolism. For example, your nerves and muscles can't work without a specific concentration of potassium and sodium.

CHECK YOUR PROGRESS

- ✓ What do you mean by basal metabolic rate (BMR)?
- ✓ Define respiration and its types.
- ✓ Define carbohydrates with examples.
- ✓ Write a short note on respiratory quotient (R.Q).
- ✓ Write a significance of R.Q.

2.6.1. FACTORS AFFECTING BASAL METABOLISM

Several factors influence your basal metabolism. Some people have a higher metabolic rate thanks to their genes. Muscles burn three times more calories than fat even when you're sleeping, so the proportion of muscle to fat changes your metabolic rate. Age makes a difference because the body loses muscle mass with aging, which slows down metabolism. When you don't consume enough calories to support your minimum energy needs, your metabolism slows down by up to 30 percent. A fever increases the body's metabolic rate by 7 percent for every 0.5 degree Centigrade over normal body temperature. When the thyroid gland doesn't produce the right amount of hormones, metabolic rate may drop by 30 to 40 percent.

2.6.2. RESTING METABOLIC RATE (RMR)

It is whole-body mammal (and other vertebrate) metabolism during a time period of strict and steady resting conditions that are defined by a combination of assumptions of physiological homeostasis and biological equilibrium. RMR differs from basal metabolic rate (BMR) because BMR measurements must meet total physiological equilibrium whereas RMR

conditions of measurement can be altered and defined by the contextual limitations. Therefore, BMR is measured in the elusive perfect steady state, whereas RMR measurement is more accessible and thus, represents most, if not all measurements or estimates of daily energy expenditure. Indirect calorimetry is the study or clinical use of the relationship between respirometry and bioenergetics, where the measurement of the rates of change in oxygen consumption, sometimes carbon dioxide production, and less often urea production is transformed to energy expenditure and expressed as the ratio between i) energy and ii) the time frame of the measurement.

2.6.3. ENERGY BALANCE

Energy balance is when the energy we get from food and drinks equals the energy our bodies use. Energy is a vital element in the body for growth, development, normal functioning of body processes. A requirement of energy varies from person to person and the amount of energy intake and expenditure depends on that person's diet and lifestyle. It is the relationship between energy in (food calories taken into the body through food and drink) and energy out (calories being used in the body for our daily energy requirements).

This relationship, which is defined by the laws of thermodynamics, dictates whether weight is lost, gained, or remains the same. According to these laws, energy is never really created and it's never really destroyed. Rather, energy is transferred between entities. We convert potential energy that's stored within our food (measured in Calories or Kcals) into three major destinations; work, heat and storage. As the image below shows, the average number of available calories per person in the US is increasing.

In general, there is more energy in. When it comes to energy out the body's energy needs include the amount of energy required for maintenance at rest, physical activity and movement, and for food digestion, absorption, and transport. We can estimate our energy needs by measuring the amount of oxygen we consume. We eat, we digest, we absorb, we circulate, we store, we transfer energy, we burn the energy, and then we repeat.

2.6.4. IMPORTANCE OF ENERGY

Energy balance also has to do with what's going on in your cells. When you are in a positive energy balance (more in than out) and when you're in a negative energy balance (more out than in), everything from your metabolism, to your hormonal balance, to your mood is impacted. There are two types of energy balance.

- **Negative energy balance**
- **Positive energy balance**

2.6.5. NEGATIVE ENERGY BALANCE

A severe negative energy balance can lead to a decline in metabolism, decreases in bone mass, reductions in thyroid hormones, reductions in testosterone levels, an inability to concentrate, and a reduction in physical performance. Yet a negative energy balance does lead to weight loss. The body detects an energy deficit and fat reserves are called upon to make up the difference. The body doesn't know the difference between a strict diet monitored by a physician at a Beverly Hills spa and simply running out of food in a poor African village. The body just knows it isn't getting enough energy, so it will begin to slow down all non-survival functions.

2.6.6. POSITIVE ENERGY BALANCE

Overfeeding has its own ramifications not only in terms of weight gain but in terms of health and cellular fitness. With too much overfeeding, plaques can build up in arteries, the blood pressure and cholesterol in our body can increase, we can become insulin resistant and suffer from diabetes, we can increase our risk for certain cancers, and so on. The relationship between the amount of calories we eat in the diet and the amount of energy we use in the body determines our body weight and overall health. The body is highly adaptable to a variety of energy intakes/outputs. It must be adaptable in order to survive. Therefore, mechanisms are in place to ensure stable energy transfer regardless of whether energy imbalances exist.

2.6.7. FACTORS THAT AFFECT ENERGY IN

- Calorie intake.
- Energy digested and absorbed (90-99%).

Factors that affect energy out Work

Physical work (exercise and activity).

Heat

- Heat produced with physical work.
- Heat produced via the thermic effect of food (TEF).
- Heat produced by resting metabolism.
- Heat produced; adipose creation.
- Heat produced; adipose thermoregulation.

Storage

- Efficiency of work.

- Efficiency of food metabolism.
- Energy stored in adipose tissue.

2.7. SUMMARY

In this unit, we have……

Basal metabolic rate (BMR) is often used interchangeably with resting metabolic rate (RMR). While BMR is a minimum number of calories required for basic functions at rest, RMR — also called resting energy expenditure (REE) — is the number of calories that your body burns while it's at rest. Typically about 60% of our total energy needs come from resting metabolism (see above), but this varies greatly depending on our activity level. The average BMR for an American woman is about 1,400 calories, while for a man its about 1,80 calories. The factors that affect the BMR are body temperature, age, sex, race, emotional state, climate and circulating levels of hormones like catecholamine's (epinephrine and norepinephrine) and those secreted by the thyroid gland. The energy requirement of man can be determined either directly by measuring his output in a calorimeter or indirectly by measuring his oxygen consumption. Energy balance also has positive energy balance (more in than out) and negative energy balance (more out than in), everything from your metabolism, to your hormonal balance, to your mood is impacted.

2.8. TERMINAL QUESTIONS

Q.1. Describe energy balance.

Answer: .....
.....
.....

Q.2. Describe basal metabolic rate (BMR) and factors influencing it.

Answer...……
……..……
…….....

Q.3. Explain basal and resting metabolism.

Answer...……
……..……
…….....

Q.4. Explain the resting metabolic rate (RMR).

Answer...……
……..……
…….....

Q.5. Write short notes on trace minerals and macrominerals.

Answer...……
……..……
…….....

Q.6. Describe measurement of fuel value of foods.

Answer...……
……..……
…….....

Q.7. Describe energy, its types and their importance.

Answer...……
……..……
…….....

Q. **8**. Describe respiratory quotients (RQ) of different foodstuffs.

Answer...……
……..……
…….....

2.9. FURTHER READINGS

1. Biochemistry- Lehninger A.L.
2. Biochemistry –J.H.Weil.
3. Biochemistry fourth edition-David Hames and Nigel Hooper.
4. Textbook of Biochemistry for Undergraduates - Rafi, M.D.
5. Biochemistry and molecular biology- Wilson Walker.

UNIT-3 BIOLOGICAL OXIDATION OF FOODSTUFF

Structure

3.1. INTRODUCTION

In this unit we will introduce you about biological oxidation of food stuffs in an unique way. Energy is required to maintain the structure and function of the living cells. This energy is derived from oxidation of carbohydrates, lipids and protein in diets. • The energy liberated is converted into ATP, which is known as the energy currency of the living cells. Each gram of carbohydrate and protein gives about 4 Kcal on oxidation, while each gram of fat gives about 9 Kcal. Oxidation is a chemical reaction that involves the moving of electrons. When iron reacts with oxygen it forms a chemical called rust because it has been oxidized (the iron has lost some electrons) and the oxygen has been reduced.

Phosphorylation is the chemical addition of a phosphoryl group (PO_3^-) to an organic molecule. The removal of a phosphoryl group is called dephosphorylation. Both phosphorylation and dephosphorylation

are carried out by enzymes (e.g., kinases, phosphotransferases). A chemical weapon agent (CWA) is a chemical substance whose toxic properties are used to kill, injure or incapacitate human beings. About 70 different chemicals have been used or stockpiled as chemical weapon agents during the 20th century. These agents may be in liquid, gas or solid form.

Objectives

- To know about biological oxidation and electron transport chain (ETC).
- To know different enzymes which are associated with biological oxidation
- To define phosphorylation and their types.
- To know about chemical warfare and measurement of energy.
- To know about thermogenesis and its types.

3.2 BIOLOGICAL OXIDATION

Biological oxidation is catalyzed by enzymes which function in combination with coenzymes and/or electron carrier proteins. The living organisms of the planet cannot exist without energy. It is vital to every process and chemical reaction. Many living organism, including human beings, can receive energy from food. Let's examine where energy comes from, and the reactions that take place at this time in the cells of living organisms.

On the basis of receiving energy lies the process of biological oxidation. This process has been studied in great detail, and there is even a whole science about it, biochemistry, which deals with all the subtleties and mechanisms of the process. Biological oxidation is the combination of oxidation-reduction transformations of substances in living organisms. Oxidation-reduction reactions are those which take place with a change in the oxidation state of atoms through the redistribution of electrons between them.

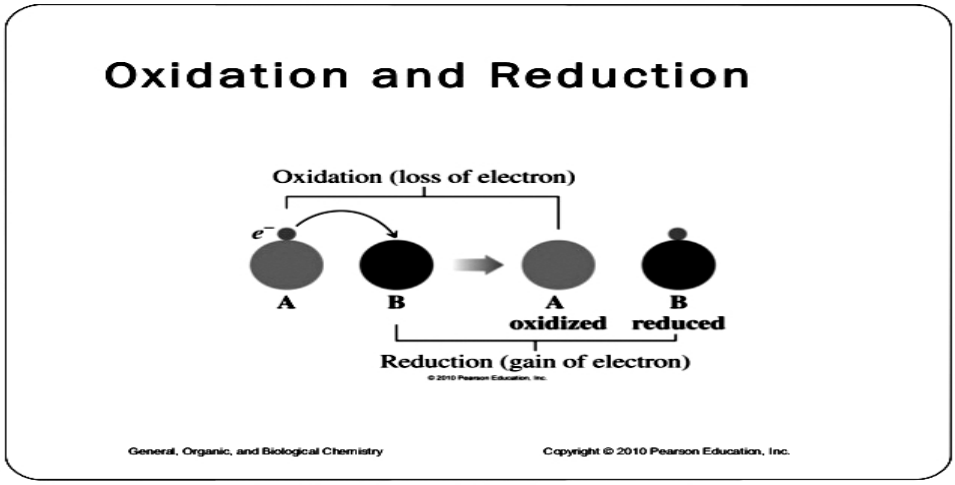

Fig.3.1 : Biological oxidation

Scientists first proposed the theory that complex chemical reactions took place inside each living organism in the 18th century. The problem was studied by the French chemist Antoine Lavoisier, who noticed that the processes of combustion and biological oxidation resembled each other.

The scientist traced the path of oxygen, which is absorbed by the living organism in the respiration process, and concluded that a process of oxidation took place in the organism, resembling the combustion process, but at a slower rate. Lavoisier discovered that molecules of oxygen, which is an oxidizer, interact with organic compounds (containing carbon and hydrogen), as a result of which their absolute transformation takes place, and the compounds break down.

Several aspects of this process are remained unclear to the scientists :

- Why oxidation takes place at a low body temperature, unlike the similar combustion process.
- Why the oxidation reaction is not accompanied by a flame and a large release of free energy.
- How nutrients can "burn" in the organism of a living creature with a body that is around 80% water.

It took many years for scientists to answer these and many other questions, and also to clarify what biological oxidation is. Chemists have now studied the connection of breathing with other metabolism processes, including the process of phosphorylation; the properties of enzymes that catalyze reactions of biological oxidation; localization of enzymes in the cell; and also the mechanism of the accumulation and transformation of energy.

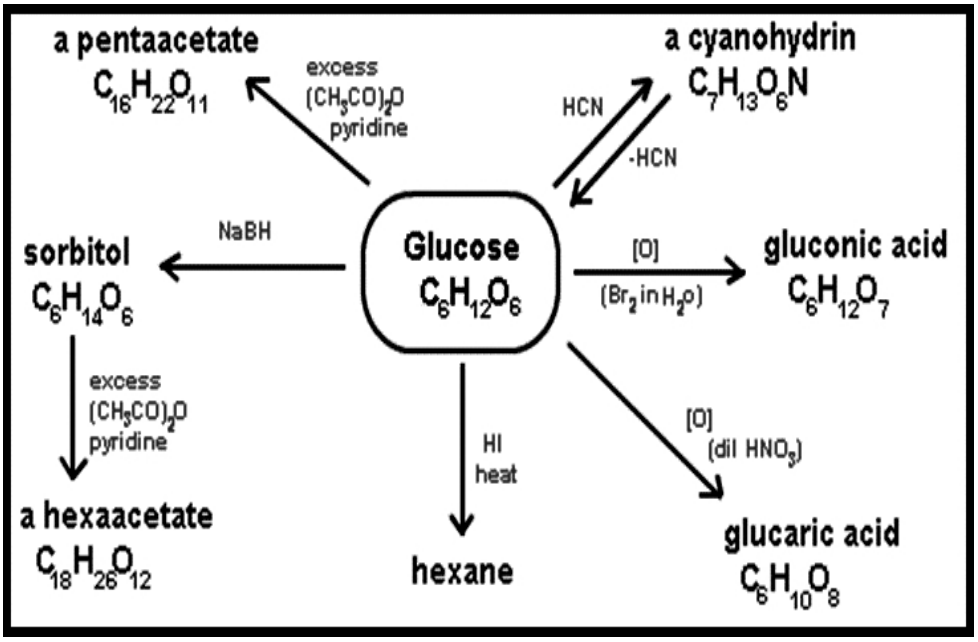

FIG.3.2 : BIOLOGICAL OXIDATION OF GLUCOSE

3.2.1. TYPES OF BIOLOGICAL OXIDATION

In different conditions, there are two types of biological oxidation can take place. Many fungi and microorganism receive energy by transforming nutrients by the anaerobic method. Anaerobic biological oxidation is a reaction that takes place without the presence of oxygen or its par-ticipation in the process in any way. This method of receiving energy is used by living organisms in an environment, into which air does not enter -in clay, under the ground, in mud, in swamps, and in rotting substances. Anaerobic biological oxidation is called *glycolysis.*

The second, more complex method of transforming nutrients into energy is of aerobic biological oxidation, or tissue respiration. This reaction takes place in all aerobic organisms which use oxygen in the respiration process. The aerobic method of biological oxidation is impossible without molecular oxygen.

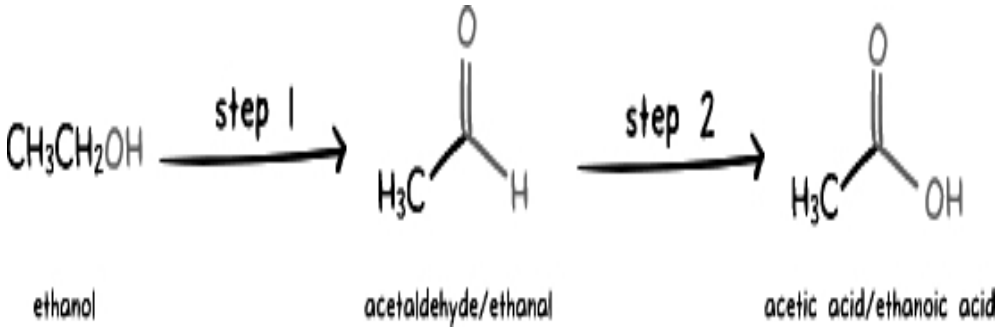

Fig. 3.3 : Biological oxidation of alcohols

Different enzymes associated with biological oxidation

1. **Oxidoreductases**

   These enzymes catalyse the removal of hydrogen from the substrate and add it to another substance, thus bringing about oxidation reduction reaction. e.g Glyceraldehyde-3 Phosphate dehydrogenase.

2. **Oxidases**

   These enzymes catalyse the removal of hydrogen from the substrate and add directly to the molecular oxygen. e.g. Cytochrome oxidases, tyrosinase, uricase.

3. **Oxygenases**

   These enzymes incorporate oxygen into the substrates.

   - **Mono-oxygenases**

     Adds only one atom of oxygen to the substrate. These are also known as mixed function oxidases.

- **Di-oxygenases**

  Adds both the atoms of oxygen to the substrate. e.g. Homogentisic acid di-oxygenase.

4. Aerobic dehydrogenases

These enzymes remove hydrogen from the substrate and add it either directly to oxygen or any other artificial acceptors like methylene blue. The product formed is hydrogen peroxide.

5. Anaerobic dehydrogenases

These enzymes use other substrates or substances to donate the hydrogen. They transfer hydrogen's to some other hydrogen acceptor, but not directly to oxygen. Thus the hydrogen acceptors are NAD, + FAD and FMN. Heme proteins like cytochromes also receive hydrogen's. The cytochromes are b, c_1, c, a and a_3.

6. Hydro peroxidases

These enzymes have either hydrogen peroxide (H_2O_2) or organic peroxide as their substrate. There are two types of hydro peroxidases. They are as follows.

- Peroxidase
- Catalase

Their prime function is destruction of H_2O_2.

3.2.2. RESPIRATORY CHAIN OR ELECTRON TRANSPORT CHAIN (ETC)

When electrons are transferred from the most electronegative system [(NADH or $FADH_2$) (-0.32V)] to the most electropositive system (+0.82V) (Oxygen), there will be liberation of all the energy at one time in an explosive manner. But, if they are transferred in a step wise manner through some intermediate systems then there will be slow release of energy and it can be captured by the cell to synthesize energy rich compounds. During biological oxidation, electrons are transferred through electron transport proteins which are arranged in a specific chain to form the electron transport chain (ETC), which is situated in the inner mitochondrial membrane.

Transfer of electrons from substrate to molecular oxygen through a chain of electron carriers is called electron transport chain or respiratory chain. Mitochondria contain a series of catalysts forming the respiratory chain which are involved in the transfer of electrons and hydrogen and their final reaction is with oxygen to form water. The components of respiratory chain are arranged sequentially in the order of increasing redox potential.

Electrons flow through the chain in a stepwise manner from lower redox potential to higher redox potential. Some amount of energy is liberated with transfer of electron from one component to another. Whenever there is a release of 7.4 Kcal of energy or a little more, then ATP formation takes place there. NADH forms 3 ATPs whereas FADH2 forms only 2 as it enters ETC at the site beyond the first site of ATP formation.

Sites of ATP formation in the ETC or respiratory chain

- Between NADH dehydrogenase (flavoprotein) and ubiquinone (coenzyme Q).
- Between cytochrome-b and cytochrome-c_1.
- Between cytochrome-a and cytochrome-a_3 (cytochrome of oxidase).

The components of ETC, their redox potential and their sequence is shown below:

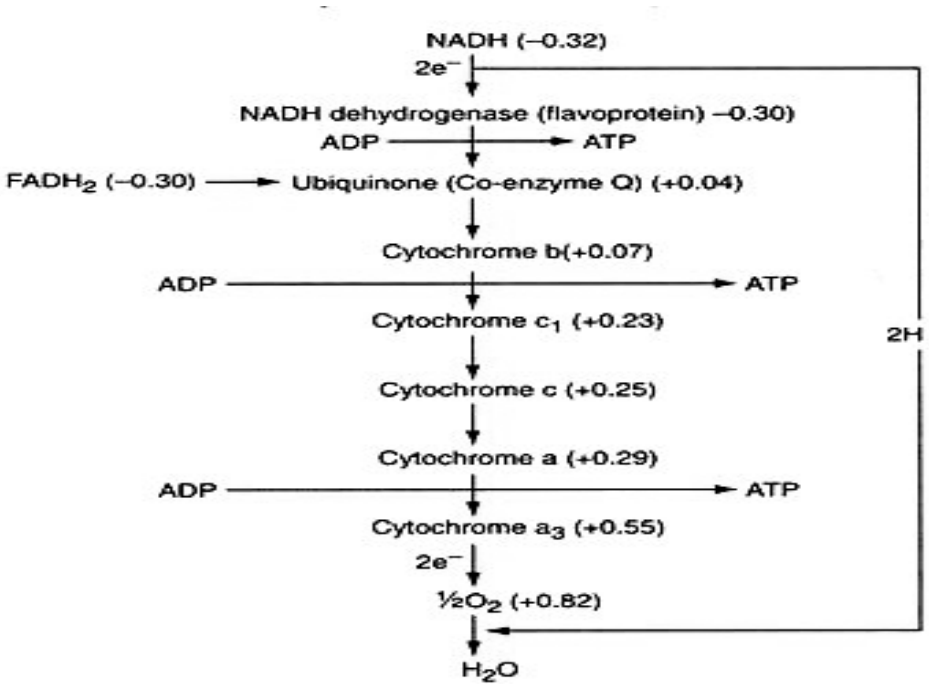

Fig.3.4: Components of electron transport chain

3.3. PHOSPHORYLATION

Esterification of a phosphate through a high energy bond (7.4 Kcal) is known as phosphorylation. Combination of inorganic phosphate (Pi) with any other compound through high energy bond is known as phosphorylation. Or formation of ATP from ADP and phosphate or NTP from NDP and P_i is known as phosphorylation.

Types of phosphorylation

There are two types of phosphorylation are as given below.

3.3.1. SUBSTRATE LEVEL PHOSPHORYLATION

Formation of high energy phosphate bond at the level of a substrate without the involvement of the respiratory chain is known as substrate level phosphorylation. e.g Phosphoenolpyruvate is converted to pyruvate by pyruvate kinase where ATP is formed from ADP.

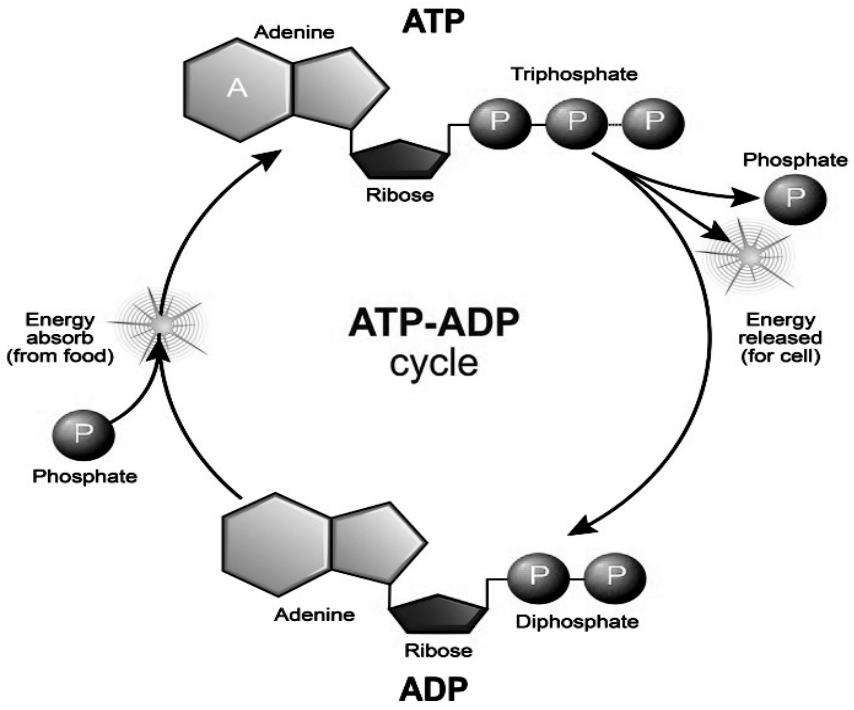

Fig. 3.5 : The ATP-ADP Cycle in substrate level phosphorylation

3.3.2. OXIDATIVE PHOSPHORYLATION

The oxidative phosphorylation of ADP happens through cellular respiration wherein enzymes are used to oxidize nutrients. This process is very efficient in releasing energy in biological systems when compared to fermentation or anaerobic glycolysis. Unlike oxidative phosphorylation, substrate level phosphorylation does not couple phosphorylation and oxidation. The enzymatic phosphorylation of ADP to ATP coupled with electron transport from a substrate to molecular oxygen is known as oxidative phosphorylation or respiratory chain phosphorylation.

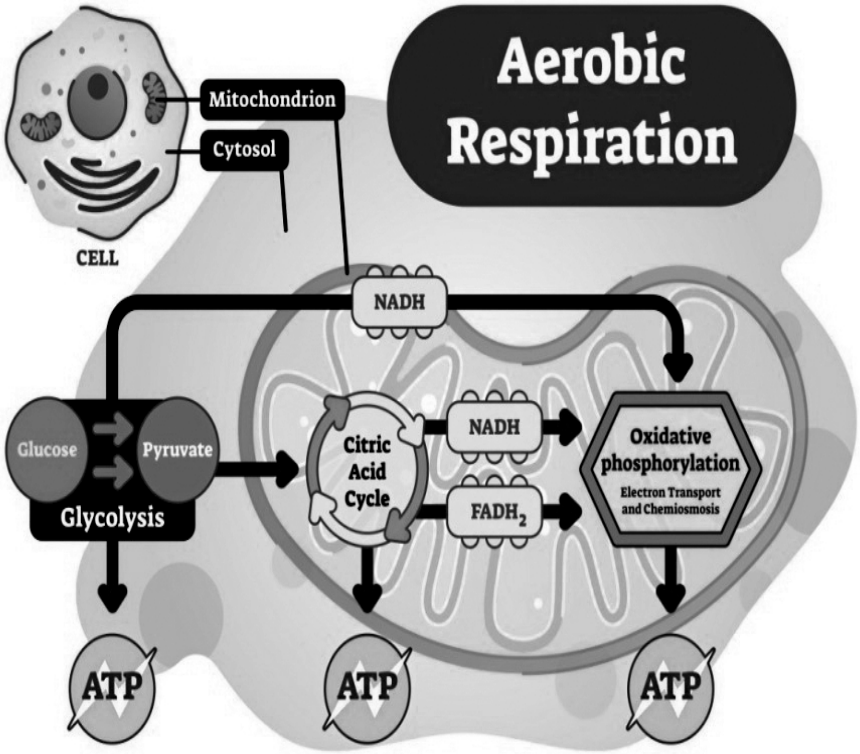

Fig. 3.6 : Oxidative phosphorylation and substrate level phosphorylation in aerobic respiration

3.3.3. MECHANISM OF OXIDATIVE PHOSPHORYLATION

There are three theories or hypothesis, explaining the formation of ATP through electron transport chain. They are as given below.

1. **Chemical coupling hypothesis**

   It states that a high energy compound is formed taking the energy liberated by electron transfer and this compound in turn phosphorylates ADP to ATP.

2. **Conformational coupling hypothesis**

   There are many proteins in the wall of inner mitochondrial membrane; one of them is F_0F_1, ATPase, which is responsible for the ATP production. According to this hypothesis the energy liberated from ETC brings a conformational change in the proteins of the membrane and is then transferred to F_oF_1ATPase which thereby also gets a conformation change and hence becomes unstable. In order to attain stability it provides energy for ATP synthesis

3. Chemiosmotic hypothesis

It states that electron transport pumps H^+ from the mitochondrial matrix across the inner mitochondrial membrane to the outer aqueous phase, thereby the matrix becomes basic and the outer phase becomes acidic. Due to this osmotic difference (i.e. more acidic outside and more basic inside the mitochondrial matrix) the H influx (diffuse) into the matrix through a pore in the F_0F_1 ATPase which provides the energy for the ATP synthesis.

P/O Ratio (inorganic phosphate/oxygen)

The number of inorganic phosphates esterified per atom of oxygen consumed is known as P/O ratio. For NADH it is 3 and FADH, it is 2.

Formation and Detoxification of H_2O_2

During ETC, O_2 accepts four electrons forming two H_2O. If by chance O_2 accepts only two electrons, the product formed is H_2O_2 and if it accepts only one electron then superoxide radical is formed. Both these damage the membrane structure by attacking the unsaturated fatty acids of the membranes.

Detoxification of Superoxide

$$2O^-_2 + 2H^+ \text{ ----- SUPEROXIDE DISMUTASE} \rightarrow H_2O_2 + O_2$$

H_2O_2 is detoxified as-----

$$2H_2O_2 \text{ -------- CATALASE} \rightarrow 2H_2O + O_2$$

Cytochrome-a_3

Cytochrome-a_3 is also known as cytochrome oxidase. It has two molecules of heme with long hydrocarbon side chains. To the other end of the heme, two copper atoms are attached which can directly react with oxygen to donate four electrons.

Inhibitors of ETC

Inhibitors of ETC are those which inhibit or stop the flow of electrons in the electron transport chain. These are as follows.

- At the first site of ATP formation, rotenone and barbital inhibit the flow of electrons
- At the second site antimycin-A and amytal inhibits the flow of electrons.
- At the third site cyanide (Cn^-), carbon monoxide (CO) and H_2S gas inhibit.

Un-couplers of Oxidative Phosphorylation :

Un-couplers are those substances which prevent oxidative phosphorylation (formation of ATP) though ETC is normally operating. Due to the effect of un-couplers there is a continuous flow of electrons but

there is no formation of ATP i.e. ETC is not coupled to the ATP formation, so the energy is dissipated as heat. Some of the un-couplers are as follows.

1. **2, 4-Dinitrophenol (DNP):**

   It transfers protons across the mitochondrial membrane thereby diverting its flow from F_0F_1 ATPase.

2. **Valinomycin**

   It transfers K^4 ions, disturbing the osmotic pressure.

3. **Gramicidin**

   It transfers Na^+ ions, across the membrane. All the above three are known as 'ionophores' i.e. those which disrupt the membrane permeability to ions, thereby uncoupling phosphorylation with ETC.

4. **Oligomycin**

   It inhibits F_0F_1 ATPase.

5. **Atractyloside**

   It inhibits adenine nucleotide transport protein of the mitochondrial membrane which transport ATP in exchange of ADP.

Mechanisms/Applications of Un-couplers

- The mechanism by which body heat is increased during fever is by uncoupling.
- Increase in the heat of the penis during erection is due to uncoupling.
- Reduction in fat (weight) of obese persons is by the mechanism of uncoupling (banned).
- Newly born infants have special type of mitochondria called brown fat mitochondria which are highly porous containing more cytochromes. They help in release of more heat by uncoupling, thus helping in maintaining the body temperature in the infants as they do not have sub-cutaneous fat resulting in loss of more heat.

3.4. CHEMICAL WARFARE

It involves using the toxic properties of chemical substances to kill, injure or incapacitate an enemy. The offensive use of living organisms (such as anthrax) is considered to be biological warfare rather than chemical warfare. The use of non-living toxic products produced by living organisms, ex. toxins such as botulinum toxin, ricin, or saxitoxin is

considered as chemical warfare. Chemical used in warfare is called a ‘chemical warfare agent (CWA).

3.4.1. MEASUREMENT OF ENERGY CONTENT OF FOOD MATERIALS FOOD

Food is any substance normally eaten or drunk by living things. The term food also includes liquid drinks. Food is the main source of energy and of nutrition for animals, and is usually of animal or plant origin. There are 4 basic food energy sources: fats, proteins, carbohydrates and alchol. Humans and other animals need a minimum intake of food energy to sustain their metabolism and to drive their muscles. Foods are composed chiefly of carbohydrates, fats, proteins, water, vitamins, and minerals.

Carbohydrates, fats, proteins, and water represent virtually all the weight of food, with vitamins and minerals making up only a small percentage of the weight. Carbohydrates, fats, and proteins comprise ninety percent of the dry weight of foods. Organisms derive food energy from carbohydrates, fats and proteins as well as from organic acids, polyols, and ethanol present in the diet. Some diet components that provide little or no food energy, such as water, minerals, vitamins, cholesterol and insoluble fiber, may still be necessary to health and survival for other reasons. Water, minerals, vitamins, and cholesterol are not broken down (they are used by the body in the form in which they are absorbed) and so cannot be used for energy. Fiber cannot be completely digested by most animals, including humans, who can only extract 2 kcal/g of food energy. Ruminants can extract nearly 4 kcal/g from fiber because of the bacteria in their rumens.

Using the International System of Units, researchers measure energy in joules (J) or in its multiples; the kilojoule (kJ) is most often used for food-related quantities. An older metric system unit of energy, still widely used in food-related contexts, is the calorie; more precisely, the "food calorie", "large calorie" or kilocalorie (kcal or Cal), equal to 4184 joules. (Contrast the "small calorie" (cal), equal to 1/1000 of a food calorie, that is often used in chemistry and in physics. In the European Union, both the kilocalorie (kcal) and kilojoule (kJ) appear on nutrition labels. In many countries, only one of the units is displayed; in Canada and the United States labels spell out the unit as Calorie.

Fats and ethanol have the greatest amount of food energy per gram, 37 and 29 kJ/g (8.8 and 6.9 kcal/g), respectively. Proteins and most carbohydrates both have about 17 kJ/g (4 kcal/g). The differing energy density of foods (fat, alcohols, carbohydrates and proteins) lies mainly in their varying proportions of carbon, hydrogen, and oxygen atoms. Carbohydrates that are not easily absorbed, such as fiber, or lactose in lactose-intolerant individuals, contribute less food energy. Polyols (including sugar alcohols) and organic acids contribute 10 kJ/g (2.4 kcal/g) and 13 kJ/g (3.1 kcal/g) respectively.

3.4.2. HISTORICAL DEVELOPMENT

Humans are omnivorous animals that can consume both plant and animal products. We changed from gatherers to hunter gatherers. After the experience of the Ice Age it is probable that humans wanted to create some feeling of security by controlling what plants were growing and which animals were available. This led to agriculture, which has continually improved and altered the way in which food is obtained.

3.4.3. TYPES OF FOOD

Fats

In biochemistry, fat is a generic term used for a class of lipids. Fats are produced by organic processes in animals and plants. All fats are insoluble in water and have a density significantly below that of water (i.e. they float on water.) Fats that are liquid at room temperature are often referred to as oil. Most fats are composed primarily of triglycerides; some monoglycerides and diglycerides are mixed in, produced by incomplete esterification. These are extracted and used as an ingredient. Products with a lot of saturated fats tend to be solid at room temperature, while products containing unsaturated fats, which include monounsaturated fats and polyunsaturated fats, tend to be liquid at room temperature. Predominantly saturated fats (solid at room temperature) include all animal fats as well as palm oil, coconut oil, cocoa fat and hydrogenated vegetable oil.

All other vegetable fats, such as those coming from olive, peanut, maize (corn oil), cottonseed, sunflower, safflower, and soybean, are predominantly unsaturated and remain liquid at room temperature. However, both vegetable and animal fats contain saturated and unsaturated fats. Some oils (such as olive oil) contain in majority monounsaturated fats, while others present quite a high percentage of polyunsaturated fats (sunflower oil, rape seed oil).

Energy Usage in Human Body

The human body uses the energy released by respiration for a wide range of purposes: about 20% of the energy is used for brain metabolism, and much of the rest is used for the basal metabolic requirements of other organs and tissues. In cold environments, metabolism may increase simply to produce heat to maintain body temperature. Among the diverse uses for energy, one is the production of mechanical energy by skeletal muscle to maintain posture and produce motion.

The conversion efficiency of energy from respiration into mechanical (physical) power depends on the type of food and on the type of physical energy usage (e.g., which muscles are used, whether the muscle is used aerobically or anaerobically). In general, the efficiency of muscles is rather low: only 18 to 26% of the energy available from respiration is converted into mechanical energy. This low efficiency is the

result of about 40% efficiency of generating ATP from the respiration of food, losses in converting energy from ATP into mechanical work inside the muscle, and mechanical losses inside the body. The latter two losses are dependent on the type of exercise and the type of muscle fibers being used (fast-twitch or slow-twitch). For an overall efficiency of 20%, one watt of mechanical power is equivalent to 4.3 kcal (18 kJ) per hour.

If a manufacturer of rowing equipment shows calories released from 'burning' food as four times the actual mechanical work, plus 300 kcal (1,300 kJ) per hour, which amounts to about 20% efficiency at 250 watts of mechanical output. It can take up to 20 hours of little physical output (e.g., walking) to burn off 4,000 kcal (17,000 kJ), more than a body would otherwise consume. For reference, each kilogram of body fat is roughly equivalent to 32,300 kilojoules or 7,700 kilocalories of food energy (i.e., 3,500 kilocalories per pound).

Changes in body temperature -either hotter or cooler - increase the metabolic rate, thus burning more energy. Prolonged exposure to extremely warm or very cold environments increases the basal metabolic rate (BMR). People who live in these types of settings often have BMRs 5-20% higher than those in other climates.

Physical energy value

The sample preparation is a main part in determining the energy value. Food should generally be placed in the calorimeter already freeze-dried and homogenized. The result is influenced mostly by the water content of the sample. The calorimeter provides the so-called physical energy value.

This means that the sample was fully combusted. In our bodies, however, these processes do not work in the same way as in a combustion calorimeter, but are rather staged in a great number of individual steps during which a comparably tiny amount of energy is released. This energy is used for the synthesis of substances needed by the body and for maintaining the body temperature. Special energy-rich molecules are built up that can be used later and at other points for the biosynthesis of compounds.

In other words, one does not need to constantly eat in order to have energy available and to build up materials. This means that the organism never fully breaks down the material it took in; it eliminates a part thereof, primarily a part that it cannot break down, but which can be physically burned. The energy values measured in the calorimeter are thus generally higher than those listed on the food identification label, because these figures describe the value that is actually released from the organism-the so-called physiological energy value.

Physiological energy value

In order for a person to eat food optimally, one prerequisite is first to crush it well, to chew it, to allow the saliva to act, then it can be better

digested and the individual components optimally processed by the healthy body. Fats are in some cases stored or, to cover basic energy needs, are accessed directly and converted into energy. However, the preparation of food is important here. Some foods may be poorly digested in its raw state and poorly utilized by the body. In order to know the optimal personal energy value for food, one would first have to determine one's own basic energy expenditure. There are studies in which people were evaluated specifically in that regard. This includes, among other things, breathing, CO_2 output (combustion efficiency of the body), at rest and while working.

Energy expenditure

Measurement of energy expenditure in humans is required to assess metabolic needs, fuel utilisation, and the relative thermic effect of different food, drink, drug and emotional components. Indirect and direct calorimetric and non-calorimetric methods for measuring energy expenditure are reviewed, and their relative value for measurement in the laboratory and field settings is assessed. Where high accuracy is required and sufficient resources are available, an open-circuit indirect calorimeter can be used.

There are three components to total energy expenditure in humans are as follows.

- Basal metabolic rate (BMR).
- Thermic effect of food.
- The energy expenditure of activity (activity thermogenesis).

BMR is the energy expended when an individual is lying at complete rest, in the morning after sleep in the post-absorptive state. In individuals with sedentary occupations basal metabolic rate accounts for approximately 60% of the total daily energy expenditure and is highly predicted by lean body mass within and across species. Resting energy expenditure, in general, is within 10% of the BMR and is measured in subjects at complete rest in the postabsorptive state.

Thermic effect of food is the increase in energy expenditure associated with digestion, absorption and storage of food, and accounts for approximately 10% of the total daily energy expenditure; many believe there exist facultative as well as fixed components. Activity thermogenesis is the thermogenesis that accompanies physical activities and, therefore, can be divided into exercise and non-exercise activity thermogenesis. Most individuals do not partake in purposeful sporting exercise and so their exercise-related activity thermogenesis is zero; for those who do exercise regularly, exercise related energy expenditure is generally,10% of the total daily energy expenditure.

Measurement of energy expenditure

Open-circuit indirect calorimeters can employ a mask, hood, canopy or room/chamber for collection of expired air. For short-term measurements, mask, hood or canopy systems suffice. Chamber-based systems are more accurate for the long-term measurement of specified activity patterns but behaviour constraints mean they do not reflect real life.

Where resources are limited and/or optimum precision can be sacrificed, flexible total collection systems and non-calorimetric methods are potentially useful if the limitations of these methods are appreciated. The use of the stable isotope technique, doubly labelled water, enables total daily energy expenditure to be measured accurately in free-living subjects. The factorial method for combining activity logs and data on the energy costs of activities can also provide detailed information on free-living subjects.

3.4.4. THERMOGENESIS

Thermogenesis means the generation of heat, and it is what is keeping you alive right now. A lot of people are aware of thermogenesis, but many think that it applies solely to your metabolism. Whilst they're not wrong - thermogenesis directly affects your metabolism, there is a lot more to it than that. The first thing you should understand is that your body can only withstand a drop in body temperature of 10 degrees, and a rise in temperature of 5 degrees. That really isn't much is it? Luckily your Hypothalamus has you covered.

The Hypothalamus is situated in the center of your brain and is responsible for a process known as thermoregulation (finding a temperature balance). When you are very cold your Hypothalamus (or more accurately the primary motor center that is found within the Hypothalamus) can cause your muscles to shiver. This can increase your metabolism five-fold and will raise your body temperature.

On the other hand, if you begin to get too hot, either from the weather or from aerobic/anaerobic exercise your Hypothalamus will cause you to begin to sweat. This will lower your body temperature. Both of these are examples of thermoregulation.

The purpose of thermoregulation is to keep your body temperature at the perfect balance, this is known as Homeostasis. Thermoregulation is one control for Homeostasis but it is not the only one, the body also regulates blood glucose, calcium levels, the partial pressure of O_2 and CO_2, blood pressure etc.

Thermogenesis, literally defined as heat production, is an important physiological variable as well as a normal by-product of metabolic processes. Increased thermogenesis is a common feature of the acute-phase response and can be observed following injury, inflammation, infection, physical or emotional stress, and in certain chronic diseases such

as malignancy. Thermogenesis is also a primary effector of thermoregulation in homeotherms, and an important mediator of fever. It is the process of heat production in organisms. It occurs in all warm-blooded animals, and also in a few species of thermogenic plants such as the Eastern skunk cabbage, the Voodoo lily, and the giant water lilies of the genus *Victoria*. The lodgepole pine dwarf mistletoe, *Arceuthobium americanum* disperses its seeds explosively through thermogenesis.

Cytokines have been proposed to mediate many aspects of the acute-phase response, including activation of thermogenesis and fever. Experimental studies have now demonstrated potent effects and probable mechanisms of action of a number of cytokines on thermogenesis.

Types of Thermogenesis

Depending on whether or not they are initiated through locomotion and intentional movement of the muscles, thermogenic processes can be classified as one of the following:

- Exercise-associated thermogenesis (EAT)
- Non-exercise activity thermogenesis (NEAT)
- Diet-induced thermogenesis (DIT)

Shivering

One method to raise temperature is through shivering. It produces heat because the conversion of the chemical energy of ATP into kinetic energy causes almost all of the energy to show up as heat. Shivering is the process by which the body temperature of hibernating mammals (such as some bats and ground squirrels) is raised as these animals emerge from hibernation.

Non-shivering

Non-shivering thermogenesis occurs in brown adipose tissue (brown fat) that is present in almost all eutherians (swine). Brown adipose tissue has a unique uncoupling protein that allows the uncoupling of protons (H^+) moving down their mitochondrial gradient from the synthesis of ATP, thus allowing the energy to be dissipated as heat. In this process, substances such as free fatty acids (derived from triacylglycerols) remove purine (ADP, GDP and others) inhibition of thermogenin, which causes an influx of H^+ into the matrix of the mitochondrion and bypasses the ATP synthase channel. This uncouples oxidative phosphorylation, and the energy from the proton motive force is dissipated as heat rather than producing ATP from ADP, which would store chemical energy for the body's use.

Thermogenesis can also be produced by leakage of the sodium-potassium pump and the Ca^{2+} pump. Thermogenesis is contributed to by futile cycles, such as the simultaneous

occurrenceof lipogenesis and lipolysis or glycolysis and gluconeogenesis. Acetylcholine stimulates muscle to raise metabolic rate.

Regulation

Non-shivering thermogenesis is regulated mainly by thyroid hormone (secreted by thyroid gland) and the sympathetic nervous system. Some hormones, such as norepinephrine and leptin, may stimulate thermogenesis by activating the sympathetic nervous system. Rising insulin levels after eating may be responsible for diet-induced thermogenesis (thermic effect of food). Progesterone also increases body temperature.

Check your progress

- ✓ Explain measurement of energy content of foods.
- ✓ Define physical energy and physiological energy values.
- ✓ Define energy expenditure.
- ✓ Define basal metabolic rate (BMR).
- ✓ Define thermogenesis and thermic effect of food.

Factors

There are three factors that make up your metabolism, these are: Your resting metabolic rate (RMR), the thermic effect of food (TEF), and the thermic effect of exercise. Add all of these together and you will have an idea of how many calories you are using each day. Your RMR is responsible for between 60 and 75% of your daily calories burned, whilst your TEF is 10% and your TEE is between 15 and 30% (depending on how active you are).

When we talk about exercises or foods that can boost your metabolism, a lot of people think that this means that they boost it for life and your metabolism is like a savings account that you add money to. But these exercises and foods will only temporarily boost your TEF and TEE and as you can see, they only make up 25-40% of your calories per day. Making long term changes to your metabolism is something that is difficult to do, but it is what is responsible for long term weight maintenance. Temperature can also affect your daily calories burned.

3.5. SUMMARY

Biological oxidation is catalyzed by enzymes which function in combination with coenzymes and/or electron carrier proteins. The living organisms of the planet cannot exist without energy. It is vital to every

process and chemical reaction. In different conditions, there are two types of biological oxidation can take place. Many fungi and microorganism receive energy by transforming nutrients by the anaerobic method. Anaerobic biological oxidation is a reaction that takes place without the presence of oxygen or its participation in the process in any way.

Etherification of a phosphate through a high energy bond (7.4 Kcal) is known as phosphorylation. Combination of inorganic phosphate (Pi) with any other compound through high energy bond is known as phosphorylation. Or formation of ATP from ADP and phosphate or NTP from NDP and P_i is known as phosphorylation. Carbohydrates, fats, proteins, and water represent virtually all the weight of food, with vitamins and minerals making up only a small percentage of the weight. Carbohydrates, fats, and proteins comprise ninety percent of the dry weight of foods. Organisms derive food energy from carbohydrates, fats and proteins as well as from organic acids, polyols, and ethanol present in the diet. Measurement of energy expenditure in humans is required to assess metabolic needs, fuel utilization, and the relative thermic effect of different food, drink, drug and emotional components. Indirect and direct calorimetric and non-calorimetric methods for measuring energy expenditure are reviewed, and their relative value for measurement in the laboratory and field settings is assessed.

3.6. TERMINAL QUESTIONS.

Q.1. Define biological oxidation and its types.

Answer.....
.....
.....

Q.2. Discuss different enzymes which are associated with biological oxidation.

Answer.....
.....
.....

Q.3. Describe electron transport chain (ETC) and its role in respiration.

Answer.....
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.....

Q.4. Explain different types of food materials.

Answer.....
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.....

Q.5. Explain thermogenesis and its types.

Answer...……
……..……
…….....

Q.6. Explain phosphorylation and its types.

Answer...……
……..……
…….....

3.7. FURTHER READINGS

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Uttar Pradesh Rajarshi Tandon
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UGBCH-102

Nutritional Biochemistry

BLOCK

2

NUTRITION OF CARBOHYDRATES, PROTEINS AND VITAMINS

UNIT-4

Dietary Carbohydrate

UNIT-5

Proteins

UNIT-6

Minerals and Vitamins

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COURSE INTRODUCTION

This the second block on nutrition of carbohydrates, proteins and Vitamins. It consists of following three units:

Unit-4 : In this unit we cover the introduction carbohydrates. This unit discuss about fundaments of carbohydrates and its biological significance. Carbohydrate availability is increased by consuming carbohydrate contain food material. Digestion, absorption, storage and utilization of carbohydrates are briefly discussed in this unit along with it hormonal regulation of blood glucose.

Unit-5 : In this unit we cover the Sources, functions, digestions and absorptions of proteins. The nature and types of essential and nonessential amino acids is also mentioned in this unit. Role of nutrient and their toxicity of different nutrient discuss briefly.

Unit-6 : This unit discuss the nutrition importance of dietary elements such as of Structure importance of dietary calcium, phosphorus, magnesium, iron, iodine, zinc and copper etc. the source and limitations of these elements also discuss. The requirements and deficiency diseases associated with different vitamins also mentioned in this unit.

UNIT-4 CARBOHYDRATE

Structure

4.1 INTRODUCTION

We described carbohydrate, which are a class of biomolecules that essential for human being. Carbohydrates are important component of living organisms and are main source of energy in living organism. Here we described the basic definition, functions, digestion, absorption, storage and utilization of carbohydrates like- monosaccharides, disaccharides, and polysaccharides etc. Our body can convert excess carbohydrates into

triglyceride molecules and store them as fat. The carbohydrate are mains molecules that daily require for human body. According to National Institute of Health, the recommended daily amount (RDA) of carbohydrates for adults is 135 grams. Generally carbohydrates are classified as monosaccharides, disaccharides, oligosaccharides and polysaccharides. Here in this unit you will study the structure of aldose and ketose forms of carbohydrates

Objectives

After going through the course of this unit student will be able to:

- Know about the carbohydrates and their functions.
- Understand the mechanism of digestion and absorption of carbohydrates.
- Studies the different types of metabolic pathways.
- Understand the hormonal regulation of blood glucose.

4.2 CARBOHYDRATES OVERVIEW

Carbohydrates may be defined as polyhydroxyaldehydes or ketones or compounds which produce them on hydrolysis. Carbohydrates are the major source of energy for the living cells. Glucose (normal fasting blood level 70-100 mg/dl) is the central molecule in carbohydrate metabolism, actively participating in a number of metabolic pathways--glycolysis, gluconeogenesis, glycogenesis, glycogenolysis, hexose monophosphate shunt, uronic acid pathway etc.

4.2.1 FUNCTIONS

- They are the most abundant dietary source of energy (4 Cal/g) for all organisms.
- Carbohydrates are precursors for many organic compounds (fats, amino acids).
- Carbohydrate (as glycoproteins and glycolipids) participates in the structure of cell membrane and cellular functions such as cell growth, adhesion and fertilization.
- They are structural components of many organisms. These include the fiber (cellulose) of plants, exoskeleton of some insects and the cell wall of microorganisms.
- Carbohydrates also serve as the storage form of energy (glycogen) to meet the immediate energy demands of the body.

4.2.2 DIGESTION

The principal dietary carbohydrates are polysaccharides (starch, glycogen), disaccharides (lactose, sucrose) and, to a minor extent, monosaccharides (glucose, fructose). The digestion of carbohydrates occurs briefly in mouth and largely in the intestine. The polysaccharides get hydrated during heating which is essential for their efficient digestion. The hydrolysis of glycosidic bonds is carried out by a group of enzymes called glycosidases. These enzymes are specific to the bond, structure and configuration of monosaccharide units.

- **Digestion in the mouth**: Carbohydrates are the only nutrients for which the digestion begins in the mouth to a significant extent. During the process of mastication, salivary a-amylase (ptyalin) acts on starch randomly and cleaves α-1,4-glycosidic bonds. The products formed include α-limit dextrins (containing about 8 glucose units with one or more α-1,6-glycosidic bonds) maltotriose and maltose.

- **Carbohydrates not digested in the stomach:** The enzyme salivary amylase is inactivated by high acidity (low pH) in the stomach.

- **Digestion in the small intestine:** The acidic dietary contents of the stomach, on reaching small intestine, are neutralized by bicarbonate produced by pancreas. The pancreatic α-amylase acts on starch and continues the digestion process. Amylase specifically acts on α-l,4-glycosidic bonds and not on α-1,6-bonds. The resultant products are disaccharides (maltose, isomaltose) and oligosaccharides.

The final digestion of di-and oligosaccharides to monosaccharides primarily occurs at the mucosal lining of the upper jejunum. This is carried out by oligosaccharidases (e.g. glucoamylase acting on amylose) and disaccharidases (e.g. maltase, sucrase, lactase). The enzyme sucrase is capable of hydrolysing a large quantity of table sugar (sucrose). In contrast, lactase (β-galactosidase) is the rate limiting and consequently, the utilization of milk sugar (lactose) is limited in humans.

4.2.3 ABSORPTION

The principal monosaccharides produced by the digestion of carbohydrates are glucose, fructose and galactose. Of these, glucose accounts for nearlv 80 o/o of the total monosaccharides. The absorption of sugars mostly takes place in the duodenum and upper jejunum of small intestine. There exists a considerable variation in the absorption of different monosaccharides. It is observed that hexoses are more rapidly absorbed than pentoses. Among the monosaccharides, galactose is most

efficiently absorbed followed by glucose and fructose. Insulin has no effect on the absorption of sugars.

Different sugars possess different mechanisms for their absorption. Glucose is transported into the intestinal mucosal cells by a carrier mediated and energy requiring process. Glucose and Na^+ share the same transport system (symport) which is referred to as sodium dependent glucose transporter. The concentration of Na^+ is higher in the intestinal lumen compared to mucosal cells. Na^+, therefore, moves into the cells along its concentration gradient and simultaneously glucose is transported into the intestinal cells. This is mediated by the same carrier system. Thus, when Na+ diffuses into the cell and it drags glucose along with it.

The mechanism of absorption of galactose is similar to that of glucose. The inhibitor phlorizin blocks the Na^+ dependent transport of glucose and galactose. Fructose absorption does not require energy and is independent of Na^+ transport. Fructose is transported by facilitated diffusion mediated by a carrier. Inside the epithelial cell, most of the fructose is converted to glucose. The latter then enters the circulation. Pentoses are absorbed by a process of simple diffusion.

4.2.4 STORAGE AND UTILIZATION

The monosaccharide glucose is the central molecule in carbohydrate metabolism. Glucose is utilized as a source of energy, it is synthesized from non-carbohydrate precursors and stored as glycogen to release glucose as and when the need arises. The other important monosaccharides in carbohydrate metabolism are fructose, galactose and mannose. The important pathways for utilization of carbohydrates are :

4.3 GLYCOLYSIS

Glycolysis is derived from the Greek words (glycose-sweet or sugar; lysis-dissolution). This pathway is often referred to as Embden-Meyerhof Parnaspathway (EMP pathway) in honour of the two biochemists who made a major contribution to the knowledge of glycolysis. Glycolysis is defined as the sequence of reactions converting glucose (or glycogen) to pyruvate or lactate, with the production of ATP.

1. Glycolysis takes place in all cells of the body. The enzymes of this pathway are present in the cytosomal fraction of the cell.

2. It occurs in the absence of oxygen (anaerobic) or in the presence of oxygen (aerobic). Lactate is the end product under anaerobic condition. In the aerobic condition, pyruvate is formed, which is then oxidized to CO_2 and H_2O.

3. Glycolysis is a major pathway for ATP synthesis in tissues lacking mitochondria, e.g. erythrocytes, cornea, lens etc.

4. Glycolysis is very essential for brain which is dependent on glucose for energy.

The pathway of glycolysis can be divided into three distinct phases:

A. Energy investment phase or priming stage

B. Splitting phase

C. Energy generation phase

A. Energy investment phase

1. Glucose is phosphorylated to glucose 6-phosphate by hexokinase or glucokinase (both are isoenzymes).This is an irreversible reaction, dependent on ATP and Mg^{2+}. Glucokinase present in liver, catalyses the phosphorylation of only glucose, has high K_m for glucose (10 mM) and is not inhibited by glucose 6-phosphate. Due to high affinity (low K_m), glucose is utilized by hexokinase even at low concentration, whereas glucokinase acts only at higher levels of glucose i.e., after a meal when blood glucose concentration is above 100 mg/dl. Glucose 6-phosphate is impermeable to the cell membrane. lt is a central molecule with a variety of metabolic fates – glycolysis, glycogenesis, gluconeogenesis and pentose phosphate pathway.

2. Glucose 6 –phosphate undergoes isomerization to give fructose 6-phosphate in the presence of the enzyme phosphohexose isomerase and Mg^{2+}.

3. Fructose 6-phosphate is phosphorylated to fructose1,6-bisphosphate by phosphofructokinase (PFK). This is an irreversible and a regulatory step in glycolysis.

B. Splitting phase

4. The six carbon fructose 1,6- bisphosphate is split (hence the name glycolysis) to two three-carbon compounds, glyceraldehyde 3-phosphate and dihydroxyacetone phosphate by the enzyme aldolase (fructose 1,6- bisphosphate aldolase).

5. The enzyme phosphotriose isomerase catalyses the reversible interconversion of glyceraldehyde 3-phosphate and dihydroxyacetone phosphate. Thus, two molecules of glyceraldehydes 3-phosphate are obtained from one molecule of glucose.

C. Energy generation phase

6. Glyceraldehyde 3-phosphate dehydrogenase converts glyceraldehydes 3-phosphate to 1,3-bisphosphoglycerate. This step is important as it is involved in the formation of $NADH^{+}$ H^{+} and a high energy compound 1,3-bisphosphoglycerate. lodoacetate and arsenate inhibit the enzyme glyceraldehyde 3-phosphate dehydrogenase. ln aerobic condition, NADH passes through the electron transport chain and 6 ATP (2 x 3 ATP) are synthesized by oxidative phosphorylation.

7. The enzyme phosphoglycerate kinase acts on 1,3-bisphosphoglycerate resulting in the synthesis of ATP and formation of 3-phosphoglycerate. This step is a good example of substrate Ievel phosphorylation, since ATP is synthesized from the substrate without the involvement of electron transport chain. Phosphoglycerate kinase reaction is reversible, a rare example among the kinase reactions.

8. 3-Phosphoglycerate is converted to 2-phosphoglycerate by phosphoglycerate mutase. This is an isomerization reaction.

9. The high energy compound phosphoenol pyruvate is generated from 2-phosphoglycerate by the enzyme enolase. This enzyme requires Mg^{2+} or Mn^{2+} and is inhibited by fluoride. For blood glucose estimation in the laboratory, fluoride is added to the blood to prevent glycolysis by the cells, so that blood glucose is correctly estimated.

10. The enzyme pyruvate kinase catalyses the transfer of high energy phosphate from phosphoenol pyruvate to ADP, leading to the formation of ATP. This step also is a substrate level phosphorylation. This reaction is irreversible.

Production of ATP in glycolysis

Under anaerobic conditions, 2 ATP are synthesized while, under aerobic conditions, 8 or 6 ATP are synthesized-depending on the shuttle pathway that operates.

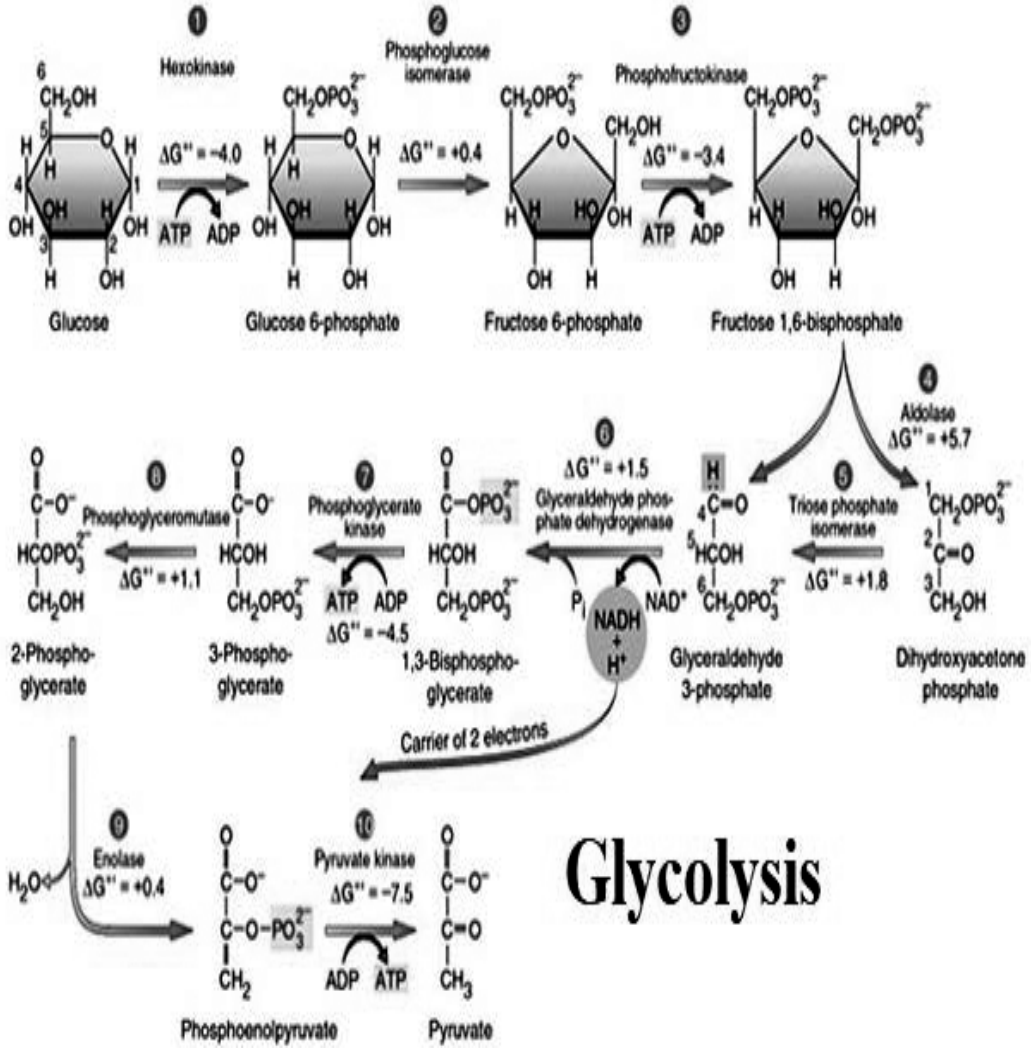

Fig. 4.1 : Process of Glycolysis

Source: http://www.biosciencenotes.com/glycolysis/

4.3.1 CITRIC ACID CYCLE (KREBS CYCLE)

The citric acid cycle (Krebs cycle or tricarboxylic acid-TCA cycle) is the most important metabolic pathway for the energy supply to the body. About 65-70% of the ATP is synthesized in Krebs cycle. Citric acid cycle essentially involves the oxidation of acetyl CoA to CO_2 and H_2O. This cycle utilizes about two thirds of total oxygen consumed by the body. Krebs cycle is the most important central pathway connecting almost all the individual metabolic pathways (either directly or indirectly). The enzymes of TCA cycle are located in mitochondrial matrix, in close proximity to the electron transport chain. Oxidative decarboxylation of pyruvate to acetyl CoA by pyruvate dehydrogenase complex is a connecting link between glycolysis and TCA cycle. The events of TCA cycle are as follows:

1. **Formation of citrate:** Krebs cycle proper starts with the condensation of acetyl CoA and oxaloacetate, catalysed by the enzyme citrate synthase.

2. 2 & 3. **Citrate is isomerized to isocitrate**: by the enzyme aconitase. This is achieved in a two stage reaction of dehydration followed by hydration through the formation of an intermediate-cis-aconitate.

3. 4 & 5. **Formation of α-ketoglutarate** : The enzyme isocitrate dehydrogenase catalyses the conversion (oxidative decarboxylation) of isocitrate to oxalosuccinate and then to α-ketoglutarate. The formation of NADH and the liberation of CO_2 occur at this stage.

4. **Conversion of α-ketoglutarate to succinyl CoA**: occurs through oxidative decarboxylation, catalysed by α-ketoglutarate dehydrogenase complex. This enzyme is dependent on five cofactors-TPP (Thymine pyrophosphate), lipoamide, NAD^+, FAD and CoA.

    a. The mechanism of the reaction is analogous to the conversion of pyruvate to acetyl CoA. At this stage of the TCA cycle, second NADH is produced and the second CO_2 is liberated.

5. **Formation of succinate** : Succinyl CoA is converted to succinate by succinate thiokinase. This reaction is coupled with the phosphorylation of GDP to GTP. This is a substrate level phosphorylation. GTP is converted to ATP bv the enzvme nucleoside diphosphate kinase.

6. **Conversion of succinate to fumarate :** Succinate is oxidized by succinate dehydrogenase to fumarate. This reaction results in the production of $FADH_2$ and not NADH.

7. **Formation of malate:** The enzyme fumarase catalases the conversion of fumarate to malate with the addition of H_2O.

8. **Conversion of malate to oxaloacetate :** Malate is then oxidized to oxaloacetate by malate dehydrogenase. The third and final synthesis of NADH occurs at this stage. The oxaloacetate is regenerated which can combine with another molecule of acetyl CoA, and continue the cycle.

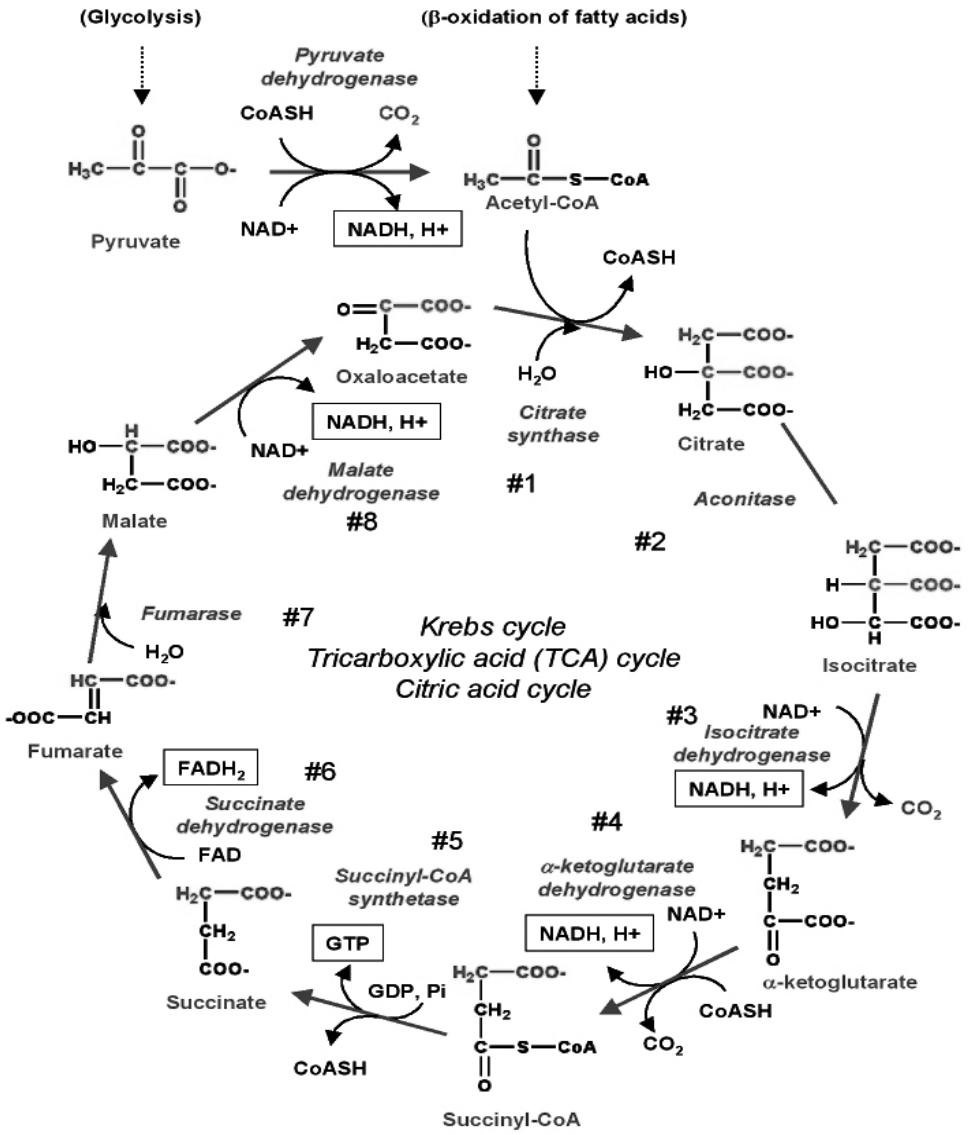

Fig.4.2: Krebs cycle

4.4 GLUCONEOGENESIS

The synthesis of glucose from noncarbohydrate compounds is known as gluconeogenesis. The major substrates / precursors for gluconeogenesis are lactate, pyruvate, glucogenic amino acids, propionate and glycerol.

Gluconeogenesis occurs mainly in the cytosol, although some precursors are produced in the mitochondria. Gluconeogenesis mostly takes place in liver (about 1 kg glucose synthesized everyday) and, to some extent, in kidney matrix (about one-tenth of liver capacity).

Reactions of gluconeogenesis

Gluconeogenesis closely resembles the reversed pathway of glycolysis, although it is not the complete reversal of glycolysis.

Essentially 3, (out of 10) reactions of glycolysis are irreversible. The seven reactions are common for both glycolysis and gluconeogenesis. The three irreversible steps of glycolysis are catalysed by the enzymes, namely hexokinase, phosphofructokinase and pyruvate kinase. These three stages-bypassed by alternate enzymes specific to gluconeogenesis are.

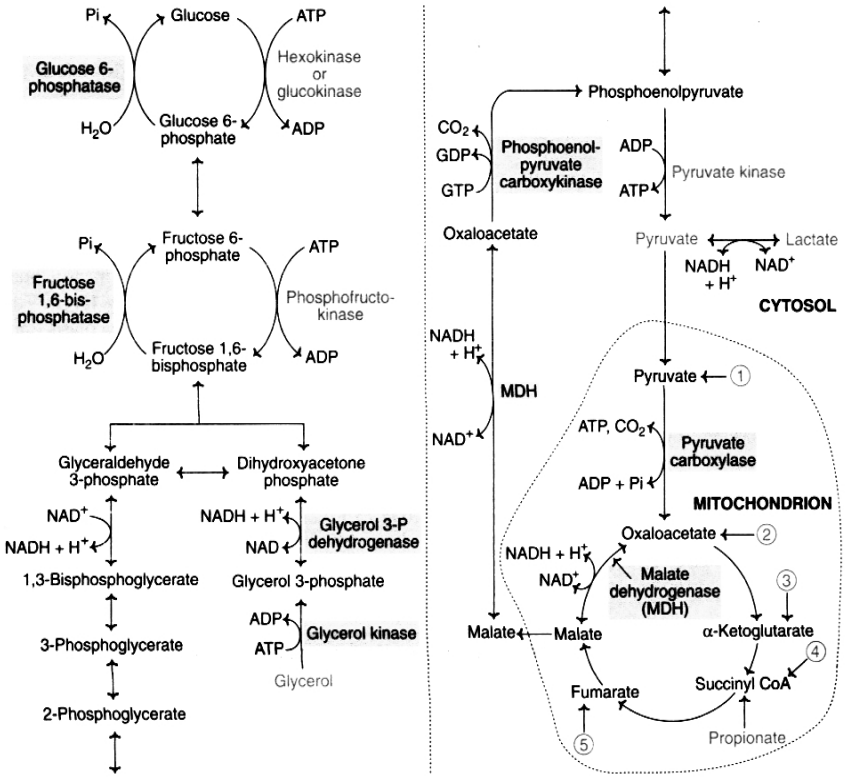

Fig.4.3 : Gluconeogenesis

1) **Conversion of pyruvate to phosphoenol pyruvate:** This takes place in two steps. Pyruvate carboxylase is a biotin dependent mitochondrial enzyme that converts pyruvate to oxaloacetate in presence of ATP and CO_2. This enzyme regulates gluconeogenesis and requires acetyl CoA for its activity. Oxaloacetate is synthesized in the mitochondrial matrix. lt has to be transported to the cytosol to be used in gluconeogenesis where the rest of the pathway occurs. ln the cytosol, phosphoenolpyruvate carboxykinase converts oxaloacetate to phosphoenolpyruvate.

2) **Conversion of fructose 1,6-bisphosphate to fructose 6-phosphate:** Phosphoenolpyruvate undergoes the reversal of glycolysis until fructose 1,6-bisphosphateis produced. The enzyme fructose l,6-bisphosphatase converts fructose 1,6-bisphosphate to fructose 6-phosphate.This enzyme requires Mg^{2+} ions.

3) Conversion of glucose 6-phosphate to glucose: Glucose 6-phosphatase catalyses the conversion of glucose 6-phosphate to

glucose. The presence or absence of this enzyme in a tissue determines whether the tissue is capable of contributing glucose to the blood or not. lt is mostly present in liver and kidney but absent in muscle, brain and adipose tissue.

4.5 GLYCOGENESIS

The synthesis of glycogen from glucose is glycogenesis. Glycogenesis takes place in the cytosol and requires ATP and UTp, besides glucose

1. **Synthesis of UDP-glucose:** The enzymes hexokinase (in muscle) and glucokinase (in liver) convert glucose to glucose 6-phosphate. Phosphoglucomutase catalyses the conversion of glucose 6-phosphate to glucose 1-phosphate. Uridine diphosphate glucose (UDPG) is synthesized from glucose 1-phosphate and UTP by UDP-glucose pyrophosphorylase.

2. **Requirement of primer to initiate glycogenesi**s: A small fragment of pre-existing glycogen must act as a 'primer to initiate glycogen synthesis. lt is recently found that in the absence of glycogen primer, a specific protein namely glycogenin can accept glucose from UDPG.

3. **Glycogen synthesis by glycogen synthase:** Glycogen synthase is responsible for the formation of 1,4-glycosidic linkages. This enzyme transfers the glucose from UDP-glucose to the non-reducing end of glycogen to form α- 1,4 linkages.

4. **Formation of branches in glycogen:** The formation of branches is brought about by the action of a branching enzyme, namely glucosyl α-4-6 transferase.. This enzyme transfers a small fragment of five to eight glucose residues from the non-reducing end of glycogen chain (by breaking α-1 ,4 linkages) to another glucose residue where it is linked by α-1,6 bond. This leads to the formation of a new non-reducing end, besides the existing one. Glycogen is further elongated and branched, respectively, by the enzymes glycogen synthase and glucosyl 4-6 transferase.

   The overall reaction of the glycogen synthesis for the addition of each glucose residue is

$(Glucose)_n$ + Glucose + 2ATP ------ $(Glucose)n_{+1}$ +2 ADP + Pi. Of the two ATP utilized, one is required for the phosphorylation of glucose while the other is needed for conversion of UDP to UTP.

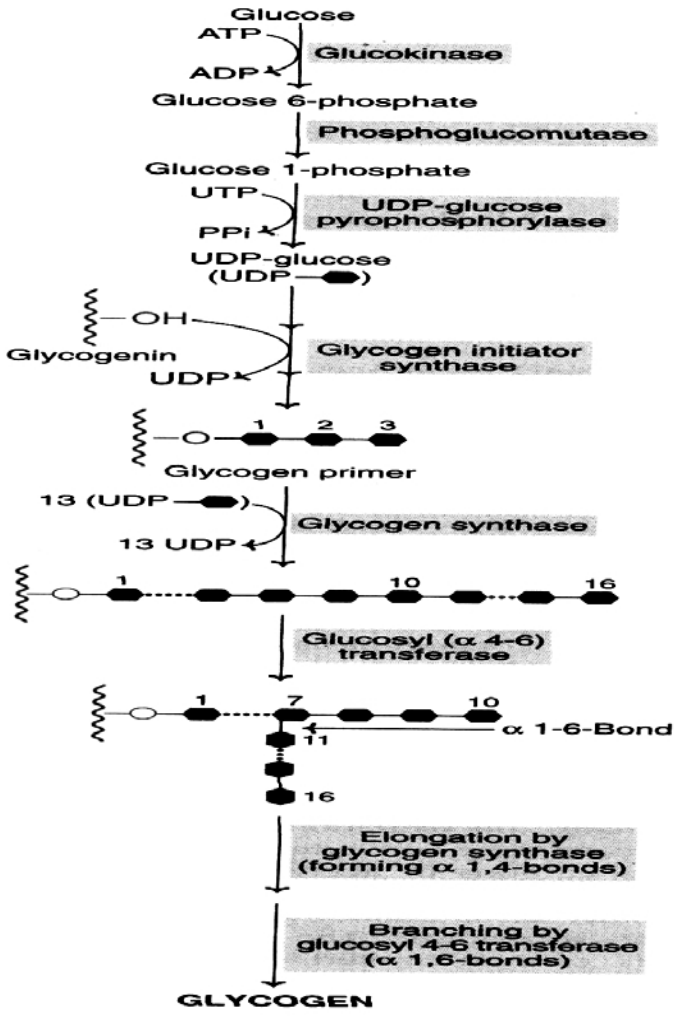

Fig.4.4: Process of glycogenesis

4.6 GLYCOGENOLYSIS

The degradation of stored glycogen in liver and muscle constitutes glycogenolysis. The pathways for the synthesis and degradation of glycogen are not reversible. An independent set of enzymes present in the cytosol carry out glycogenolysis.

i. **Action of glycogen phosphorylase:** The α-1,4-glycosidic bonds (from the non-reducing ends) are cleaved sequentially by the enzyme glycogen phosphorylase to yield glucose 1-phosphate. This process-called phosphorolysis continues until four glucose residues remain on either side of branching point (α-1,6-glycosidic link). The glycogen so formed is known as limit dextrin which cannot be further degraded by phosphorylase.

ii. **Action of debranching enzyme:** The branches of glycogen are cleaved by two enzyme activities present on a single polypeptide called debranching enzyme, hence it is a bifunctional enzyme. Glycosyl 4 : 4 transferase (oligo α.-1,4 1 ,4 glucan transferase)

activity removes a fragment of three or four glucose residues attached at a branch and transfers them to another chain. Here, one α-1,4-bond is cleaved and the same α-1,4 bond is made, but the places are different. Amylo α-1,6- glucosidase breaks the α,-1,6 bond at the branch with a single glucose residue and releases a free glucose.

iii. **Formation of glucose 6-phosphate and glucose:** Through the combined action of glycogen phosphorylase and debranching enzyme, glucose 1-phosphate and free glucose in a ratio of 8 : 1 are produced. Glucose1- phosphate is converted to glucose 6–phosphate by the enzyme phosphoglucomutase. The fate of glucose 6-phosphate depends on the tissue.

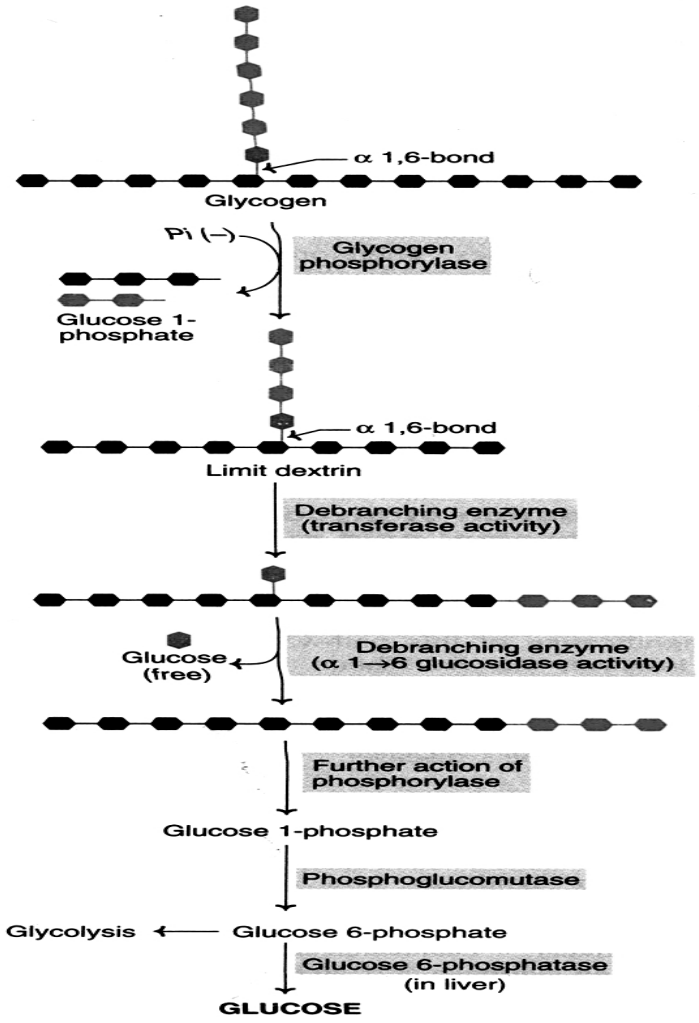

Fig.4.5 : Process of glycogenolysis

4.7 HEXOSE MONOPHOSPHATE SHUNT (HMP)

Hexose monophosphate pathway or HMP shunt is also called pentose phosphate pathway or phosphogluconate pathway. This is an alternative pathway to glycolysis and TCA cycle for the oxidation of

glucose. HMP shunt is more anabolic in nature, it is concerned with the biosynthesis of NADPH and pentoses.

It is a unique multifunctional pathway. The pathway starts with glucose 6-phosphate. As such, no ATP is directly utilized or produced. There are several interconvertible substances produced which may proceed in different directions in the metabolic reactions.

The enzymes of HMP shunt are located in the cytosol. The tissues such as liver, adipose tissue, adrenal gland, erythrocytes, testes and lactating mammary gland, are highly active in HMP shunt. Most of these tissues are involved in the biosynthesis of fatty acids and steroids which are dependent on the supply of NADPH. The sequence of reactions of HMP shunt is divided into two phases-oxidative and non-oxidative.

4.7.1 OXIDATIVE PHASE

Glucose 6-phosphate dehydrogenase (G6PD) is an NADP-dependent enzyme that converts glucose 6-phosphate to 6-phosphogluconolactone. The latter is then hydrolysed by the gluconolactone hydrolase to 6-phosphogluconate. The next reaction involving the synthesis of NADPH is catalysed by 6-phosphogluconate dehydrogenase to produce 3 keto 6-phosphogluconate which then undergoes decarboxylation to give ribulose 5-phosphate. **G6PD regulates HMP shunt:** The first reaction catalysed by G6PD is most regulatory in HMP shunt. This enzyme catalyses an irreversible reaction. NADPH competitively inhibits G6PD. lt is the ratio of NADPH / NAD^+ that ultimately determines the flux of this cycle.

4.7.2 NON-OXIDATIVE PHASE

The non-oxidative reactions are concerned with the interconversion of three, four, five and seven carbon monosaccharides. Ribulose 5-phosphate is acted upon by an epimerase to produce xylulose 5-phosphate while ribose 5-phosphate ketoisomerase converts ribulose 5 – phosphate to ribose 5-phosphate. The enzyme transketolase catalyses the transfer of two carbon moiety from xylulose 5-phosphate to ribose 5-phosphate to give a 3-carbon glyceraldehyde 3-phosphate and a 7-carbon sedoheptulose 7-phosphate. Transketolase is dependent on the coenzyme thiamine pyrophosphate (TPP) and Mg^{2+} ions. Transaldolase brings about the transfer of a 3-carbon fragment (active dihydroxyacetone) from sedoheptulose 7-phosphate to glyceraldehyde 3-phosphate to give fructose 6-phosphate and four carbon erythrose 4-phosphate. Transketolase acts on xylulose 5-phosphate and transfers a 2-carbon fragment (glyceraldehyde) from it to erythrose 4-phosphate to generate fructose 6-phosphate and glyceraldehyde 3-phosphate. Fructose 6-phosphate and glyceraldehyde 3-phosphate can be further catabolized through glycolysis and citric acid cycle. Glucose may also be synthesized from these two compounds.

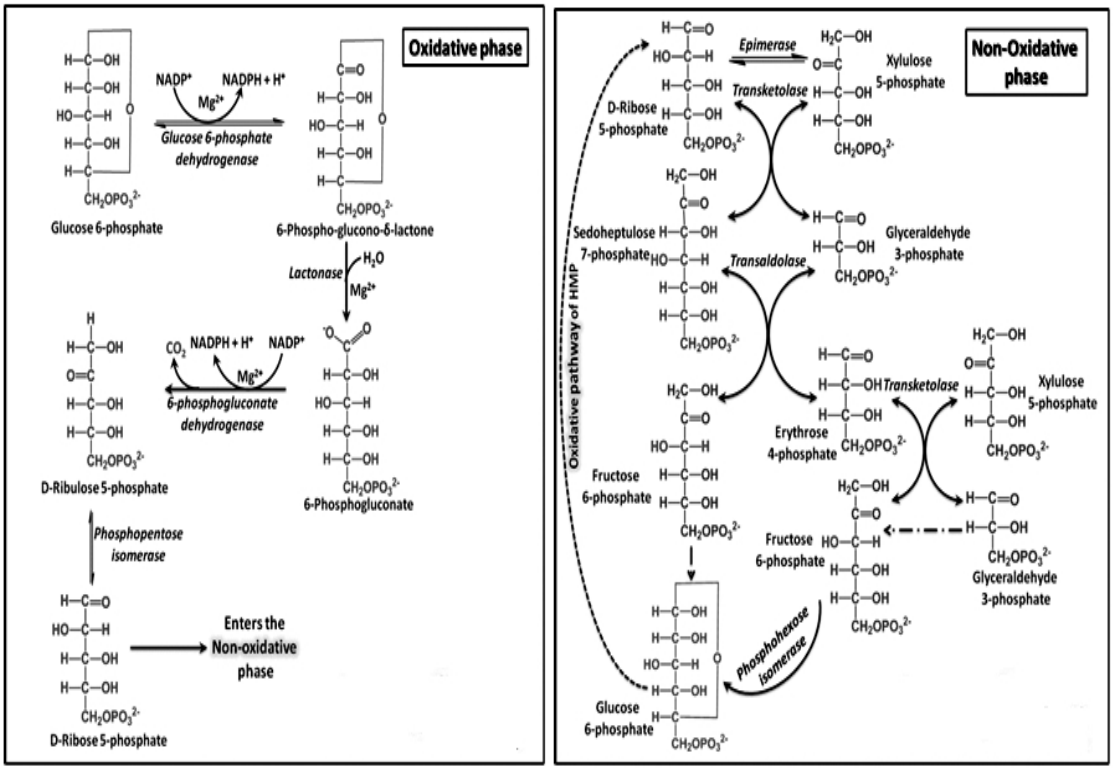

Fig.4.6: Hexose Monophosphate Shunt

Source;https://pharmaxchange.info/2013/10/hexose-monophosphate-pathway-or-pentose-phosphate-pathway-with-animation/

4.8 URONIC ACID PATHWAY

This is an alternative oxidative pathway for glucose and is also known as glucuronic acid pathway. lt is concerned with the synthesis of glucuronic acid, pentoses and vitamin, ascorbic acid. Dietary xylulose enters uronic acid pathway through which it can participate in other metabolism

1. **Formation and importance of UDPglucuronate :** Glucose 6-phosphate is first converted to glucose1-phosphate. UDP-glucose is then synthesized by the enzyme UDP-glucose pyrophosphorylase. Till this step, the reactions are the same as described in glycogenesis. UDP-glucose dehydrogenase oxidizes UDP-glucose to UDP-glucuronate.

2. **Conversion of UDP-glucuronate to L-gulonate :** UDP-glucuronate loses its UDP moiety in a hydrolytic reaction and releases D - glucuronate which is reduced to L-gulonate by an NADPH-dependent reaction.

3. **Synthesis of ascorbic acid in some animals :** L-Gulonate is the precursor for the synthesis of ascorbic acid (vitamin C) in many animals. The enzyme L-gulonolactone oxidase which converts

gulonate to ascorbic acid, is absent in man, other primates and guinea pigs.

4. **Oxidation of L-gulonate :** L-Gulonate is oxidized to 3-ketogulonate and then decarboxylated to a pentose, L-xylulose. L-Xylulose is converted to D-xylulose via xylitol by a reduction(NADPH-dependent) followed by an oxidation(NAD^+-dependent) reaction. This is necessary since the D-xylulose (and not L-form)-after getting phosphorylated can enter the hexose monophosphate shunt, for further metabolism.

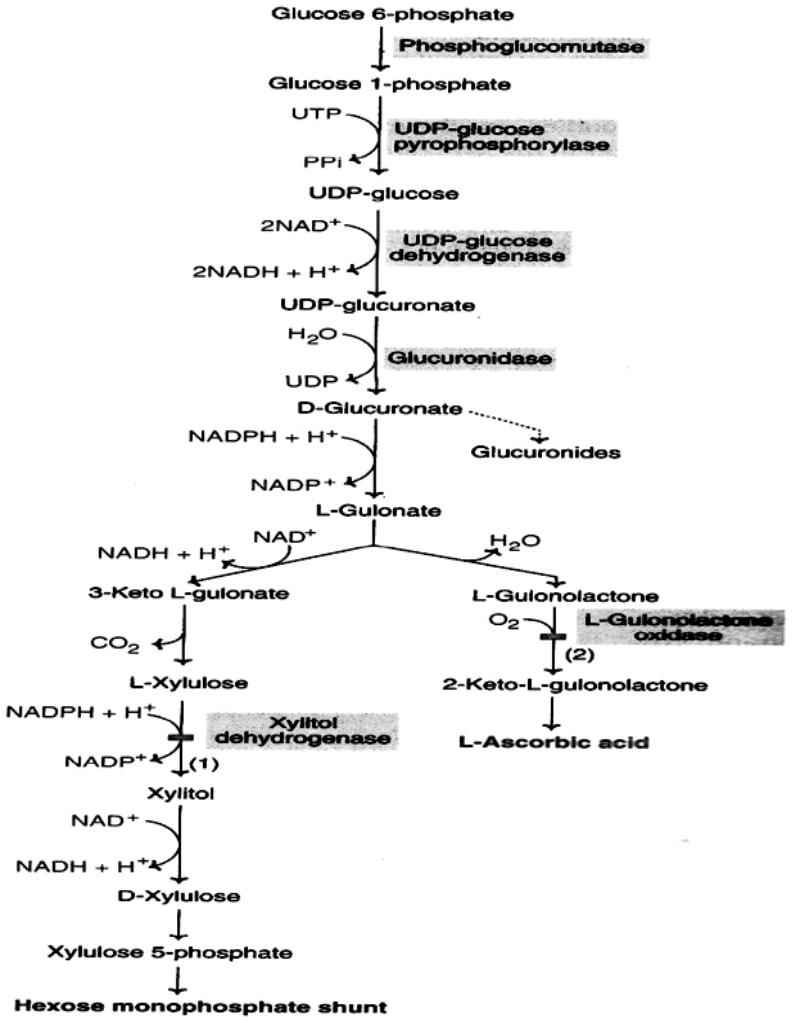

Fig.4.7 : Uronic acid pathway

4.9 GALACTOSE METABOLISM

The disaccharide lactose, present in milk and milk products, is the principal dietary source of galactose. Lactase (β-galactosidase) of intestinal mucosal cells hydrolyses lactose to galactose and glucose. Galactose is also produced within the cells from the lysosomal degradation of glycoproteins and glycolipids.

The specific enzyme, namely galactokinase, phosphorylates galactose to galactose 1-phosphate. This reacts with UDP-glucose in an exchange reaction to form UDP-galactose in presence of the enzyme galactose 1- phosphate uridyltransferase. UDP-galactose is an active donor of galactose for many synthetic reactions involving the formation of compounds like lactose, glycosaminoglycans, glycoproteins, cerebrosides and glycolipids. UDP-galactose can be converted to UDP-glucose by UDP hexose 4 –epimerase. In this way, galactose can enter the metabolic pathways of glucose. Galactose is not an essential nutrient since UDP-glucose can be converted to UDP-galactose by the enzyme UDP hexose 4-epimerase.

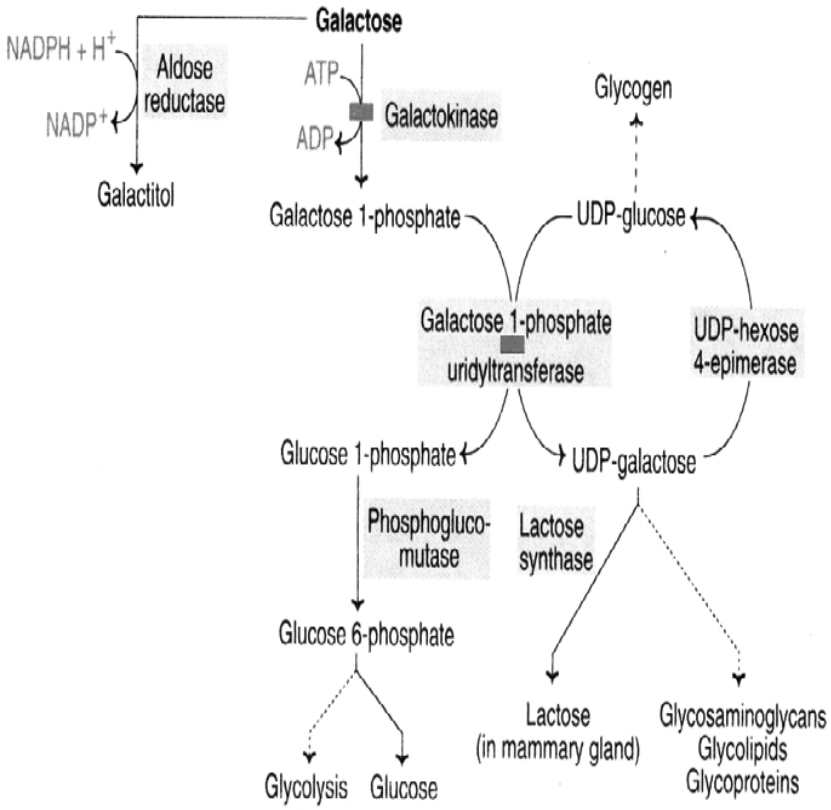

Fig. 4. 8. Metabolism of Galactose

4.10 FRUCTOSE METABOLISM

The major dietary source of fructose is the disaccharide sucrose (cane sugar), containing equimolar quantities of fructose and glucose. It is also found in free form in honey and many fruits. Fructose entry into the cells is not controlled by the hormone insulin. This is in contrast to glucose which is regulated for its entry into majority of the tissues. Fructose is mostly phosphorylated by fructokinase to fructose1 – phosphate. Fructokinase has been identified in liver, kidney and intestine. Hexokinase, which phosphorylates various monosaccharides, can also act on fructose to produce fructose 6-phosphate. However, hexokinase has low affinity (high K_m) for fructose, hence this is a minor pathway.

Fructose1 –phosphate is cleaved to glyceraldehyde and dihydroxyacetone phosphate (DHAP) by aldolase B. This is in contrast to fructose 6-phosphate which is converted to fructose 1, 6-bisphosphate and split by aldolase A.

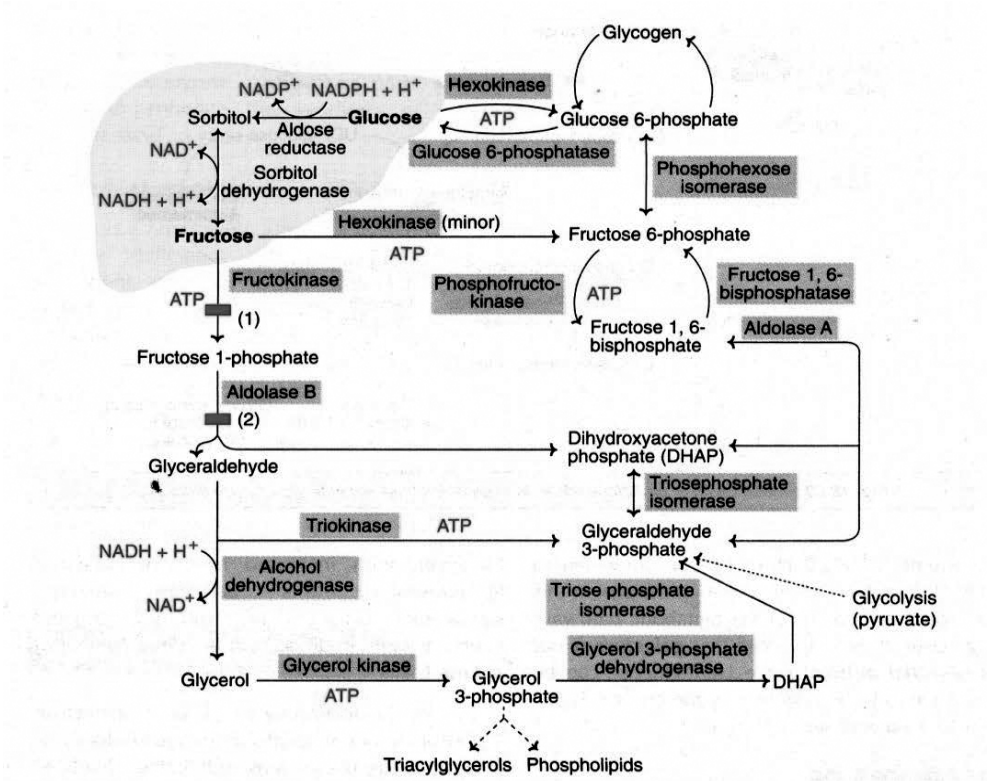

Fig. 4.9 : Metabolism of Fructose

Glyceraldehyde is phosphorylated by the enzyme triokinase to glyceraldehyde 3- phosphate which, along with DHAP, enters glycolysis or gluconeogenesis. The fructose is more rapidly metabolized (via glycolysis) by the liver than glucose. This is due to the fact that the rate limiting reaction in glycolysis catalysed by phosphofructokinase is bypassed.

Increased dietary intake of fructose significantly elevates the production of acetyl CoA and lipogenesis (fatty acid, triacylglycerol and very low density lipoprotein synthesis).

4.11 AMINO SUGAR AND MUCOPOLYSACCHARIDE METABOLISM

When a hydroxyl group of a sugar is replaced by an amino group, the resultant compound is an amino sugar. The important amino sugars are glucosamine, galactosamine, mannosamine, sialic acid etc. They are essential components of glycosaminoglycans, glycolipids (gangliosides) and glycoproteins. They are also found in some oligosaccharides and certain antibiotics. lt is estimated that about 20% of the glucose is utilized

for the synthesis of amino sugars, which mostly occurs in the connective tissue. Fructose 6-phosphate is the major precursor for glucosamine, N-acetylgalactosamine and N-acetylneuraminic acid (NANA).

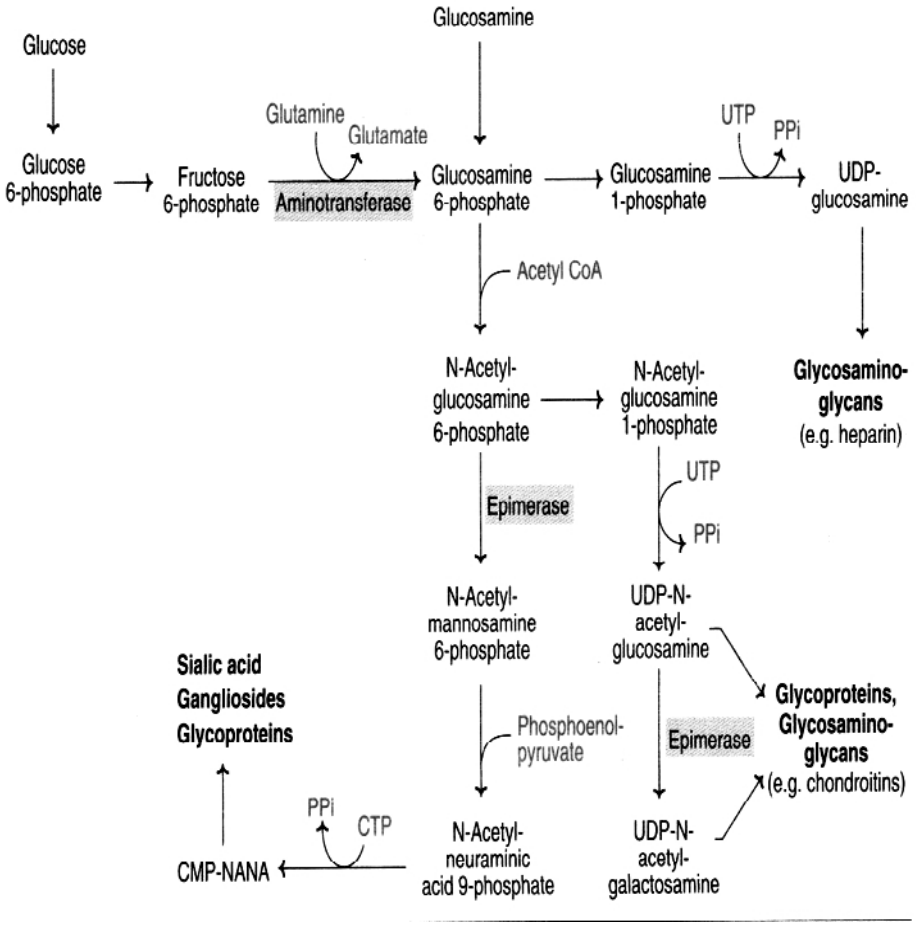

Fig. 4.10 : Metabolism of Amino Sugars

4.12 HORMONAL REGULATION OF BLOOD GLUCOSE

Glucose has an extremely important role to perform in the body. However, if the level of free glucose in the blood are higher than a certain level for longer periods it can have dreadful consequences. Thus the level of glucose must be maintained in the blood within a specific spectrum of concentration.

- **Insulin :** secreted by the β-cells of pancreas. It is activated by amino acids, free fatty acids, ketone bodies, glucagon, secretin and tolbutamide. Epinephrine and norepinephrine block the release of insulin. Insulin transporters increase glycolysis by stimulating phosphofructokinase. Gluconeogenesis, glycogenolysis and ketogenesis are decreased where as lipogenesis and protein synthesis are increased by insulin.

- **Anterior pituitary hormones :** Growth hormone is stimulated by hypoglycaemia and causes decreased uptake of glucose while adrenocorticotrophin (ACTH) mobilizes free fatty acids from adipose tissue and produces hyperglycaemia.
- **Adrenal cortex hormones :** Glucocorticoids such as cortisol act antagonistic to insulin. Therefore, gluconeogenesis increases, utilization of glucose occurs in extrahepatic tissue and increased formation of glucose in liver by stimulating glucose-6-phosphatase fructose1,6-bisphosphatase occurs.
- **Epinephrine :** In muscle, glycogen breakdown is aided by phosphorylase, which in turn is activated by epinephrine. The glucose formed by degradation of glycogen is converted to lactate via Cori's cycle. There is decreased release of insulin, glucose gets used up in the liver.
- **Glucagon :** secreted by the α-cells of pancreas, stimulated by hypoglycaemia. It causes glycogenolysis in the liver. It stimulates glucose-6- phosphatase and enhances gluconeogenesis.
- Thyroid hormones stimulate glycogenolysis.
- Sex hormones oestrogens are responsible for decreased levels of insulin and decrease in the blood sugar levels.

4.13 SUMMARY

Carbohydrates may be defined as polyhydroxyaldehydes or ketones or compounds which produce them on hydrolysis. They are structural components of many organisms. These include the fiber (cellulose) of plants, exoskeleton of some insects and the cell wall of microorganisms and also serve as the storage form of energy (glycogen) to meet the immediate energy demands of the body. The digestion of carbohydrates occurs briefly in mouth and largely in the intestine. The hydrolysis of glycosidic bonds is carried out by a group of enzymes called glycosidases. These enzymes are specific to the bond, structure and configuration of monosaccharide units.

Carbohydrates are the only nutrients for which the digestion begins in the mouth. During the process of mastication, salivary a-amylase (ptyalin) acts on starch randomly and cleaves α-1,4-glycosidic bonds. The absorption of sugars mostly takes place in the duodenum and upper jejunum of small intestine. Glucose is utilized as a source of energy, it is synthesized from non-carbohydrate precursors and stored as glycogen to release glucose as and when the need arises.

The important metabolic pathways are – glycolysis, gluconeogenesis, glycogenesis, glycogenolysis, hexose monophosphate shunt, uronic acid pathway etc. Glucose is oxidized in glycolysis, either in anaerobic (2 ATP formed) or aerobic (8 ATPformed) conditions, resulting

in the lormation of 2 moles ol lactate or pyruvate respectively. Acetyl CoA is produced from pyruvate which is completely oxidized in citric acid cycle, the final common oxidative pathway for all foodstuffs. The complete oxidation of one mole of glucose generates 38 ATP. Gluconeogenesis is the synthesis of glucose from noncarbohydrate precursors like amino acids (except leucine and lysine), lactate, glycerol, propionate etc. Glycogen is the storage form of glucose. The degradation of glycogen (glycogenolysis) in muscle meets the immediate fuel requirements, whereas the liver glycogen maintains the blood glucose level. Hexose monophosphate shunt (HMP shunt) is the direct oxidative pathway of glucose. It generates NADPH and pentoses, respectively required for the synthesis of lipids and nucleic acids. Glucose can be converted to fructose by sorbitol pathway. Amino sugars (glucosamine, galactosamine, mannosamine etc.), synthesized from Fructose 6-phosphate are essential components of glycosaminoglycans, glycolysis and glycoproteins.

4.14 SELF ASSESSMENT QUESTIONS

Q.1. Write an account of the digestion and absorption of carbohydrates.

Answer:----------

Q.2. Write about the important functions of carbohydrates.

Answer:----------

Q.3. Write about the Kreb's cycle.

Answer:----------

Q.4. Describe briefly the metabolism of glucose 6-phosphate.

Answer:----------

Q.5. Give an account of glycogen metabolism.

Answer:----------

Q.6. Describe the hexose monophosphate shunt and its significance.

Answer:----------

Q.7. Short notes:

i. Glycogenolysis

ii. Glycolysis

iii. Uronic acid pathway

Answer:----------

4.15 FURTHER READINGS

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UNIT-5 PROTEIN

Structure

5.1 INTRODUCTION

This unit covers the basic unit of proteins means amino acids function, sources and types of proteins. It also covers the basic digestions and absorptions of essential and nonessential amino acids. Protein is a macronutrient and one of the three essential nutrients found in food that the body needs in large amounts. Proteins are the polymers of L-α-amino acids. It is essential for the maintenance and building of body tissues and muscle. The straight chain amino acids are combined which gives primary structure of proteins. The spatial arrangement of two or more polypeptides or tertiary structures unites by different types of bond to form quarternary structure of protein.

Objectives

- Understand the nature and functions of proteins.
- Know about the types of amino acids and its importance.

- Understand the mechanism of digestion and absorption of protein.
- Define Antagonism, Imbalance and Toxicity and its examples.
- Study of Effects of Deficiency and Kwashiorkor

5.2 PROTEINS OVERVIEW

Proteins are categories in different types. The primary structure of proteins defined as covalent backbone structure of polypeptide chains. In this unit describes the primary, secondary, tertiary and quaternary structure of proteins. The chemical composition of proteins reveals that carbon, hydrogen, nitrogen, oxygen and rare sulfur are the chief elements while others such as phosphorous, iron, zinc and copper also may be part of proteins. Some protein contains only one peptide chain and some two or more. There are 20 amino acids which constitutes the proteins structure while arranged in special sequences.

5.2.1 SOURCES

The best animal sources are fish, seafood, chicken, beef, mutton, milk, meat, and eggs. Soy, quinoa, red beans or lentils, wholegrain rice or peanut butter, yogurt, Nuts and seeds are vegetable sources.

5.2.2 FUNCTIONS

Proteins perform a great variety of specialized and essential functions in the living cells. These functions may be broadly grouped as static (structural) and dynamic.

Structural functions

Perform brick and mortar roles and are primarily responsible for structure and strength of body. For example collagen and elastic found in bone matrix, vascular system and other organs and α-keratin present in epidermal tissues.

Dynamic functions : Proteins performing dynamic functions are appropriately regarded as the working horses of cell. Proteins acting as –

- Enzymes.
- Hormones.
- Blood clotting factors.
- Immunoglobulins.
- Membrane receptors and storage proteins.
- Besides their function in genetic control, muscle contraction and respiration etc.

5.2.3 DIGESTIONS AND ABSORPTIONS

The digestion and absorption are obtained from two sources – dietary and endogenous. Dietary proteins are denatured on cooking and therefore, easily digested. Proteins are degraded by a class of enzymes namely hydrolases- which specifically cleave the peptide bonds, hence known as peptidases. They are divided into two groups-

a) **Endopeptidases (proteases) :** which attack the internal peptide bonds and release peptide fragments, e.g. pepsin, trypsin.

b) **Exopeptidases :** which act on the peptide bonds of terminal amino acids. Exopeptidases are subdivided into carboxypeptidases (act on C-terminal amino acid) and amino peptidases (act on N-terminal amino acid).

The proteolytic enzymes responsible for the digestion of proteins are produced by the stomach, the pancreas and the small intestine. Proteins are not digested in the mouth due to the absence of proteases in saliva.

i. **Digestion by gastric secretion :** Protein digestion begins in the stomach. Gastric juice produced by stomach contains hydrochloric acid and a protease proenzyme pepsinogen. Hydrochloric acid performs two important functions – denaturation of proteins and killing of certain microorganisms. The denatured proteins are more susceptible to proteases for digestion. Pepsin is produced by the serous cells of the stomach as pepsinogen, the inactive zymogen or proenzyme. Pepsin A is the most predominant gastric protease which cleaves peptide bonds formed by amino groups of phenylalanine or tyrosine or leucine. Pepsin digestion of proteins results in peptides and a few amino acids which act as stimulants for the release of the hormone cholecystokinin from the duodenum. Rennin enzyme, also called chymosin, is found in the stomach of infants and children. It is involved in the curdling of milk. lt converts milk protein casein to calcium paracaseinate which can be effectively digested by pepsin. Rennin is absent in adults.

ii. **Digestion by pancreatic proteases :** The proteases of pancreatic juice are secreted as zymogens (proenzymes) and then converted to active forms. These processes are initiated by the release of two polypeptide hormones, namely cholecystokinin and secretin from the intestine. Trypsin, chymotrypsin and elastase are endopeptidases active at neutral pH. Gastric HCl is neutralized by pancreatic $NaHCO_3$ in the intestine and this creates favourable pH for the action of proteases. Trypsin cleaves the peptide bonds, the carbonyl (-CO-) group of which is contributed by arginine or lysine. The amino acid serine is essential at the active centre to bring about the catalysis of all the three pancreatic proteases, hence

these enzymes are referred to as serine proteases. The pancreatic carboxypeptidases (A and B) are metalloenzymes that are dependent on Zn^{2+} for their catalytic activity hence, also called Zn proteases. Carboxypeptidase B acts on peptide bonds of COOH- terminal amino acid, the amino group of which is contributed by arginine or lysine.

iii. **Digestion by small intestinal enzymes :** The luminal surface of intestinal epithelial cells contains aminopeptidases and dipeptidases. Aminopeptidase is a non-specific exopeptidase which repeatedly cleaves N-terminal amino acids one by one to produce free amino acids and smaller peptides. The dipeptidases act on different dipeptides to liberate amino acids.

The free amino acids, dipeptides and to some extent tripeptides are absorbed by intestinal epithelial cells. The di- and tripeptides, after being absorbed are hydrolysed into free amino acids in the cytosol of epithelial cells. The activities of dipeptidases are high in these cells. Therefore, after a protein meal, only the free amino acids are found in the portal vein. The small intestine possesses an efficient system to absorb free amino acids. L-Amino acids are more rapidly absorbed than D-amino acids. The transport of L-amino acids occurs by an active process (against a concentration gradient), in contrast to D-amino acids which takes place by a simple diffusion. Amino acids absorption mechanism is basically a Na^+ dependent active process linked with the transport of Na^+. As the Na^+ diffuses along the concentration gradient, the amino acid also enters the intestinal cell. Both Na^+ and amino acids share a common carrier and are transported together. The energy is supplied indirectly by ATP.

Another transport system to explain the mechanism of amino acid transfer across membrane in the intestine and kidney known as γ-glutamyl cycle or Meister cycle and involves a tripeptide namely glutathione (γ-glutamylcysteinylglycine). This cycle appears to be important for the metabolism of glutathione.

5.3 ESSENTIAL AND NONESSENTIAL AMINO ACIDS

The twenty amino acids are required for the synthesis of variety of proteins. Based on the nutritional requirements amino acids are grouped into two classes essential and nonessential.

Essential or indispensable amino acids

The amino acids which cannot be synthesized by the body and, therefore, need to be supplied through the diet are called essential amino acids. They are required for proper growth and maintenance of the individual. The ten amino acids essential for humans are – Arginine, Valine, Histidine, lsoleucine, Leucine, Lysine, Methionine, Phenylalanine,

Threonine, Tryptophan. Of the ten listed above, two amino acids namely Arginine and Histidine can be partly synthesized by adults and not by growing children, hence these are considered as semi-essential amino acids. Thus, 8 amino acids are absolutely essential while 2 are semi-essential.

Non-essential or dispensabte amino acids

The body can synthesize about 10 amino acids to meet the biological needs, hence they need not be consumed in the diet. These are followings

Glycine

Alanine

Serine

Cysteine,

Aspartate

Asparagines

Glutamate

Glutamine

Tyrosine

Proline

5.4 AMINO ACID INTERACTIONS

Amino acid interactions have been recognized as a nutritional phenomenon. Harper 1956 first categorized amino acid interactions as imbalances, antagonisms, and toxicities.

5.4.1 ANTAGONISM

Antagonisms have been defined as specific interactions in which the requirement for one essential amino acid, not necessarily the first limiting amino acid, is increased by the addition of a structurally related amino acid to the diet. Two well recognized examples are the lysine-arginine antagonisn in which excess dietary lysine increases the requirement for arginine and the branched chain amino acid antagonism involving leucine, isoleucine and valine in which an excess of one (or two) branched chain amino acids increases the requirement for the other branched chain amino acid(s). Growth depression can be overcome by supplementation with an amino acids structurally similar to the antagonist for e.g. Lysine and Arginine of structure similar. Excess of lysine→ growth depress →improve by addition of arginine.

One other interaction that could be categorized as an antagonism involves methionine, glycine and arginine. In this interaction excess arginine and glycine increase the requirement for methionine. Occurrence of antagonisms is more limited than that of imbalances because these interactions are more specific, influencing the requirements for only a few amino acids, they are likely to occur mainly in practical diets of unusual composition. For example, diets based on corn, contain relatively high proportions of leucine , yet dietary levels of isoleucine or valine generally appear sufficient to prevent an antagonism. The branched chain amino acid antagonism in poultry and swine has been observed only when large supplements of leucine have been added to practical or semi purified diets.

5.4.2 IMBALANCE

Imbalances occur when a diet that is limiting in two amino acids is supplemented with the second limiting amino acid or with all essential amino acids, except the first limiting amino acid. This results in depression of growth (and other measures of performance) which can only be corrected by supplementation of the imbalanced diet with the first limiting amino acid. In theory this applies to diets first limiting in any essential amino acid. Thus imbalance is the most common form of interaction.

Imbalances significantly impact upon nutrition in ways that are not always obvious. It was demonstrated that increased dietary protein increased the requirement for lysine and sulfur amino acids. The dietary requirement for lysine for chicks increased from 0.85% to 1.35% as the protein level increased from 20% to 40%. Excess amino acids cause a growth depression that can only be overcome by providing a higher dietary level of the first limiting amino acid. Thomas et al. (1975) determined whether lysine imbalance was practical significance in broiler diets. They did not observe a marked shift in lysine requirement as the protein content of the diet was increased over a smaller range from 23 to 27%. Nonetheless their data suggest that the requirement increased. In practice, therefore, one should consider that the requirement for the most limiting amino acid will increase as the dietary protein content increases. Imbalances also influence the assessment of amino acid availability by conventional growth assay. These assays involve a comparison of the growth of rats or chicks fed a basal diet limiting in the amino acid to be tested, The basal diet containing graded levels of the amino acid being tested (reference diets), or the basal diet supplemented with graded levels of the test feedstuff. Amino acid availability is calculated from the relative slopes of the response curves for animals fed the reference and test diets. The relative performance is greatly affected by the other amino acids in the test feedstuff. When these amino acids are also included as free amino acids in the reference diet they depress the response curve of the animals fed these diets, thereby improving the relative response of animals fed the test feedstuff. The depression is due to amino acid imbalance.

5.4.3 TOXICITY

Adverse effect of an amino acid in excess cannot be overcome by supplementation with another amino acid for example-

Methionine toxicity in pig and poultry: In pigs and poultry 40 g per kg diet of methionine showed most growth depression. Excess methionine in chicks also increases the requirements of the vitamin B_6. In calves, methionine toxicity leads to decreased food intake, depressed N retention and body weight loss.

Methionine toxicity in cats: Cats given DL- methionine (1 g/kg of body weight/day) developed severe hemolytic anemia with marked increase of methemoglobin (MetHb) concentration and Heinz-body formation at treatment-day 6 to 10. Excessive methionine intake leads to production of an intermediate of the methionine catabolism that may affect RBC directly as an intensive oxidizing agent, resulting in an excessive oxidation of hemoglobin to MetHb and Heinz-body formation.

Tryptophan toxicity: More amount of tryptophan are administered via oral or intraruminal, it produced respiratory distress and pulmonary leisons. This change happened by the enzyme oxidase, to form a reactive free radical which is having of damaging the tissue in the lung. Severity is reduced by supplementing tissue glutathione. Threonine depressed growth in chicks but not in pigs. Arginine more toxic to pig than fowl.

5.5 EFFECT OF DEFICIENCY OF PROTEINS

Protein deficiency or Protein-energy malnutrition (PEM) also called protein-calorie malnutrition (PCM). It is widely prevalent in the infants and pre-school children. Kwashiorkor and marasmus are the two extreme forms of protein-energy malnutrition.

5.5.1 MARASMUS

Marasmus literally means to waste. It mainly occurs in children under one year age. Marasmus is predominantly due to the deficiency of calories. This is usually observed in children given watery gruels (of cereals) to supplement the mother's breast milk. The symptoms of marasmus include growth retardation, muscle wasting (emaciation), anemia and weakness. A marasmic child does not show edema or decreased concentration of plasma albumin. This is a major difference to distinguish marasmus from kwashiorkor.

5.5.2 KWASHIORKOR

The term kwashiorkor was introduced by Cicely Williams (1933) to a nutritional disease affecting the people of Gold Coast (modern Ghane) in Africa. Kwashiorkor literally means sickness of the deposed child i.e. a disease the child gets when the next baby is born.

- **Occurrence and causes :** Kwashiorkor is predominantly found in children between 1-5 years of age. This is primarily due to insufficient intake of proteins, as the diet of a weaning child mainly consists of carbohydrates.
- **Clinical symptoms :** stunted growth, edema (particularly on legs and hands), diarrhea, discoloration of hair and skin, anemia, apathy and moon face.
- **Biochemical manifestations :** Kwashiorkor is associated with a decreased plasma albumin concentration (<2 g/dl against normal 3-4.5g/dl), fatty liver, deficiency of K^+ due to diarrhea. Edema occurs due to lack of adequate plasma proteins to maintain water distribution between blood and tissues. Disturbances in the metabolism of carbohydrate, protein and fat are also observed. Several vitamin deficiencies occur. Plasma retinol binding protein (RBP) is reduced. The immunological response of the child to infection is very low.
- **Treatment :** Ingestion of protein-rich foods or the dietary combinations to provide about 3-4 g of protein/kg body weight/day will control kwashiorkor. The treatment can be monitored by measuring plasma albumin concentration, disappearance of edema and gain in bodyweight.

5.6 SUMMARY

Protein is a macronutrient. It is one of the three essential nutrients found in food that the body needs in large amounts. The best sources are fish, seafood, chicken, soy, quinoa, and red beans. Proteins functions may be broadly grouped as static (structural) and dynamic. The digestion and absorption are obtained from two sources – dietary and endogenous. Proteins are degraded by a class of enzymes namely hydrolases- which specifically cleave the peptide bonds, hence known as peptidases. They are divided into two group- Endopeptidases and Exopeptidases. The twenty amino acids are required for the synthesis of variety of proteins. Based on the nutritional requirements amino acids are grouped into two classes essential and nonessential.The amino acids which cannot be synthesized by the body and, therefore, need to be supplied through the diet are called essential amino acids. The body can synthesize about 10 amino acids to meet the biological needs, hence they need not be consumed in the diet. Amino acid interactions have been recognized as a nutritional phenomenon. Harper 1956 first categorized amino acid interactions as imbalances, antagonisms, and toxicities. Protein deficiency or Protein-energy malnutrition (PEM) also called protein-calorie malnutrition (PCM). It is widely prevalent in the infants and pre-school children. Kwashiorkor and marasmus are the two extreme forms of protein-energy malnutrition.

5.7 SELF ASSESSMENT QUESTIONS

Q.1. Discuss the protein-energy malnutrition with special reference to kwashiorkor.

Answer:----------

Q.2. Define the essential and non essential amino acids.

Answer:----------

Q.3. What is antagonism and toxicity? Discuss briefly.

Answer:----------

Q.4. Describe briefly the digestion of proteins.

Answer:----------

Q.5. Write about the functions of Protein.

Answer:----------

Q.6. Classify amino acids on the basis of nutritional requirement.

Answer:----------

5.8 FURTHER READINGS

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UNIT-6 MINERALS AND VITAMINS

Structure

6.1 INTRODUCTION

Minerals are inorganic substances that play an important role in a variety of metabolic reactions as cofactors. Minerals perform several vital functions which are absolutely essential for the existence of the organism. These include calcification of bone, blood coagulation, neuromuscular irritability, acid-base equilibrium, fluid balance and osmotic regulation. The minerals are classified as principal elements and trace elements. The principal elements are required in amounts greater than 100 mg/day. The seven principal elements (macrominerals) are calcium, phosphorus, magnesium, sodium, potassium, chloride and sulfur.

The trace elements (microminerals) are required in amounts less than 100 mg/day. They are Iron, manganese, zinc, cobalt, fluorine, nickel etc.

Vitamins are essential dietary factors required in small amounts. These are organic compounds which cannot synthesize in human body but required for normal growth and development therefore vitamins needs to be supplied in diet. They are divided into two classses – water soluble (B complex & Vitamin C) and fat soluble (Vitamin A, D, E & K). Deficiency of one or more vitamins produces avitaminosis, symptoms are characteristic for particular vitamin.

Objectives

After going through the course of this unit student will be able to:

- Understand the nutritional importance of minerals.
- To know about the effect of deficiencies of these minerals.
- Studies about the Vitamins and their source of requirement.
- To know about the diseases caused due to deficiency of these Vitamins.

6.2 MINERALS OVERVIEW

Minerals are solid substances that are present in nature and can be made of one element or more elements combined together. They are called native elements. Instead, ordinary kitchen salt is a chemical compound that is called rock salt, which is a mineral formed of sodium and chlorine ions. Atoms, ions and molecules that form a mineral are present in the space in a tidy way and according to well-defined geometrical shapes, which are called crystal lattices. Minerals found in the Earth's crust include things like salt, coal, iron, ore, shale, and diamonds, just to name a few. While there are a number of elements on the periodic table that can be extracted from the Earth's crust. Minerals are usually solid, inorganic, have a crystal structure, and form naturally by geological processes. The study of minerals is called mineralogy

6.2.1 CALCIUM

It is the most abundant among the minerals in the body. About half of calcium present in blood is ionized and rest in unionized form.99% of calcium is present in the bones and teeth. A small fraction(1%) found outside the skeletal tissues, performs a wide variety of functions. Calcium taken in the diet in the form of calcium phosphate or carbonate. The best sources of calcium are Milk, egg, fish and vegetables.

Dietary requirements

Adult men and women – 800 mg/day

Women during pregnancy, – 1.5 g/day

lactation and post menopause

Children (1-18 yrs) – 0.8-1.2 g/day

The absorption of calcium mostly occurs in the duodenum by an energy dependent active process. It is influenced by several factors. The factors that increase the calcium absorption are vitamin D, parathyroid hormone, acidity (low pH), Lactose and amino acids such as lysine and arginine. The factors that decrease the calcium absorption are phytates and oxalates form insoluble salts, high content of dietary phosphate results in the formation of insoluble calcium phosphate prevents Ca uptake, alkaline condition and high content of dietary fiber.

Biochemical Functions

1. It requires for development of bones and teeth.
2. Calcium interacts with troponin C to trigger muscle contraction.
3. It plays a role in blood coagulation. Ionic calcium helps in the production of thromboplastin and in the conversion of prothrombin into thrombin.
4. It is necessary for the transmission of nerve impulse.
5. Calcium influences the membrane integrity and permeability and transport of water and several ions across it.
6. It is necessary for the direct activation of enzymes such as lipase, ATPase and succinate dehydrogenase.
7. Ca-calmodulin complex activates certain enzymes e.g. adenylate cyclase, Ca^{2+} dependent protein kinases.
8. Calcium is regarded as a second messenger for some hormonal action of e.g. epinephrine in liver glycogenolysis. It also serve as third messenger for some hormonal action for e.g. antidiuretic hormone (ADH) acts through cAMP and then calcium.
9. The release of certain hormones (insulin, PTH, calcitonin) from the endocrine glands is facilitated by calcium.
10. It regulates microfilament and microtubule mediated processes such as endocytosis, exocytosis and cell motility.
11. It acts on myocardium and prolongs systole.
12. Calcium is involved in cell to cell contact and adhesion of cells in a tissue.

Clinical Manifestation

Deficiency of calcium leads to rickets, osteoporosis and hyper excitability. Inadequate intake of calcium may result in hypertension.

Hypercalcaemia

Symptoms are : Lethargy, nausea, loss of appetite and tendency to fracture bones. It may occur in the following conditions:

- Hyperparathyroidism
- Multiple myeloma
- Metastatic carcinoma of bone
- Milk-alkali syndrome
- Treatment with drugs such as diuretics
- Hypervitaminosis D

Hypocalcaemia

It is observed in the following:

- Tetany. Calcium levels fall below 7 mg/dl.
- Hypoparathyroidism
- Fanconi's syndrome (disorder of tubular reabsorption)
- Acute pancreatitis
- Vitamin D deficiency
- Chronic renal failure.

6.2.2 PHOSPHORUS

Total body phosphate weighs about 1 kg, 80% of which is present in bone and teeth, while 10% is in muscles. The best sources are cheese, milk, nuts, eggs etc.

Dietary requirements

Adult men and women – 500 mg/day

Women during pregnancy, – 1.0 g/day

Children –400-600 mg/day

The absorption is mainly from jejunum and stimulated by parathormone (PTH) and vitamin D.

Biochemical Functions

1. It is essential for the development of bones and teeth.
2. It plays a central role for the formation and utilization of high-energy phosphate compounds e.g. ATP, GTP, creatine phosphate etc.
3. It is required for the formation of phospholipids, phosphoproteins and nucleic acids (DNA and RNA).
4. It is an essential component of several nucleotide coenzymes e.g. NAD^+, $NADP^+$, pyridoxal phosphate, ADP, AMP.
5. Several proteins and enzymes are activated by phosphorylation.
6. Phosphate buffer system is important for the maintenance of pH in the blood (around 7.4) as well as in the cells.

Clinical Manifestation

Deficiency of phosphorus results in osteomalacia, renal rickets and cardiac arrhythmia.

Hyperphosphataemia

It is observed in the following:

- Diabetes mellitus, starvation
- Renal insufficiency
- Hypothyroidism
- Hypervitaminosis D

Hypophosphataemia

It is observed in the following:

- Rickets
- Fanconi's syndrome
- Intake of drugs such as antacids

6.2.3 MAGNESIUM

It is found both in intracellular and extracellular fluids. The adult body contains about 20 g magnesium, 70% of which is found in bones with calcium and phosphorus. The remaining 30% occurs in the soft tissues and body fluids. The best sources are cereals, nuts, beans, vegetables, meat, milk and fruits.

Dietary requirements

Adult man – 350 mg/day

Adult women – 300 mg/day

Magnesium is absorbed by the intestinal cells through a specific carrier system. Vitamin D, PTH, high protein intake and neomycin therapy are the factors which increase the absorption of magnesium. Factors that decrease the absorption are increased calcium intake, fatty acids, phytates and phosphate.

Biochemical Functions

1. It is required for the formation of bones and teeth.
2. It serves as a cofactor for several enzymes requiring ATP e.g. hexokinase, glucokinase, phosphofructokinase, adenylate cyclase.
3. It is necessary for proper neuro-muscular function. Low magnesium level lead to neuromuscular irritability.

Clinical Manifestation

Deficiency of magnesium causes muscular tremor, confusion, vasodilation and hyperirritability.

Hypermagnesaemia

It is observed in the following:

- Diabetes mellitus
- Acute Renal failure
- Hypothyroidism

Hypomagnesaemia

It is observed in the following:

- Hyperthyroidism
- Chronic alcoholism
- Malnutrition
- Prolonged use of diuretics
- Portal cirrhosis

6.2.4 IRON

Iron is present in all organisms and in all cells. It is a transient metal capable of being present in Fe^{2+} (ferrous) and Fe^{3+} (ferric) forms. The total content in an adult body is 3-5 g. about 70% occurs in the

erythrocytes of blood as a constituent of hemoglobin. At least 5% of body iron is present in myoglobin of muscle. Heme is the most predominant iron containing substance. It is a constituent of several proteins/enzymes (hemoproteins) – hemoglobin, myoglobin, cytochromes, xanthine oxidase, catalase, tryptophan pyrrolase, peroxidase. Certain other proteins contain non-heme iron e.g. transferrin, ferritin, hemosiderin.

Dietary requirements

Adult man – 10 mg/day

Menstruating woman −18 mg/day

Pregnant and lactating woman – 40 mg/day

The best sources are Organ meats (liver, heart, kidney), leafy vegetables, pulses, cereals, milk etc. It is mainly absorbed in the stomach and duodenum. Acidity, ascorbic acid and cystein promote iron absorption.

Biochemical Functions

1. Hemoglobin and myoglobin are required for the transport of O_2 and CO_2**.**
2. Cytochromes and certain non-heme proteins are necessary for electron transport chain and oxidative phosphorylation.
3. Peroxidase, the lysosomal enzyme is required for phagocytosis and killing of bacteria by neutrophils.
4. Iron is associated with effective immuno-competence of the body.

Clinical Manifestation

- Iron deficiency anemia
- Hemosiderosis is a disorder due to excessive iron in the body
- Hemochromatosis is a disease in which iron is directly deposited in the tissues.

6.2.5 IODINE

It is an essential component of thyroid hormones. The total body contains about 20 mg iodine, 80% being present in the thyroid gland. Muscle, salivary glands and ovaries also contain some amount of iodine.

Dietary requirements

Adults – 100-150 µg/day

Pregnant woman – 200 µg/day

The best sources are sea foods, drinking water, vegetables and fruits. They are absorbed from the small intestine as iodide. About 80% stored in the organic form as iodothyroglobulin in the thyroid gland.

Biochemical Functions

- It is required for the synthesis of thyroid hormones T_3 (triiodothyronine) and T_4 (thyroxine) which carries out the following functions:
- Increases metabolism and oxygen consumption of tissues. Increase basal metabolic rate.
- Increases conversion of glycogen to glucose leading to increase in blood sugar level.
- Increase heart rate.
- Depletes calcium and phosphorus of bones and increases urinary calcium excretion.

Clinical Manifestation

Iodine deficiency

- Abortions
- Congenital heart anomalies
- Mental retardation and neurological defects

Hyperthyroidism

- Grave's disease- increased production of thyroid-stimulating immunoglobulin (TSI) that activates TSH receptor, LATS (long acting thyroid stimulating factor).
- Hashimoto's disease due to destruction of thyroid tissues, effects of antithyroid antibiotics, overproduction of TSH and hyperthyroidism.

6.2.6 ZINC

The total content of zinc in the body is about 2.3 g. High concentrations of zinc are found in choroid of eyes, prostrate, kidneys, liver and muscles.

Dietary requirements

Lactation – 10 mg

Pregnancy – 5 mg

The best sources are sea foods, meat, liver, eggs, vegetables and whole gram. They are absorbed mainly in the duodenum. Zinc absorption

appears to be dependent on a transport protein-metallothionein. Phytate, calcium, copper and iron interfere while small peptides and amino acids promote Zinc absorption.

Biochemical Functions

1. Zinc is an essential component of several enzymes e.g. carbonic anhydrate, alcohol dehydrogenase, alkaline phosphatase, carboxyl peptidase, superoxide dismutase.
2. It may be regarded as an antioxidant since the enzyme superoxide dismutase protects the body against free radical damage.
3. It require for the storage and secretion of insulin from the β-cells of pancreas.
4. It enhances cell growth and division require for wound healing.
5. Gustin, is a zinc containing protein of the saliva, which is important for taste sensation.
6. It is necessary to maintain the normal level of Vitamin A in serum. It promotes the synthesis of retinol binding protein.

Clinical Manifestation

Zinc deficiency

- Acrodermatitis enteropathica is a rare inherited metabolic disease.
- Growth retardation, poor wound healing, anernia.
- loss of appetite, taste sensation, impaired spermatogenesis.
- Myocardial infarction, malignancies, alcoholism, liver disease and malabsorption.
- Inhalation of zinc oxide leads to acute illness and headache. Poisoning due to ingestion from containers causes nausea and fever.

6.2.7 COPPER

The body contains about 100 mg copper distributed in different organs. It is transported in the bound form as ceruloplasm. It is stored in liver, muscles and bones of the body.

Dietary requirements

Adults	2-3 mg/day
Infants and children	0.5-2 mg/day

The best sources are liver, kidney, meat, egg yolk, cereals, nuts and green leafy vegetables. Milk is a poor source. About dietary copper is absorbed, mainfy in the duodenum. Metallothionein is a transport protein that facilitates copper absorption. Phytate, zinc and molybdenum decrease copper uptake.

Biochemical Functions

1. Copper is an essential constituent of several enzymes and involved in several metabolic reactions. The enzymes are cytochrome oxidase, catalase, tyrosinase, superoxide dismutase, ascorbic acid etc.
2. It is necessary for the synthesis of hemoglobin needed for heme synthesis. Cu is a constituent of ALA (aminolerulinic acid) synthase.
3. Ceruloplasmin serves as ferroxidase and is involved in the conversion of iron from Fe^{+2} to Fe^{+3} in which form iron (transferrin) is transported in plasma.
4. It is necessary for the synthesis of melanin and phospholipids.
5. It is required for bone formation and maintenance of myelin.
6. It plays a important role in lipid and amino acid metabolism.

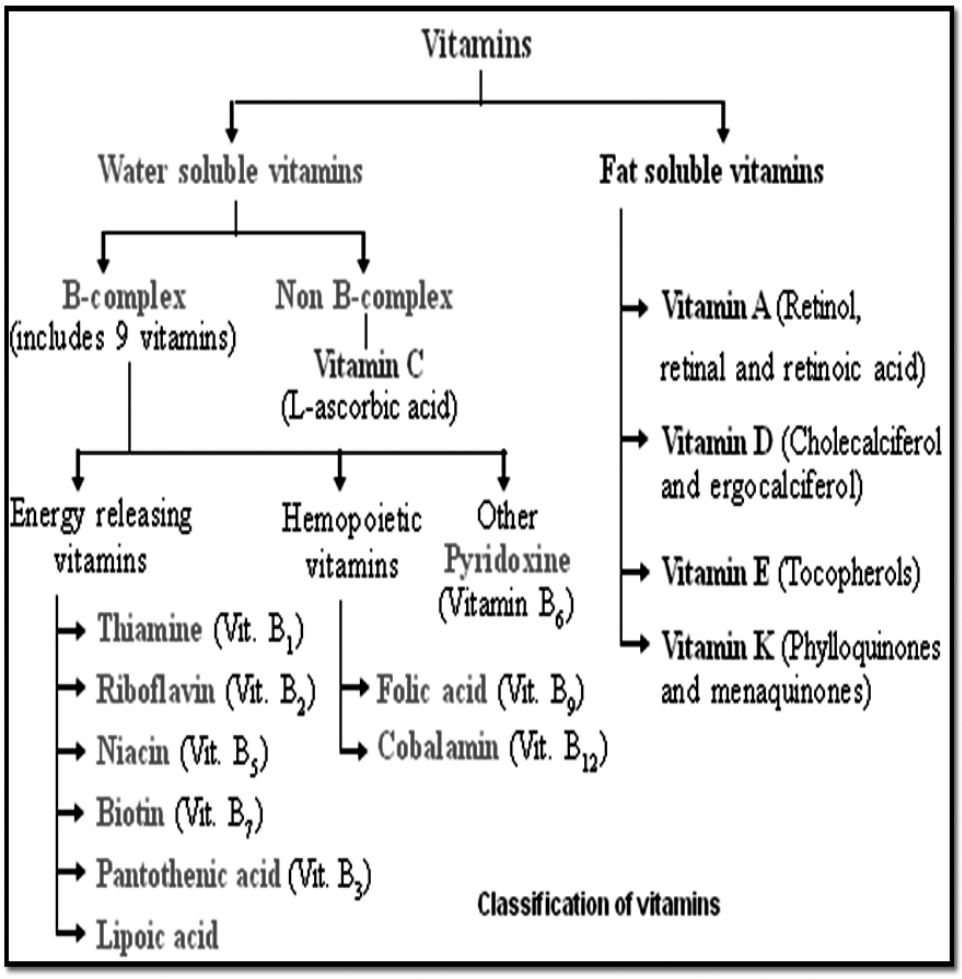
Clinical Manifestation

Copper deficiency causes :

- Demineralization of bones,demyelination of neural tissue, anemia, fragility of arteries, myocardial fibrosis, hypopigmentation of skin, greying of hair.
- Menke's disease a genetic disorder: defect in the intestinal absorption of copper.
- Wilson's disease (hepatolenticular degeneration): lt is a rare disorder of abnormal copper metabolism. This may lead to hepatic cirrhosis and brain necrosis. Copper deposition in kidney causes renal damage.

Vitamins

Vitamins are organic compounds required in the diet in small amounts to perform specific biological functions for normal maintenance of optimum growth and health of the organism.



Classification of vitamins

6.3.1 VITAMIN A

The fat soluble vitamin A is present only in foods of animal origin. However, its provitamins carotenes are found in plants. The term vitamin A is collectively used to represent many structurally related and biologically active molecules The term retinoids is often used to include the natural and synthetic forms of vitamin A. Retinol, retinal and retinoic acirl arc regarded as vitamers of vitamin A.

Retinol (vitamin A alcohol) is a primary alcohol containing β-ionone ring. The side chain has two isoprenoid units, four double bonds and one hydroxyl group. Retinal (vitamin A aldehyde) is an aldehyde form obtained by the oxidation of retinol. Retinoic acid (vitamin A acid) is produced by the oxidation of retinal and β-Carotene (provitamin A) is found in plant foods.

Dietary sources :

The best sources are liver, kidney, egg yolk, milk, cheese, butter. Fish (cod or shark) liver oils are very rich in vitamin A. Vegetable sources contain the provitamin A-carotenes. Yellow and dark green vegetables and fruits are good sources of carotenes e.g. carrots, spinach, amaranths' , pumpkins, mango, papaya etc.

Vitamin A and its provitamins are absorbed in the small intestine. The liver contains almost all the body stores of vitamin.

Daily requirement :

Man 1000 retinol (= 3,500 IU)

Woman 800 retinol (= 2,500 IU)

Functions :

1. Role in vision (Wald's visual cycle or rhodopsin cycle.
2. Vitamin A is essential to maintain healthy epithelial tissue.
3. Retinol and retinoic acid function almost like steroid hormones. They regulate the protein synthesis and thus are involved in the cell growth and differentiation.
4. Retinol and retinoic acid are involved in the synthesis of transferrin, the iron transport protein.
5. Retinyl phosphate synthesized from retinol is necessary for the synthesis of certain glycoproteins which are required for growth and mucus secretion.
6. Carotenoids (most important β-carotene) function as antioxidants and reduce the risk of cancers initiated by free radicals and strong oxidants. β-Carotene is helpful to prevent heart attacks.
7. Cholesterol synthesis requires vitamin A.
8. Vitamin A is considered to be essential for the maintenance of proper immune system to fight against various infections.

Deficiency causes :

- Night blindness (nyctalopia): difficulty to see in dim light since the dark adaptation time is increased. Prolonged deficiency irreversibly damages a number of visual cells.
- Xerophthalmia characterized by dryness in conjunctiva and cornea, and keratinization of epithelial cells. White triangular plaques known as Bitot's spots are seen in certain areas of conjunctiva. lf this condition persisits for a long time,corneal ulceration and degeneration occur. This results in the destruction of cornea, a condition referred to as keratomalacia, causing total blindness.
- Vitamin A deficiency results in growth retardation due to impairment in skeletal formation.
- The reproductive system is adversely affected in vitamin A deficiency. Degeneration of germinal epithelium leads to sterility in males.

- The skin becomes rough and dry. Keratinization of epithelial cells of gastrointestinal tract, urinary tract and respiratory tract is noticed. This leads to increased bacterial infection.
- Vitamin A deficiencv is associated with formation of urinary stones.
- **Hypervitaminosis A:** Total serum vitamin A level (normal 20-50 µg/dl) is elevated in hypervitaminosis A. Excessive consumption of vitamin A leads to toxicity. The symptoms include dermatitis (drying and redness of skin), enlargement of liver, skeletal decalcification, tenderness of long bones, loss of weight, irritability, loss of hair, joint pains etc.

6.3.2 B-COMPLEX

As the building blocks of a healthy body, B vitamins have a direct impact on your energy levels, brain function, and cell metabolism. Vitamin B complex helps prevent infections and helps support or promote cell health growth of red blood cells. It is group of water-soluble vitamins that are found especially in yeast, seed germs, eggs, liver and flesh, and vegetables.

Thiamine (B_1)

Thiamine (anti-beri-beri or antineuritic vitamin) is water soluble. lt has a specific coenzyme/ thiamine pyrophosphate (TPP) which is mostly associated with carbohydrate metabolism. Thiamine contains a pyrimidine ring and a thiazole ring held by a methylene bridge . Thiamine is the only natural compound with thiazole ring. The alcohol (OH) group of thiamine is esterfied with phosphate (2 moles) to form the coenzyme, thiamine pyrophosphate (TPP or cocarboxylase). The pyrophosphate moiety is donated by ATP and the reaction is catalysed by the enzyme thiamine pyrophosphate transferase.

Dietary sources :

Cereals, pulses, oil seeds, nuts and yeast are good sources. Thiamine is mostly concentrated in the outer layer (bran) of cereals. Vitamin B, is also present in animal foods like pork, liver, heart, kidney, milk etc.

Functions :

1. The enzyme pyruvate dehydrogenase catalyses (oxidative decarboxylation) the irreversible conversion of pyruvate to acetyl CoA.
2. α-Ketoglutarate dehydrogenase is an enzyme of the citric acid cycle.

3. Thiamine pyrophosphate plays an important role in the transmission of nerve impulse.

4. The branched chain α-keto acid dehydrogenase (decarboxylase) catalyses the oxidative decarboxylation of branched chain amino acids (valine, leucine and isoleucine) to the respective keto acids.This enzyme also requires thiamine pyrophosphate.

5. Transketolase is an enzyme of the hexose monophosphate shunt, which is dependent on thiamine pyrophosphate.

   a. Daily requirement:

   b. Adult person – 1-1.5 mg/day

   c. Children – 0.7-1.2 mg/day

Vitamin B_1 Deficiency causes :

- **Beri-Beri**: In adults two types of beri-beri occur. lnfantile beriberi is also seen.
- **Wet beri-beri** : This is characterized by edema of legs, face, trunk and serous cavities. breathlessness and palpitation. The calf muscles are slightly swollen. The systolic blood pressure is elevated while diastolic is decreased. Fast and bouncing pulse is observed.
- **Dry beri-beri** : This is associated with neuro- logical manifestations resulting in peripheral neuritis. Edema is not commonly seen. The muscles become progressively weak and walking becomes difficult.
- **Infantile beri-beri :** characterized by sleeplessness, restlessness, vomiting, convulsions and bouts of screaming that resemble abdominal colic.
- Carbohydrate metabolism is impaired. Accumulation oI pyruvate occurs in the tissues which is harmful. Pyruvate concentration in plasma is elevated and it is also excreted in urine.
- Pyruvate accumulation in brain results in disturbed metabolism that may be responsible for polyneuritis
- Thiamine deficiency leads to impairment in nerve impulse transmission due to lack of thiamine pyrophosphate.
- The transketolase activity in erythrocytes is decreased. Measurement of RBC transketolase activity is a reliable diagnostic test to assess thiamine deficiency
- Wernicke-Korsakoff syndrome: This is a disorder mostly seen in chronic alcoholics. It is characterized by loss of memory, apathy and a rhythmical to and formation of the eye balls.

Riboflavin (B_2)

Riboflavin through its coenzymes takes part in a variety of cellular oxidation-reduction reactions. Riboflavin contains 6,7-dimethyl isoalloxazine (a heterocyclic 3 ring structure) attached to D-ribitol by a nitrogen atom. Ribitol is an open chain form of sugar ribose with the aldehyde group (CHO) reduced to alcohol (CH2OH). Riboflavin is stable to heat but sensitive to light. Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) are the two coenzyme forms of riboflavin.

Dietary sources :

The best sources are Milk and milk products, meat, eggs, liver, kidney. Cereals, fruits, vegetables and fish are moderate sources.

Daily requirement:

Adult person – 1.2-1.7 mg/day

Functions:

1. The flavin coenzymes participate in many redox reactions responsible for energy production.
2. Enzymes that use flavin coenzymes (FMN or FAD) are called flavoproteins. Many flavoproteins contain metal atoms (iron, molybdenum etc.) which are known as metalloflavoproteins. The coenzymes, FAD and FMN are associated with certain enzymes involved in carbohydrate, lipid, protein and purine metabolisms besides the electron transport chain.

Vitamin B_2 Deficiency causes:

- Cheilosis (fissures at the corners of the mouth).
- Glossitis (tongue smooth and purplish).
- Dermatitis.

Niacin (vitamin $B_{3)}$

Niacin or nicotinic acid is also known as pellagra preventive factor. The coenzymes of niacin (NAD^+ and $NADP^+$) can be synthesized by the essential amino acid, tryptophan. Niacin is a pyridine derivative. Structurally, it is pyridine3–carboxylic acid. The amide form of niacin is known as niacinamide or nicotinamide.

Dietary sources :

The rich sources are liver, yeast, whole grains, cereals, pulses like beans and peanuts. Milk, fish, eggs and vegetables are also good source.

Daily requirement :

Adult person – 15-20 mg/day

Children – 10-15mg/day

Functions :

1. The coenzymes NAD^+ and $NADP^+$ are involved in a variety of oxidation-reduction reactions.
2. A large number of enzymes (about 40) belonging to the class oxidoreductases are dependent on NAD^+ or $NADP^+$.
3. NAD^+ or $NADP^+$ participate in almost all the metabolisms (carbohydrate, lipid, protein etc.).
4. NADH produced is oxidized in the electron transport chain to generate ATP. NADPH is also important for many biosynthetic reactions as it donates reducing equivalents.

Vitamin B_3 causes :

Pellagra: The symptoms of disease are -

Dermatitis : (inflammation of skin) is usually found in the areas of the skin exposed to sunlight (neck, dorsal part of feet, ankle and parts of face).

Diarrhea : in the form of looses tools, often with blood and mucus. Prolonged diarrhea leads to weight loss.

Dementia : associated with degeneration of nervous tissue. The symptoms of dementia include anxiety, irritability, poor memory, insomnia(sleeplessness) etc.

Pyridoxine (vitamin B_6)

Vitamin B_6 is used to collectively represent the three compounds namely pyridoxine, pyridoxal and pyridoxamine (the vitamers of B_6). Vitamin B_6 compounds are pyridine derivatives. They differ from each other in the structure of a functional group attached to 4th carbon in the pyridine ring. Pyridoxine is a primary alcohol, pyridoxal is an aldehyde form while pyridoxamine is an amine. The active form of vitamin B_6 is the coenzyme pyridoxal phosphate (PLP).

Dietary sources

Good animal sources are egg yolk, fish, milk, meat. Wheat, corn, cabbage, roots and tubers are good vegetable sources.

Daily requirement :

Adult person – 2-2.2 mg/day

Functions :

1. Transamination : Pyridoxal phosphate is involved in the transamination reaction converting amino acids to keto acids. The keto acids enter the citric acid cycle and get oxidized to generate

energy. It is an energy releasing vitamin which integrates carbohydrate and amino acid metabolisms.

2. Decarboxylation : Some of the α-amino acids undergo decarboxylation to form the respective amines.
3. Pyridoxal phosphate is required for the synthesis of δ-amino levulinic acid, the precursor for heme synthesis.
4. Pyridoxal phosphate plays an important role in the metabolism of sulfur containing amino acids. Transsulfuration (transfer of sulfur) from homo-cysteine to serine occurs in the synthesis of cysteine.
5. Deamination of hydroxyl group containing amino acids requires pyridoxal phosphate.
6. Serine is synthesized from glycine by a pyridoxal phosphate dependent enzyme hydroxymethyltransferase.
7. Pyridoxal phosphate is needed for the absorption of amino acids from the intestine.
8. Adequate intake of vitamin B_6 is useful to prevent hyperoxaluria and urinary stone formation.

Vitamin B_6 deficiency causes :

Pyridoxine deficiency is associated with neurological symptoms such as depression, irritability, nervousness and mental confusion. Convulsions and peripheral neuropathy are observed in severe deficiency. Decrease in hemoglobin levels, associated with hypochromic microcytic anaemia due to a reduction in heme production. Xanthurenic acid, produced in high quantities is excreted in urine.

BIOTIN (Vitamin B_7)

Biotin (formerly known as anti-egg white injury factor, vitamin B_7 or vitamin H) is a sulfur containing B-complex vitamin. lt directly participates as a coenzyme in the carboxylation reactions. Biotin is a heterocyclic sulfur containing monocarboxylic acid. The structure is formed by fusion of imidazole and thiophene rings with a valeric acid side chain. It is covalently bound to ε-amino group of lysine to form biocytin in the enzymes. Biocytin may be regarded as the coenzyme of biotin

Dietary sources :

The rich sources are liver, kidney, egg yolk, milk, tomatoes, grains etc.

Daily requirement :

Adult person – 100-300 mg/day

Functions :

1. Biotin serves as a carrier of CO_2 in carboxylation reactions.

2. Gluconeogenesis and citric acid cycle : The conversion of pyruvate to oxaloacetate by biotin dependent pyruvate carboxylase is essential for the synthesis of glucose from many non-carbohydrate sources.

3. Fatty acid synthesis : Acetyl CoA is the starting material for the synthesis of fatty acids.

4. Propionyl CoA is produced in the metabolism of certain amino acids (valine, isoleucine, threonine etc.) and degradation of odd chain fatty acids. lts further metabolism is dependent on biotin.

Biotin deficiency causes :

- Anemia, loss of appetite, nausea, dermatitis, glossitis etc.
- Depression, hallucinations, muscle pain.
- Destruction of intestinal flora due to prolonged use of drugs such as sulfonamides.
- High consumption of raw eggs. The raw egg white contains a glycoprotein-avidin, which tightly binds with biotin and blocks its absorption from the intestine.

Pantothenic acid (vitamin B_5)

Pantothenic acid formerly known as chick anti-dermatitis factor (or filtrate factor) is widely distributed in nature. lt's metabolic role as coenzyme A is also widespread. Pantothenic acid consists of two components, pantoic acid and β-alanine, held together by a peptide linkage.

Dietary sources :

The rich sources are egg, liver, meat, yeast, milk etc.

Daily requirement :

Adult person – 5-10 mg/day

Functions :

1. The functions of pantothenic acid are exerted through coenzyme A or CoA (A for acetylation). Coenzyme A is a central molecule involved in all the metabolisms (carbohydrate, lipid and protein). lt plays a unique role in integrating various metabolic pathways.

2. Coenzyme A serves as a carrier of activated acetyl or acyl groups (as thiol esters). This is comparable with ATP which is a carrier of activated phosphoryl groups.

3. Coenzyme A may be regarded as a coenzyme of metabolic integration, since acetyl CoA is a central molecule for a wide variety of biochemical reactions.

4. Succinyl CoA is also involved in many reactions, including the synthesis of porphyrins of heme.

5. Pantothenic acid itself is a component of fatty acid synthatase complex and is involved in the formation of fatty acids.

Deficiency causes :

- Burning feet syndrome (pain and numbness in the toes, sleeplessness, fatigue etc.)
- Anemia, fatty liver, decreased steroid synthesis etc.

FOLIC ACID (Vitamin B_9)

Folic acid or folacin (Latin: folium-leaf) is abundantly found in green leafy vegetables. lt is important for one carbon metabolism and is required for the synthesis of certain amino acids, purines and the pyrimidine-thymine.

Folic acid consists of three components pteridine ring, p-amino benzoic acid (PABA) and glutamic acid (1 to 7 residues). Folic acid mostly has one glutamic acid residue and is known as pteroyl-glutamic acid (PGA). The active form of folic acid is tetrahydrofolate (THF or FH_4). lt is synthesized from folic acid by the enzyme dihydrofolate reductase.

Dietary sources :

The rich sources are green leafy vegetables, whole grains, cereals, liver, kidney, yeast and eggs.

Daily requirement :

Adult person – 200 μg /day

Pregnant women – 400 μg /day

Lactating women – 300 μg /day

Functions :

Tetrahydrofolate (THF or FH_4) the coenzyme of folic acid, is actively involved in the one carbon metabolism. THF serves as an acceptor or donor of one carbon units (formyl, methyl etc.) in a variety of reactions involving amino acid and nucleotide metabolism.

Folic acid deficiency causes :

- Decreased production of purines and dTMP is observed which impair DNA synthesis. Due to block in DNA synthesis, the

maturation of erythrocytes is slowed down leading to macrocytic RBC.

- Macrocytic anemia (abnormally large RBC) associated with megaloblastic changes in bone marrow.
- In pregnant women may cause neural defects in the fetus.
- Formiminoglutamate (FIGLU) accumulates and is excreted in urine.

COBALAMIN (Vitamin B_{12})

Vitamin B_{12} is also known as anti-pernicious anemia vitamin. lt is a unique vitamin, synthesized by only microorganisms and not by animals and plants. The empirical formula of vitamin B_{12} (cyanocobalamin) is $C_{63}H_{90}N_{14}$ $O_{l4}PCo$. The structure of vitamin B_{12} consists of a corrin ring with a central cobalt atom. There are two coenzyme forms of vitamin B_{12}

a. 5'-Deoxyadenosyl cobalamin, cyanide is replaced by 5' deoxyadenosine forming an unusal carbon cobalt bond.

b. Methylcobalamin in which cyanide is replaced by methyl group.

Dietary sources :

Foods of animal origin are the only sources for vitamin B12. The rich sources are liver, kidney, milk, curd, eggs, fish, pork and chicken. Curd is a better source than milk, due to the synthesis of B_{12} by *Lactobacillus*.

Daily requirement :

Adult person – 3 µg /day

Pregnant & Lactating women – 4 µg /day

Children – 0.5-1.5 µg /day

Functions :

1. Synthesis of methionine from homocysteine: Vitamin B_{12}, as methylcobalamin is used in this reaction. This is an important reaction involving N^5-methyl tetrahydrofolate from which tetrahydrofolate is liberated (enzyme-homocysteine methyltransferase or methionine synthase).

2. lsomerization of methylmalonyl CoA to succinyl CoA : The degradation of odd chain fatty acids, certain amino acids (valine, isoleucine etc.) and pyrimidines (thymine and uracil) produce directly or through the mediation of propionyl CoA, an important compound methylmalonyl CoA. This is converted by the enzyme methylmalonyl CoA mutase to succinyl CoA in the presence of B_{12} coenzyme, deoxyadenosyl cobalamin.

Deficiency causes :

- Pernicious anemia : characterized by low hemoglobin levels, decreased number of erythrocytes and neurological manifestations.
- Neuronal degeneration and demyelination of nervous system: symptoms include paresthesia (numbness and tingling) of fingers and toes, confusion, loss of memory and psychosis.

6.3.3 VITAMIN C (ASCORBIC ACID)

Vitamin C is a water soluble versatile vitamin. It plays an important role in human health and disease. Ascorbic acid is a hexose (6 carbon) derivative and closely resembles monosaccharides in structure (Fig.7.15). The acidic property of vitamin C is due to the enolic hydroxyl groups.

Dietary sources :

Citrus fruits, gooseberry (amla), guava/ green vegetables (cabbage, spinach), tomatoes, potatoes are rich in ascorbic acid. High content of vitamin C is found in adrenal gland and gonads. M ilk is a poor source of ascorbic acid.

Vitamin C is rapidly absorbed from the intestine. lt is not stored in the body to a significant extent. Ascorbic acid is excreted in urine as such, or as its metabolites-diketogulonic acid and oxalic acid.

Functions :

1. Collagen formation : It plays the role of a coenzyme in hydroxylation of proline and lysine while protocollagen is converted to collagen.
2. Bone formation: It is required for bone formation.
3. Tyrosine metabolism: It is required for the oxidation of p-hydroxy phenylpyruvate.
4. Folic acid metabolism: The active form of the vitamin folic acid is tetrahydrofolate(F H_4). Vitamin C is needed for the formation of FH_4 (enzyme-folic acid reductase).
5. Ascorbic acid is a strong antioxidant. lt spares vitamin A, vitamin E, and some B-complex vitamins from oxidation.
6. Vitamin C enhances the synthesis of immunoglobulins (antibodies) and increases the phagocytic action of leucocytes.
7. Vitamin C reduces the risk of cataract, cancer, and coronary heart diseases.
8. Synthesis of corticosteroid hormones: Adrenal gland possesses high levels of ascorbic acid, particularly in periods of stress. lt is

necessary for the hydroxylation reactions in the synthesis of corticosteroid hormones.

9. lron and hemoglobin metabolism : Ascorbic acid enhances iron absorption by keeping it in the ferrous form. Vitamin C is useful in the reconversion of methemoglobin to hemoglobin.The degradation of hemoglobin to bile pigments requires ascorbic acid.

Daily requirement :

Adult person - 60-70 mg/day.

Deficiency causes :

Scurvy : This disease is characterized by spongy and sore gums, loose teeth, anemia, swollen joints, fragile blood vessels, decreased immunocompetence, delayed wound healing, sluggish hormonal function of adrenal cortex and gonads, haemorrhage, osteoporosis etc.

6.3.4 VITAMIN D

Vitamin D is a fat soluble vitamin, resembles sterols in structure and functions like a hormone. It is also regarded as sun-shine vitamin. The synthesis of vitamin D_3 in the skin is proportional to the exposure to sunlight. Dark skin pigment (melanin) adversly influences the synthesis of cholecalciferol. Ergocalciferol (vitamin D_2) is formed from ergosterol and is present in plants. Cholecalciferol (vitamin D_3) is found in animals. Both the sterols are similar in structure except that ergocalciferol has an additional methyl group and a double bond. Ergocalciferol and cholecalciferol are sources for vitamin D activity and are referred to as provitamins. Vitamin D is absorbed in the small intestine for which bile is essential. Through lymph, vitamin D enters the circulate ion bound to plasma a2-globulin and is distributed throughout the body. Liver and other tissues stores mall amounts of vitamin D.

Dietary sources

Best sources are fatty fish, fish liver oils, egg yolk etc. Vitamin D can be provided to the body in three ways: Exposure of skin to sunlight for synthesis of vitamin D; Consumption of natural foods and by irradiating foods (like yeast) that contain precursors of vitamin D and fortification of foods (milk, butter etc.).

Daily requirement :

400 IU (International Units) or 10 mg / day

200 IU or 5 mg / day in India (Due to Good sunlight)

Functions :

1. Calcitriol(1,25-DHCC) is the biologically active form of vitamin D . lt regulates the plasma levels of calcium and phosphate.

2. Calcitriol increases the intestinal absorption of calcium and phosphate.

3. In the osteoblasts of bone, calcitriol stimulates calcium uptake for deposition as calcium phosphate.

4. Calcitriol is also involved in minimizing the excretion of calcium and phosphate through the kidney, by decreasing their excretion and enhancing reabsorption.

Deficiency causes :

- Rickets : characterized by bone deformities due to incomplete mineralization, resulting in soft and pliable bones and delay in teeth formation. The weight-bearing bones are bent to form bow-legs. Plasma level of calcitriol is decreased and alkaline phosphatase activity is elevated.
- Osteomalacia (adult rickets): demineralization of the bones occurs, increasing their susceptibility to fractures.
- Renal rickets: due to decreased synthesis of calcitriol in kidney.

Hypervitaminosis D

Vitamin D is stored mostly in liver and slowly metabolised. Vitamin D is the most toxic in overdoses (10-100 times RDA). Toxic effects of hypervitaminosis D include demineralization of bone (resorption) and increased calcium absorption from the intestine, leading to elevated calcium in plasma (hypercalcemia). Prolonged hypercalcemia is associated with deposition of calcium in many soft tissues such as kidney and arteries which may lead to formation of stones in kidneys (renal calculi). High consumption of vitamin D is associated with loss of appetite, nausea, increased thirst, loss of weight etc.

6.3.5 VITAMIN E

Vitamin E (tocopherol) is a naturally occurring antioxidant. lt is essential for normal reproduction in many animals, hence known as anti-sterility vitamin. Vitamin E is the name given to a group of tocopherols and tocotrienols. About eight tocopherols (vitamin E vitamers) have been identified- α, β, γ, δ etc. Among these, α-tocopherol is the most active. The tocopherols are derivatives of 6-hydroxy chromane (tocol) ring with isoprenoid (3 units) side chain. The antioxidant property is due to the chromane ring.

Dietary sources

Many vegetable oils are rich sources of vitamin E. e.g. wheat germ oil, cotton seed oil, peanut oil, corn oil and sunflower oil. It is also present in meat, milk, butter and eggs. Vitamin E is absorbed along with fat in the small intestine. Bile salts are necessary for the absorption. In the liver, it is

incorporated into lipoproteins (VLDL and LDL) and transported. It stored in adipose tissue, liver and muscle.

Daily requirement :

Man 10 mg (= 15 IU) α-tocopherol

Woman 8 mg (= 12 IU) α-tocopherol

Functions :

Most of the functions of vitamin E are related to its antioxidant property.

1. It is essential for the membrane structure and integrity of the cell.
2. Prevents the peroxidation of polyunsaturated fatty acids in various tissues and membranes.
3. Vitamin E is closely associated with reproductive functions and prevents sterility. It preserves and maintains germinal epithelium of gonads for proper reproductive function.
4. lt increases the synthesis of heme by enhancing the activity of enzymes δ- aminolevulinic acid (ALA) synthase and ALA dehydratase.
5. lt is required for cellular respiration through electron transport chain (believed to stabilize coenzyme Q).
6. Vitamin E prevents the oxidation of vitamin A and carotenes.
7. It is required for proper storage of creatine in skeletal muscle.
8. Vitamin E is needed for optimal absorption of amino acids from the intestine.
9. lt is involved in proper synthesis of nucleic acids.
10. Vitamin E protects liver from being damaged by toxic compounds such as carbon tetrachloride.
11. lt works in association with vitamins A , C and β-carotene, to delay the onset of cataract.
12. Vitamin E has been recommended for the prevention of chronic diseases such as cancer and heart diseases.

Deficiency causes :

- Sterility,
- Degenerative changes in muscle,
- megaloblastic anaemia and changes in central nervous system.

6.3.6 VITAMIN K

Vitamin K is the only fat soluble vitamin with a specific coenzyme function. lt is required for the production of blood clotting factors, essential for coagulation (in German-Koagulation; hence the name K for this vitamin). Vitamin K exists in different forms (K_1, K_2 & K_3). All the three vitamins (K_1, K_2, K_3) are naphthoquinone derivatives.Vitamin K_1 (phylloquinone) is present in plants. Vitamin K_2 (menaquinone) is produced by the intestinal bacteria and also found in animals. Vitamin K_3 (menadione) is a synthetic form. The three vitamins are stable to heat. Their activity is, however, lost by oxidizing agents, irradiation, strong acids and alkalies. Vitamin K is taken in the diet or synthesized by the intestinal bacteria. Its absorption takes place along with fat (chylomicrons) and is dependent on bile salts. Vitamin K is transported along with LDL and is stored mainly in liver and, to a lesser extent, in other tissues

Dietary sources :

The best sources are Cabbage, cauliflower, tomatoes, alfa alfa, spinach and other green vegetables. lt is also present in egg yolk, meat, liver, cheese and dairy products.

Daily requirement :

Adult person - 70-140 µg/day.

Deficiency causes :

Deficiency of vitamin K leads to the lack of active prothrombin in the circulation. The result is that blood coagulation is adversely affected. The individual bleeds profusely even for minor injuries. The blood clotting time is increased.

Hypervitaminosis K

Causes hemolytic anaemia and jaundice, particularly in infants. The toxic effect is due to increased breakdown of RBC.

6.4 SUMMARY

The minerals or inorganic elements are required for normal growth and maintenance of the body. They are classified as principal elements and trace elements. There are seven principal elements-Ca, P, Mg, Na, K, Cl and S. The trace elements include Fe, Cu, I, Zn, Mn, Mo, Co, F, Se and Cr. Calcium is required for the development of bones and teeth, muscle contraction, blood coagulation, nerve transmission etc. Calcium level is elevated in hyperparathyroidism and diminished in hypoparathyroidism. Phosphorus, besides being essential for the development of bones and teeth, is a constituent of high energy phosphate compounds (ATP, GTP) and nucleotide coenzymes (NAD^+, $NADP^+$). Iron is mainly required for O_2 transport and cellular respiration. It is stored as ferritin in liver, spleen and bone marrow. Iron deficiency anemia causes microcytic hypochromic

anemia.Copper is an essenial constituent of several enzymes e.g. catalase, cytochrome oxidase, tyrosinase. lodine is of important as a component of thyroid hormones(T_4 and T_3). Zinc is necessary for the storage and secretion of insulin and maintenance of normal vitamin A levels in serum, besides being a component of several enzymes (e.g. carbonic anhydrase, alcohol dehydrogenase).

Vitamins are accessory food factors required in the diet. They are classified as fat soluble (A, D, E and K) and water soluble (B-complex and C). Vitamin A is involved in vision, proper growth, differentiation and maintenance of epithelial cells. lts deficiency results in night blindness. The active form of vitamin D is calcitriol which functions like a steroid hormone and regulates plasma levels of calcium and phosphate.Vitamin D deficiency leads to rickets in children and osteomalacia in adults.Vitamin E is a natural antioxidant necessary for normal reproduction in many animals. Vitamin K has a specific coenzyme function. lt catalyses the carboxylation of glutamic acid residues in blood clotting factors and converts them to active form. Thiamine (Bl), as a cocarboxylase (TPP) is involved in energy releasing reactions. Its deficiency leads to beri-beri. Biotin (anti-egg white injury factor) participates as a coenzyme in carboxylation reactions of gluconeogenesis fatty acid synthesis etc. Vitamin B_{12} has two coenzymes, deoxyadenosylcobalomin and methylcobalamin. B_{12} deficiency results in pernicious anemia. Vitamin C (ascorbic acid) is involved in the hydroxylation of proline and lysine in the formation of collagen. Scurvy is caused by ascorbic acid deficiency.

6.5 SELF ASSESSMENT QUESTIONS

Q.1. Discuss the biochemical functions of Vitamin C and effect of their deficiency.

Answer:----------

Q.2. Write about the nutritional importance of Calcium.

Answer:----------

Q.3. Short Notes :

Iodine (b) Zinc (c) Vitamin K (d) Vitamin A

Answer:----------

Q.4. Describe B complex and their effect of their deficiencies.

Answer:----------

Q.5. Describe the significance of Copper and Phosphorus.

Answer:----------

6.6 FURTHER READINGS

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Uttar Pradesh Rajarshi Tandon
Open University

UGBCH-102

Nutritional Biochemistry

BLOCK

3

FOOD AND DRUGS INTERACTION

UNIT-7

Lipids and fates

UNIT-8

Food and drug interaction

UNIT-9

Nutritional status

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COURSE INTRODUCTION

This the third block on nutritional biochemistry. It consists of following three units:

Unit-7 : In this unit covers the Lipids and fats. The role of lipid in dietary supplement, dietary fiber and metabolism is discussed. The blood glucose level, GI tract function and role of omega-3 fatty acids in living human body also discuss apart from essential and nonessential fatty acids. .

Unit-8 : In this unit covers the food and drug interactions. The nutrient interactions affecting on ADME of drugs discuss briefly in this unit. The alcohol and nutrient deficiency, antidepressants, psychoactive drugs and nutrient interactions also mentioned here.

Unit-9 : This unit cover the nutritional status of human being. Nutrition education is an essential component in improving dietary habits and food choices, in order to reverse the under nutrition and improve the nutritional diagnosis. The biochemical assessment, reactive oxygen species (ROS), glycosylated Hb, differential diagnosis of B12 and foliate is discussed in this unit.

UNIT-7 LIPIDS AND FATS

7.1 INTRODUCTION

A lipid is a biomolecules that is soluble in nonpolar solvents. Non-polar solvents are typically hydrocarbons used to dissolve other naturally occurring hydrocarbon lipid molecules that do not (or do not easily) dissolve in water, including fatty acids, waxes, sterols, fat-soluble vitamins (such as vitamins A, D, E, and K), monoglycerides, diglycerides, triglycerides, and phospholipids. The functions of lipids include storing energy, signalling, and acting as structural components of cell membranes. Lipids have applications in the cosmetic and food industries as well as in nanotechnology. Dietary fiber (British spelling fibre) or roughage is the portion of plant-derived food that cannot be completely broken down by human digestive enzymes. It has two main components:

- Soluble fiber-which dissolves in water – is readily fermented in the colon into gases and physiologically active by-products, such as short-chain fatty acids produced in the colon by gut bacteria. It is viscous, may be called prebiotic fiber, and delays gastric emptying which, in humans, can result in an extended feeling of fullness.
- Insoluble fiber-which does not dissolve in water – is inert to digestive enzymes in the upper gastrointestinal tract and provides bulking. Some forms of insoluble fiber, such as resistant starches, can be fermented in the colon. Bulking fibers absorb water as they move through the digestive system, easing defecation.

Dietary fibers can act by changing the nature of the contents of the gastrointestinal tract and by changing how other nutrients and chemicals are absorbed. Some types of soluble fiber absorb water to become a gelatinous, viscous substance which may or may not be fermented by bacteria in the digestive tract. Some types of insoluble fiber have bulking action and are not fermented. Lignin, a major dietary insoluble fiber source, may alter the rate and metabolism of soluble fibers. Other types of insoluble fiber, notably resistant starch, are fermented to produce short-chain fatty acids, which are physiologically active and confer health benefits. Health benefit from dietary fiber and whole grains may include a decreased risk of death and lower rates of coronary heart disease, colon cancer, and type 2 diabetes.

Food sources of dietary fiber have traditionally been divided according to whether they provide soluble or insoluble fiber. Plant foods contain both types of fiber in varying amounts, according to the plant's characteristics of viscosity and ferment ability. Advantages of consuming fiber depend upon which type of fiber is consumed and which benefits may result in the gastrointestinal system. Bulking fibers – such as cellulose, hemicellulose and psyllium – absorb and hold water, promoting regularity. Viscous fibers – such as beta-glucan and psyllium – thicken the fecal mass.

Objectives :

- To determined the role of lipid in dietary supplement
- To know the blood glucose level and GI tract functions
- Role of omega-3 fatty acids in living human body
- To know essential and nonessential fatty acids

7.2 DIETARY FIBER OVERVIEW

Dietary fiber is defined to be plant components that are not broken down by human digestive enzymes. In the late 20th century, only lignin and some polysaccharides were known to satisfy this definition, but in the early 21st century, resistant starch and oligosaccharides were included as dietary fiber components. Official definition of dietary fiber varies among different institutions:

Organization	Definition
Institute of Medicine (2001)	Dietary fiber consists of non digestible carbohydrates and lignin that are intrinsic and intact in plants. "Added Fiber" consists of isolated, no digestible carbohydrates that have beneficial physiological effects in humans.
American Association of Cereal Chemists (2001)	Dietary fiber is the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine, with complete or partial fermentation in the large intestine. Dietary fiber includes polysaccharides, oligosaccharides, lignin, and associated plant substances. Dietary fibers promote beneficial physiologic effects including laxation, and/or blood cholesterol attenuation, and/or blood glucose attenuation.
Codex Alimentarius Commission (2014; adopted by the European Commission and 10 countries internationally)	Dietary fiber means carbohydrate polymers with more than 10 monomeric units, which are not hydrolyzed by digestive enzymes in the small intestine of humans.

British Nutrition Foundation[1] (2018)	Dietary fibre refers to a group of substances in plant foods which cannot be completely broken down by human digestive enzymes. This includes waxes, lignin and polysaccharides such as cellulose and pectin. Originally it was thought that dietary fibre was completely indigestible and did not provide any energy. It is now known that some fibre can be fermented in the large intestine by gut bacteria, producing short chain fatty acids and gases.

7.3 TYPES OF DIETARY FIBERS

Nutrient	Food additive	Source/Comments
water-insoluble dietary fibers		
β-glucans (a few of which are water-soluble)		
Cellulose	E 460	cereals, fruit, vegetables (in all plants in general)
Chitin	—	in fungi, exoskeleton of insects and crustaceans
Hemicellulose		cereals, bran, timber, legumes
Hexoses	—	wheat, barley
Pentose	—	rye, oat
Arabinoxylan (a hemicellulose)	—	psyllium
Lignin	—	stones of fruits, vegetables (filaments of the garden bean), cereals
Xanthan gum	E 415	production with Xanthomonas-bacteria from sugar substrates

Resistant starch		Can be starch protected by seed or shell (type RS1), granular starch (type RS2) or retrograded starch (type RS3)
Resistant starch	—	high amylose corn, barley, high amylose wheat, legumes, raw bananas, cooked and cooled pasta and potatoes
water-soluble dietary fibers		
Arabinoxylan (a hemicellulose)	—	some types are soluble (not psyllium)
Fructans		replace or complement in some plant taxa the starch as storage carbohydrate
Insulin	—	in diverse plants, e.g. topinambour, chicory, etc.
Polyuronide		
Pectin	E 440	in the fruit skin (mainly apples, quinces), vegetables
Alginic acids (Alginates)	E 400–E 407	in Algae
Sodium alginate	E 401	
Potassium alginate	E 402	
Ammonium alginate	E 403	
Calcium alginate	E 404	
Propylene glycol alginate (PGA)	E 405	

Agar	E 406	
Carrageen	E 407	red algae
Raffinose	—	legumes
Polydextrose	E 1200	synthetic polymer, ca. 1kcal/g

7.4 FIBER CONTENTS IN FOOD

Dietary fibers are found in fruits, vegetables and whole grains. The amount of fiber contained in common foods are in the following table

Food group	**Serving mean**	**Fibermass per serving**
Fruit	120 mL (0.5 cup)	1.1 g
Dark green vegetables	120 mL (0.5 cup)	6.4 g
Orange vegetables	120 mL (0.5 cup)	2.1 g
Cooked dry beans (legumes)	120 mL (0.5 cup)	8.0 g
Starchy vegetables	120 mL (0.5 cup)	1.7 g
Other vegetables	120 mL (0.5 cup)	1.1 g
Whole grains	28 g (1 oz)	2.4 g
Meat	28 g (1 oz)	0.1 g

Dietary fiber is found in plants, typically eaten whole, raw or cooked, although fiber can be added to make dietary supplements and fiber-rich processed foods. Grain bran products have the highest fiber contents, such as crude corn bran (79 g per 100 g) and crude wheat bran (43 g per 100 g), which are ingredients for manufactured foods.

7.5 PLANT SOURCES OF FIBER

Some plants contain significant amounts of soluble and insoluble fiber. For example, plums and prunes have a thick skin covering a juicy

pulp. The skin is a source of insoluble fiber, whereas soluble fiber is in the pulp. Grapes also contain a fair amount of fiber. **Soluble fiber** is found in varying quantities in all plant foods, including:

- legumes (peas, soybeans, lupins and other beans)
- oats, rye, chia, and barley
- some fruits (including figs, avocados, plums, prunes, berries, ripe bananas, and the skin of apples, quinces and pears)
- certain vegetables such as broccoli, carrots, and Jerusalem artichokes
- root tubers and root vegetables such as sweet potatoes and onions (skins of these are sources of insoluble fiber also)
- psyllium seed husks (a mucilage soluble fiber) and flax seeds
- nuts, with almonds being the highest in dietary fiber

Sources of **insoluble fiber** include :

- whole grain foods
- wheat and corn bran
- legumes such as beans and peas
- nuts and seeds
- potato skins
- lignans
- vegetables such as green beans, cauliflower, zucchini (courgette), celery, and nopal
- some fruits including avocado, and unripe bananas
- the skins of some fruits, including kiwifruit, grapes and tomatoes

7.6 FIBER SUPPLEMENTS

These are a few example forms of fiber that have been sold as supplements or food additives. These may be marketed to consumers for nutritional purposes, treatment of various gastrointestinal disorders, and for such possible health benefits as lowering cholesterol levels, reducing risk of colon cancer, and losing weight. Soluble fiber supplements may be beneficial for alleviating symptoms of irritable bowel syndrome, such as diarrhea or constipation and abdominal discomfort. Prebiotic soluble fiber products, like those containing inulin or oligosaccharides, may contribute to relief from inflammatory bowel disease,as in Crohn's disease, ulcerative colitis, and *Clostridium difficile*, due in part to the

short-chain fatty acids produced with subsequent anti-inflammatory actions upon the bowel . Fiber supplements may be effective in an overall dietary plan for managing irritable bowel syndrome by modification of food choices. One insoluble fiber, resistant starch from high-amylose corn, has been used as a supplement and may contribute to improving insulin sensitivity and glycemic management[as well as promoting regularity and possibly relief of diarrhea. One preliminary finding indicates that resistant corn starch may reduce symptoms of ulcerative colitis.

Inulins

Chemically defined as oligosaccharides occurring naturally in most plants. Inulins have nutritional value as carbohydrates, or more specifically as fructans, a polymer of the natural plant sugar, fructose. Inulin is typically extracted by manufacturers from enriched plant sources such as chicory roots or Jerusalem artichokes for use in prepared foods. Subtly sweet, it can be used to replace sugar, fat, and flour, is often used to improve the flow and mixing qualities of powdered nutritional supplements, and has significant potential health value as a prebiotic fermentable fiber.

Inulin is advantageous because it contains 25–30% the food energy of sugar or other carbohydrates and 10–15% the food energy of fat. As a prebiotic fermentable fiber, its metabolism by gut flora yields short-chain fatty acids, which increase absorption of calcium, magnesium, and iron, resulting from upregulation of mineral-transporting genes and their membrane transport proteins within the colon wall. Among other potential beneficial effects noted above, inulin promotes an increase in the mass and health of intestinal *Lactobacillus* and *Bifidobacterium* populations.

Inulin's primary disadvantage is its tolerance. As a soluble fermentable fiber, it is quickly and easily fermented within the intestinal tract, which may cause gas and digestive distress at doses higher than 15 grams/day in most people. Individuals with digestive diseases have benefited from removing fructose and inulin from their diet. While clinical studies have shown changes in the microbiota at lower levels of inulin intake, some of the health effects require higher than 15 grams per day to achieve the benefits.

Vegetable gums

Vegetable gum fiber supplements are relatively new to the market. Often sold as a powder, vegetable gum fibers dissolve easily with no aftertaste. In preliminary clinical trials, they have proven effective for the treatment of irritable bowel syndrome. Examples of vegetable gum fibers are guar gum and gum arabic.

7.7 ACTIVITY IN THE GUT

Many molecules that are considered to be "dietary fiber" are so because humans lack the necessary enzymes to split the glycosidic bond and they reach the large intestine. Many foods contain varying types of dietary fibers, all of which contribute to health in different ways.

Dietary fibers make three primary contributions: bulking, viscosity and fermentation. Different fibers have different effects, suggesting that a variety of dietary fibers contribute to overall health. Some fibers contribute through one primary mechanism. For instance, cellulose and wheat bran provide excellent bulking effects, but are minimally fermented. Alternatively, many dietary fibers can contribute to health through more than one of these mechanisms. For instance, psyllium provides bulking as well as viscosity. Bulking fibers can be soluble (e.g. psyllium) or insoluble (e.g. cellulose and hemicellulose). They absorb water and can significantly increase stool weight and regularity. Most bulking fibers are not fermented or are minimally fermented throughout the intestinal tract.

Viscous fibers thicken the contents of the intestinal tract and may attenuate the absorption of sugar, reduce sugar response after eating, and reduce lipid absorption (notably shown with cholesterol absorption). Their use in food formulations is often limited to low levels, due to their viscosity and thickening effects. Some viscous fibers may also be partially or fully fermented within the intestinal tract (guar gum, beta-glucan, glucomannan and pectins), but some viscous fibers are minimally or not fermented (modified cellulose such as methylcellulose and psyllium). Fermentable fibers are consumed by the micro biota within the large intestines, mildly increasing fecal bulk and producing short-chain fatty acids as byproducts with wide-ranging physiological activities.

Resistant starch, inulin, fructooligosaccharide and galactooligosaccharide are dietary fibers which are fully fermented. These include insoluble as well as soluble fibers. This fermentation influences the expression of many genes within the large intestine, which affect digestive function and lipid and glucose metabolism, as well as the immune system, inflammation and more.

Dietary fibers can change the nature of the contents of the gastrointestinal tract and can change how other nutrients and chemicals are absorbed through bulking and viscosity. Some types of soluble fibers bind to bile acids in the small intestine, making them less likely to re-enter the body; this in turn lowers cholesterol levels in the blood from the actions of cytochrome P450-mediated oxidation of cholesterol.

Insoluble fiber is associated with reduced risk of diabetes, but the mechanism by which this is achieved is unknown. One type of insoluble dietary fiber, resistant starch, may increase insulin sensitivity in healthy people in type 2 diabetics, and in individuals with insulin resistance, possibly contributing to reduced risk of type 2 diabetes.

Not yet formally proposed as an essential macronutrient, dietary fiber has importance in the diet, with regulatory authorities in many developed countries recommending increases in fiber intake.

7.8 PHYSICOCHEMICAL PROPERTIES

Dietary fiber has distinct physicochemical properties. Most semi-solid foods, fiber and fat are a combination of gel matrices which are hydrated or collapsed with microstructural elements, globules, solutions or encapsulating walls. Fresh fruit and vegetables are cellular materials.

- The cells of cooked potatoes and legumes are gels filled with gelatinized starch granules. The cellular structures of fruits and vegetables are foams with a closed cell geometry filled with a gel, surrounded by cell walls which are composites with an amorphous matrix strengthened by complex carbohydrate fibers.
- Particle size and interfacial interactions with adjacent matrices affect the mechanical properties of food composites.
- Food polymers may be soluble in and/or plasticized by water. Water is the most important plasticizer, particularly in biological systems thereby changing mechanical properties.
- The variables include chemical structure, polymer concentration, molecular weight, degree of chain branching, the extent of ionization (for electrolytes), solution pH, ionic strength and temperature.
- Cross-linking of different polymers, protein and polysaccharides, either through chemical covalent bonds or cross-links through molecular entanglement or hydrogen or ionic bond cross-linking.
- Cooking and chewing food alters these physicochemical properties and hence absorption and movement through the stomach and along the intestine

7.9 DIETARY FIBER IN THE UPPER GASTROINTESTINAL TRACT

Following a meal, the stomach and upper gastrointestinal contents consist of

- food compounds
- complex lipids/micellar/aqueous/hydrocolloid and hydrophobic phases
- hydrophilic phases
- solid, liquid, colloidal and gas bubble phases.

Micelles are colloid-sized clusters of molecules which form in conditions as those above, similar to the critical micelle concentration of detergents. In the upper gastrointestinal tract, these compounds consist of bile acids and di- and monoacyl glycerols which solubilize triacylglycerols and cholesterol. Two mechanisms bring nutrients into contact with the epithelium:

1. intestinal contractions create turbulence; and
2. convection currents direct contents from the lumen to the epithelial surface.

The multiple physical phases in the intestinal tract slow the rate of absorption compared to that of the suspension solvent alone.

1. Nutrients diffuse through the thin, relatively unstirred layer of fluid adjacent to the epithelium.
2. Immobilizing of nutrients and other chemicals within complex polysaccharide molecules affects their release and subsequent absorption from the small intestine, an effect influential on the glycemic index.
3. Molecules begin to interact as their concentration increases. During absorption, water must be absorbed at a rate commensurate with the absorption of solutes. The transport of actively and passively absorbed nutrients across epithelium is affected by the unstirred water layer covering the microvillus membrane.
4. The presence of mucus or fiber, e.g., pectin or guar, in the unstirred layer may alter the viscosity and solute diffusion coefficient.

Adding viscous polysaccharides to carbohydrate meals can reduce post-prandial blood glucose concentrations. Wheat and maize but not oats modify glucose absorption, the rate being dependent upon the particle size. The reduction in absorption rate with guar gum may be due to the increased resistance by viscous solutions to the convective flows created by intestinal contractions.

Dietary fiber interacts with pancreatic and enteric enzymes and their substrates. Human pancreatic enzyme activity is reduced when incubated with most fiber sources. Fiber may affect amylase activity and hence the rate of hydrolysis of starch. The more viscous polysaccharides extend the mouth-to-cecum transit time; guar, tragacanth and pectin being slower than wheat bran.

7.10 FIBER IN THE COLON

The colon may be regarded as two organs,

1. the right side (cecum and ascending colon), a fermenter. The right side of the colon is involved in nutrient salvage so that dietary

fiber, resistant starch, fat and protein are utilized by bacteria and the end-products absorbed for use by the body.

2. the left side (transverse, descending, and sigmoid colon), affecting continence.

The presence of bacteria in the colon produces an 'organ' of intense, mainly reductive, metabolic activity, whereas the liver is oxidative. The substrates utilized by the cecum have either passed along the entire intestine or are biliary excretion products. The effects of dietary fiber in the colon are on

1. bacterial fermentation of some dietary fibers.
2. thereby an increase in bacterial mass.
3. an increase in bacterial enzyme activity.
4. changes in the water-holding capacity of the fiber residue after fermentation.

Enlargement of the cecum is a common finding when some dietary fibers are fed and this is now believed to be normal physiological adjustment. Such an increase may be due to a number of factors, prolonged cercal residence of the fiber, increased bacterial mass, or increased bacterial end-products. Some non-absorbed carbohydrates, e.g. pectin, gum arabic, oligosaccharides and resistant starch, are fermented to short-chain fatty acids (chiefly acetic, propionic and n-butyric), and carbon dioxide, hydrogen and methane. Almost all of these short-chain fatty acids will be absorbed from the colon. This means that fecal short-chain fatty acid estimations do not reflect cecal and colonic fermentation, only the efficiency of absorption, the ability of the fiber residue to sequestrate short-chain fatty acids, and the continued fermentation of fiber around the colon, which presumably will continue until the substrate is exhausted. The production of short-chain fatty acids has several possible actions on the gut mucosa. All of the short-chain fatty acids are readily absorbed by the colonic mucosa, but only acetic acid reaches the systemic circulation in appreciable amounts. Butyric acid appears to be used as a fuel by the colonic mucosa as the preferred energy source for colonic cells.

7.11 DIETARY FIBER AND CHOLESTEROL METABOLISM

Dietary fiber may act on each phase of ingestion, digestion, absorption and excretion to affect cholesterol metabolism, such as the following:

1. Caloric energy of foods through a bulking effect
2. Slowing of gastric emptying time
3. A glycemic index type of action on absorption

4. A slowing of bile acid absorption in the ileum so bile acids escape through to the cecum

5. Altered or increased bile acid metabolism in the cecum

6. Indirectly by absorbed short-chain fatty acids, especially propionic acid, resulting from fiber fermentation affecting the cholesterol metabolism in the liver.

7. Binding of bile acids to fiber or bacteria in the cecum with increased fecal loss from the entero-hepatic circulation.

An important action of some fibers is to reduce the reabsorption of bile acids in the ileum and hence the amount and type of bile acid and fats reaching the colon. A reduction in the reabsorption of bile acid from the ileum has several direct effects.

1. Bile acids may be trapped within the lumen of the ileum either because of a high luminal viscosity or because of binding to a dietary fiber.

2. Lignin in fiber adsorbs bile acids, but the unconjugated form of the bile acids are adsorbed more than the conjugated form. In the ileum where bile acids are primarily absorbed the bile acids are predominantly conjugated.

3. The enterohepatic circulation of bile acids may be altered and there is an increased flow of bile acids to the cecum, where they are deconjugated and 7alpha-dehydroxylated.

4. These water-soluble form, bile acids e.g., deoxycholic and lithocholic are adsorbed to dietary fiber and an increased fecal loss of sterols, dependent in part on the amount and type of fiber.

5. A further factor is an increase in the bacterial mass and activity of the ileum as some fibers e.g., pectin are digested by bacteria. The bacterial mass increases and cecal bacterial activity increases.

6. The enteric loss of bile acids results in increased synthesis of bile acids from cholesterol which in turn reduces body cholesterol.

The fibers that are most effective in influencing sterol metabolism (e.g. pectin) are fermented in the colon. It is therefore unlikely that the reduction in body cholesterol is due to adsorption to this fermented fiber in the colon.

1. There might be alterations in the end-products of bile acid bacterial metabolism or the release of short chain fatty acids which are absorbed from the colon, return to the liver in the portal vein and modulate either the synthesis of cholesterol or its catabolism to bile acids.

2. The prime mechanism whereby fiber influences cholesterol metabolism is through bacteria binding bile acids in the colon after

the initial deconjugation and dehydroxylation. The sequestered bile acids are then excreted in feces

3. Fermentable fibers e.g., pectin will increase the bacterial mass in the colon by virtue of their providing a medium for bacterial growth.

4. Other fibers, e.g., gum arabic, act as stabilizers and cause a significant decrease in serum cholesterol without increasing fecal bile acid excretion.

7.12 DIETARY FIBER AND FECAL WEIGHT

Faces consist of a plasticize-like material, made up of water, bacteria, lipids, sterols, mucus and fiber.

1. Faces are 75% water; bacteria make a large contribution to the dry weight, the residue being unfermented fiber and excreted compounds.

2. Fecal output may vary over a range of between 20 and 280 g over 24 hours. The amount of feces egested a day varies for any one individual over a period of time.

3. Of dietary constituents, only dietary fiber increases fecal weight.

4. Water is distributed in the colon in three ways:

    1. Free water which can be absorbed from the colon.

    2. Water that is incorporated into bacterial mass.

    3. Water that is bound by fiber.

    4. Fecal weight is dictated by:

        a. The bacterial mass the holding of water by the residual dietary fiber after fermentation.

        b. There may also be an added osmotic effect of products of bacterial fermentation on fecal mass.

Wheat bran is minimally fermented and binds water and when added to the diet increases fecal weight in a predictable linear manner and decreases intestinal transit time. The particle size of the fiber is all-important, coarse wheat bran being more effective than fine wheat bran. The greater the water-holding capacity of the bran, the greater the effect on fecal weight. For most healthy individuals, an increase in wet fecal weight, depending on the particle size of the bran, is generally of the order of 3–5 g/g fiber. The fermentation of some fibers results in an increase in the bacterial content and possibly fecal weight. Other fibers, e.g. pectin, are fermented and have no effect on stool weight.

7.13 EFFECTS OF FIBER INTAKE

Research has shown that fiber may benefit health in several different ways. Lignin and probably related materials that are resistant to enzymatic degradation, diminish the nutritional value of foods. Color coding of table entries:

- Both Applies to both soluble and insoluble fiber
- Soluble Applies to soluble fiber only
- Insoluble Applies to insoluble fiber only

Effects
• Increases food volume without increasing caloric content to the same extent as digestible carbohydrates, providing satiety which may reduce appetite.
• Attracts water and forms a viscous gel during digestion, slowing the emptying of the stomach and intestinal transit, shielding carbohydrates from enzymes, and delaying absorption of glucose, which lowers variance in blood sugar levels
• Lowers total and LDL cholesterol, which may reduce the risk of cardiovascular disease
• Regulates blood sugar, which may reduce glucose and insulin levels in diabetic patients and may lower risk of diabetes
• Speeds the passage of foods through the digestive system, which facilitates regular defecation
• Adds bulk to the stool, which alleviates constipation
• Balances intestinal pH and stimulates intestinal fermentation production of short-chain fatty acids

Fiber does not bind to minerals and vitamins and therefore does not restrict their absorption, but rather evidence exists that fermentable fiber sources improve absorption of minerals, especially calcium. Some plant foods can reduce the absorption of minerals and vitamins like calcium, zinc, vitamin C, and magnesium, but this is caused by the

presence of phytate (which is also thought to have important health benefits), not by fiber.

7.14 DIETARY FIBER AND OBESITY

Dietary fiber has many functions in diet, one of which may be to aid in energy intake control and reduced risk for development of obesity. The role of dietary fiber in energy intake regulation and obesity development is related to its unique physical and chemical properties that aid in early signals of satiation and enhanced or prolonged signals of satiety. Early signals of satiation may be induced through cephalic- and gastric-phase responses related to the bulking effects of dietary fiber on energy density and palatability, whereas the viscosity-producing effects of certain fibers may enhance satiety through intestinal-phase events related to modified gastrointestinal function and subsequent delay in fat absorption. In general, fiber-rich diets, whether achieved through fiber supplementation or incorporation of high fiber foods into meals, have a reduced energy density compared with high fat diets. This is related to fiber's ability to add bulk and weight to the diet. There are also indications that women may be more sensitive to dietary manipulation with fiber than men. The relationship of body weight status and fiber effect on energy intake suggests that obese individuals may be more likely to reduce food intake with dietary fiber inclusion.

7.15 FIBER AND FERMENTATION

The American Association of Cereal Chemists has defined soluble fiber this way: *"the edible parts of plants or similar carbohydrates resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine.* In this definition:

Edible parts of plants

Indicates that some parts of a plant we eat—skin, pulp, seeds, stems, leaves, roots—contains fiber. Both insoluble and soluble sources are in those plant components.

Carbohydrates

Complex carbohydrates, such as long-chained sugars also called starch, oligosaccharides, or polysaccharides, are sources of soluble fermentable fiber.

- **Resistant to digestion and absorption in the human small intestine**

  Foods providing nutrients are digested by gastric acid and digestive enzymes in the stomach and small intestine where the nutrients are released then absorbed through the intestinal wall for transport via the blood throughout the body. A

food resistant to this process is undigested, as insoluble and soluble fibers are. They pass to the large intestine only affected by their absorption of water (insoluble fiber) or dissolution in water (soluble fiber).

- **Complete or partial fermentation in the large intestine**

  The large intestine comprises a segment called the colon within which additional nutrient absorption occurs through the process of fermentation. Fermentation occurs by the action of colonic bacteria on the food mass, producing gases and short-chain fatty acids. It is these short-chain fatty acids—butyric, acetic (ethanoic), propionic, and valeric acids—that scientific evidence is revealing to have significant health properties.

As an example of fermentation, shorter-chain carbohydrates (a type of fiber found in legumes) cannot be digested, but are changed via fermentation in the colon into short-chain fatty acids and gases (which are typically expelled as flatulence).

According to a 2002 journal article, fiber compounds with partial or low fermentability include:

- cellulose, a polysaccharide
- hemicellulose, a polysaccharide
- lignans, a group of phytoestrogens
- plant waxes
- Fiber compounds with high fermentability include:
- resistant starches
- beta-glucans, a group of polysaccharides
- pectins, a group of heteropolysaccharides
- natural gums, a group of polysaccharides
- inulins, a group of polysaccharides
- oligosaccharides

7.18 SHORT-CHAIN FATTY ACIDS

When fermentable fiber is fermented, short-chain fatty acids (SCFA) are produced. SCFAs are involved in numerous physiological processes promoting health, including:

- stabilize blood glucose levels by acting on pancreatic insulin release and liver control of glycogen breakdown.

- stimulate gene expression of glucose transporters in the intestinal mucosa, regulating glucose absorption.
- provide nourishment of colonocytes, particularly by the SCFA butyrate
- suppress cholesterol synthesis by the liver and reduce blood levels of LDL cholesterol and triglycerides responsible for atherosclerosis
- lower colonic pH (i.e., raises the acidity level in the colon) which protects the lining from formation of colonic polyps and increases absorption of dietary minerals
- stimulate production of T helper cells, antibodies, leukocytes, cytokines, and lymph mechanisms having crucial roles in immune protection.
- improve barrier properties of the colonic mucosal layer, inhibiting inflammatory and adhesion irritants, contributing to immune functions.

SCFAs that are absorbed by the colonic mucosa pass through the colonic wall into the portal circulation (supplying the liver), and the liver transports them into the general circulatory system. Overall, SCFAs affect major regulatory systems, such as blood glucose and lipid levels, the colonic environment, and intestinal immune functions. The major SCFAs in humans are butyrate, propionate, and acetate, where butyrate is the major energy source for colonocytes, propionate is destined for uptake by the liver, and acetate enters the peripheral circulation to be metabolized by peripheral tissues.

7.19 ROLE OF FIBRES IN LIPID METABOLISM

The understanding of the involvement of dietary fiber in lipid metabolism is still quite limited. Despite the strong relationships indicated by epidemiological observations, very few concerning mechanisms involved and details concerning the specific types of dietary fiber involved are known. One viable mechanism involves the interaction of some types of dietary fiber with bile acids. The magnitude of this interaction appears to be sufficient to result in an alteration of bile acid excretion and, as a result, alter sterol balance. This alteration is involved in the hypocholesteremic effects of certain types of dietary fiber. At the same time, the resultant increase in the concentration of bile acids in the colon may be related to susceptibility to colon carcinogenesis. These data indicate the necessity of a thorough evaluation of all phases of the effects of any dietary fiber source or component before making any recommendation for its use. A dietary fiber with both bile-acid adsorption capabilities and a high water-holding capacity could result in increased total excretion without increasing bile acid concentrations.

Fat is an important foodstuff for many forms of life and fats serve both structural and metabolic functions. They are a necessary part of the diet of most heterotrophs (including humans) and are the most energy dense, thus the most efficient form of energy storage.

Some fatty acids that are set free by the digestion of fats are called essential because they cannot be synthesized in the body from simpler constituents. There are two essential fatty acids (EFAs) in human nutrition: alpha-linolenic acid (an omega-3 fatty acid) and linoleic acid (an omega-6 fatty acid). Other lipids needed by the body can be synthesized from these and other fats. Fats and other lipids are broken down in the body by enzymes called lipases produced in the pancreas.

Fats and oils are categorized according to the number and bonding of the carbon atoms in the aliphatic chain. Fats that are saturated fats have no double bonds between the carbons in the chain. Unsaturated fats have one or more double bonded carbons in the chain. The nomenclature is based on the non-acid (non-carbonyl) end of the chain. This end is called the omega end or the n-end. Thus alpha-linolenic acid is called an omega- 3 fatty acid because the 3rd carbon from that end is the first double bonded carbon in the chain counting from that end. Some oils and fats have multiple double bonds and are therefore called polyunsaturated fats. Unsaturated fats can be further divided into cis fats, which are the most common in nature, and trans fats, which are rare in nature. Unsaturated fats can be altered by reaction with hydrogen effected by a catalyst. This action, called hydrogenation, tends to break all the double bonds and makes a fully saturated fat. To make vegetable shortening, then, liquid *cis*-unsaturated fats such as vegetable oils are hydrogenated to produce saturated fats, which have more desirable physical properties e.g., they melt at a desirable temperature (30–40 °C), and store well, whereas polyunsaturated oils go rancidify when they react with oxygen in the air. However, trans fats are generated during hydrogenation as contaminants created by an unwanted side reaction on the catalyst during partial hydrogenation.

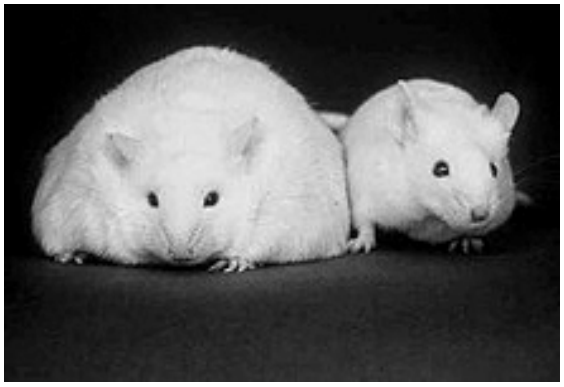
Saturated fats can stack themselves in a closely packed arrangement, so they can solidify easily and are typically solid at room temperature. For example, animal fats tallow and lard are high in saturated fatty acid content and are solids. Olive and linseed oils on the other hand are unsaturated and liquid. Fats serve both as energy sources for the body, and as stores for energy in excess of what the body needs immediately. Each gram of fat when burned or metabolized releases about 9 food calories (37 kJ = 8.8 kcal). Fats are broken down in the healthy body to release their constituents, glycerol and fatty acids. Glycerol itself can be converted to glucose by the liver and so become a source of energy.

7.20 IMPORTANCE FOR LIVING ORGANISMS

Fats are also sources of essential fatty acids, an important dietary requirement. They provide energy as noted above. Vitamins A, D, E,

and K are fat-soluble, meaning they can only be digested, absorbed, and transported in conjunction with fats. Fats play a vital role in maintaining healthy skin and hair, insulating body organs against shock, maintaining body temperature, and promoting healthy cell function. Fat also serves as a useful buffer against a host of diseases. When a particular substance, whether chemical or biotic, reaches unsafe levels in the bloodstream, the body can effectively dilute—or at least maintain equilibrium of—the offending substances by storing it in new fat tissue. This helps to protect vital organs, until such time as the offending substances can be metabolized or removed from the body by such means as excretion, urination, accidental or intentional bloodletting, sebum excretion, and hair growth.

Adipose tissue



The obese mouse on the left has large stores of adipose tissue. For comparison, a mouse with a normal amount of adipose tissue is shown on the right.

In animals, adipose tissue, or fatty tissue is the body's means of storing metabolic energy over extended periods of time. Adipocytes (fat cells) store fat derived from the diet and from liver metabolism. Under energy stress these cells may degrade their stored fat to supply fatty acids and also glycerol to the circulation. These metabolic activities are regulated by several hormones (e.g., insulin, glucagon and epinephrine). Adipose tissue also secretes the hormone leptin.

The location of the tissue determines its metabolic profile. Visceral fat is located within the abdominal wall (i.e., beneath the wall of abdominal muscle) whereas "subcutaneous fat" is located beneath the skin (and includes fat that is located in the abdominal area beneath the skin but *above* the abdominal muscle wall). Visceral fat was recently discovered to be a significant producer of signaling chemicals (i.e., hormones), among which several are involved in inflammatory tissue responses. One of these is resistin which has been linked to obesity, insulin resistance, and Type 2 diabetes. This latter result is currently controversial, and there have been reputable studies supporting all sides on the issue.

Fatty acids and human health

Dietary consumption of fatty acids has effects on human health. Studies have found that replacing saturated fats with *cis* unsaturated fats in the diet reduce risk of cardiovascular disease. For example, a 2015 systematic review of randomized control trials by the Cochrane Library concluded: "Lifestyle advice to all those at risk of cardiovascular disease and to lower risk population groups should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturated fats."

7.21 BLOOD GLUCOSE LEVEL AND G.I. TRACT INFECTION

Gastrointestinal infections are viral, bacterial or parasitic infection that causes gastroenteritis, an inflammation of the gastrointestinal tract involving both the stomach and the small intestine. Symptoms include diarrhoea, vomiting and abdominal pain. Gastroenteritis puts a stress on your body and often causes increases in blood glucose levels, in rare cases blood glucose levels will fall. Infection causes a stress response in the body by increasing the amount of certain hormones such as cortisol and adrenaline. These hormones work against the action of Insulin and as a result, the body's production of glucose increases which result in high blood sugar level.

When your body sugar is high, the white cell in your body are unable to mop up bacteria because they cannot move around at their normal speed and do not reach the infection site quickly enough to engulf and kill bacteria .In a person who does not have high sugar level or diabetics, extra insulin is produced to counter these effects but this is not possible for someone with diabetes and so hyperglycaemia persists and ketoacidosis can occur.

7.22 SOURCES OF FATS & OILS

Edible fats and oils		
Fats	**Pork fats**	Fatback Lardo Salo Salt pork Szalonna Lard

		Lardon Pork belly Bacon Pancetta Tocino Speck
	Beef/mutton fats	Dripping Suet Tallow Tail fat
	Dairy fats	Butter Clarified butter Ghee Niter kibbeh Smen
	Poultry fats	Chicken fat Duck fat Schmaltz
	Other animal fats	Blubber Muktuk Whale oil
	Vegetable fats	Borneo tallow Cocoa butter Margarine Shea butter

Digestion of Fats

Stomach

Lipase present in the stomach is unable to hydrolyze fats owing to the high acidity of the gastric contents. Therefore, the major part of the ingested fat is digested in the small intestine.

Small Intestine

The ingested fat reaching the duodenum is mixed with the bile and pancreatic juice which contains lipase. The bile salts emulsify the fat before the action of lipase. The emulsification is also brought about by monoglycerides, phospholipid and lysolecithin.

The secreted inactive pancreatic lipase is activated by bile and Ca. The surface area of the emulsified fat becomes increased for which the rate of reaction of lipase is increased. Pancreatic lipase hydrolyzes 1- and 3-positions of the triglycerides leaving a mixture of 2- monoglycerides, 1, 2- and 2, 3-diglycerides as well as the soaps of the free fatty acids.

The pancreatic juice also contains phospholipase and cholesterol-esterase which hydrolyze phospholipid and esterified cholesterol. Intestinal juice also contains a lipase whose action is not of much importance as most of the fat is hydrolyzed by the pancreatic lipase.

Absorption of Fats

Several theories have been proposed for the mechanism of absorption of fats after digestion.

The important theories are

a. Lipolytic hypothesis.

b. Partition theory.

c. More recent theory.

Lipolytic Hypothesis

1. According to this theory, fat is completely hydrolyzed to fatty acids and glycerol which are absorbed.
2. The fatty acids combining with bile salts form a miscible complex which is absorbed into the intestinal mucosa.
3. The fatty acids are then separated from bile acids and converted into triglycerides by combining with glycerol.
4. The triglycerides are passed to the lacteals. They then enter the lymphatic's and reach the systemic circulation via thoracic duct.

Partition Theory

1. According to this theory, 30 per cent of the triglycerides are hydrolyzed to fatty acids and glycerol while 70 per cent remain un-hydrolyzed.

2. The un-hydrolyzed triglycerides are emulsified by monoglycerides and diglycerides in combination with bile salts to form minute particles known as "micelles" of size about 0.1 to 0.5µ.

3. The resulting mixture is absorbed into the intestines, passed on to the lacteals and then to the lymphatic's. The mixture then reaches the systemic circulation via thoracic duct.

4. The free fatty acids are absorbed as bile salt-fatty acid complex into the intestinal mucosa. The fatty acids are absorbed into the portal blood to reach the liver.

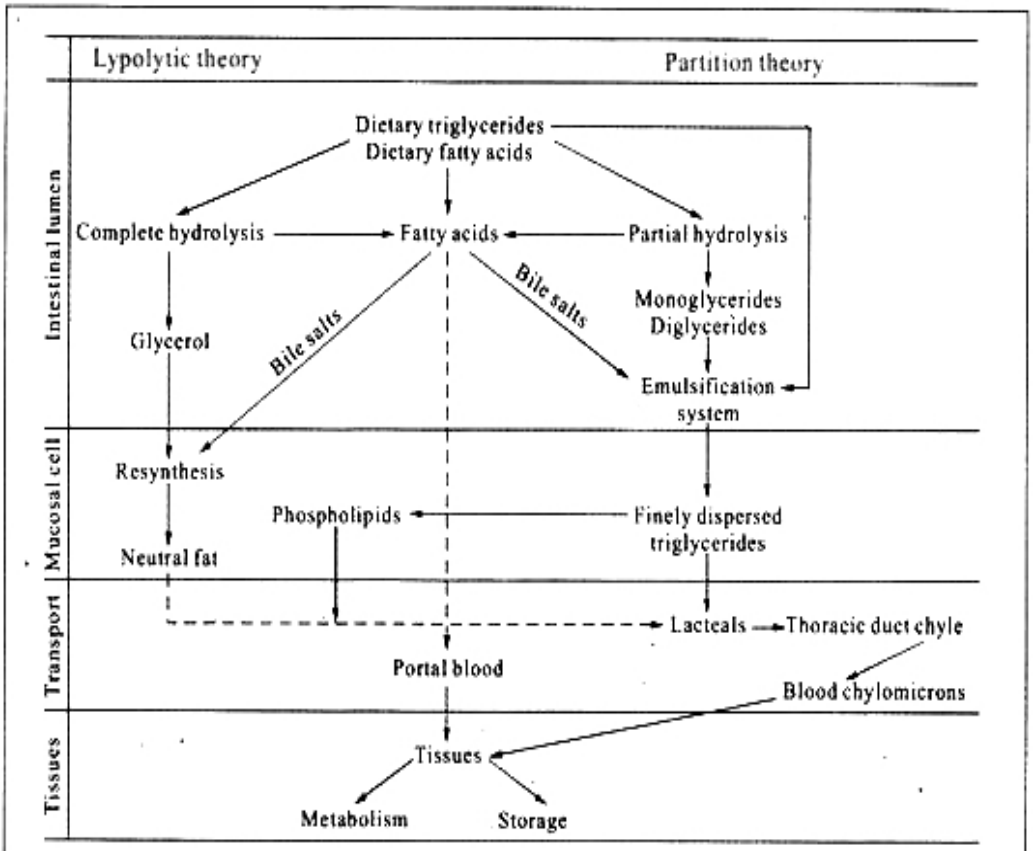


Fig : Old concept of fat absorption containing lipolytic theory and partition theory

Recent Theory

1. The removal of the ester group of 2- mono-acylglycerol requires isomerisation to a primary ester linkage. This is a slow process. As a result, monoacylglycerols are the major end products of fat digestion and less than one-fourth of the ingested fat is completely broken down to glycerol and fatty acids.

2. Within the intestinal wall, 2-monoacylglycerols are converted to triacylglycerol and l-monoacylglycerols are further hydrolyzed to form free glycerol and fatty acids.

3. The fatty acids are then activated by thiokinase in presence of ATP and coenzyme A for the resynthesize of triacylglycerol.

4. The free glycerol in the intestinal lumen is about 22 per cent of total amount of triacylglycerol originally present. This passes directly to the portal vein.

5. The glycerol within the intestinal wall is activated by glycerokinase in presence of ATP to form glycerol-3-phosphate for the synthesis of triacylglycerol followed by the combination with acyl-CoA present in the intestinal wall.

6. All long chain fatty acids present in the intestinal wall are reincorporated into triacylglycerol's which are transported to the lymphatic vessels of the abdominal region (the so-called lacteals) for distribution to the rest of the body.

7. The great majority of absorbed fat appears in the form of chylomicrons which appear first at the lymphatic vessels of the abdominal region and later in the systemic blood. The chylomicrons contain triacylglycerol, free and esterified cholesterol, phospholipid and 0.5 per cent protein.

All of the factors relating to digestion and absorption of fat are mentioned in Fig.7.1.

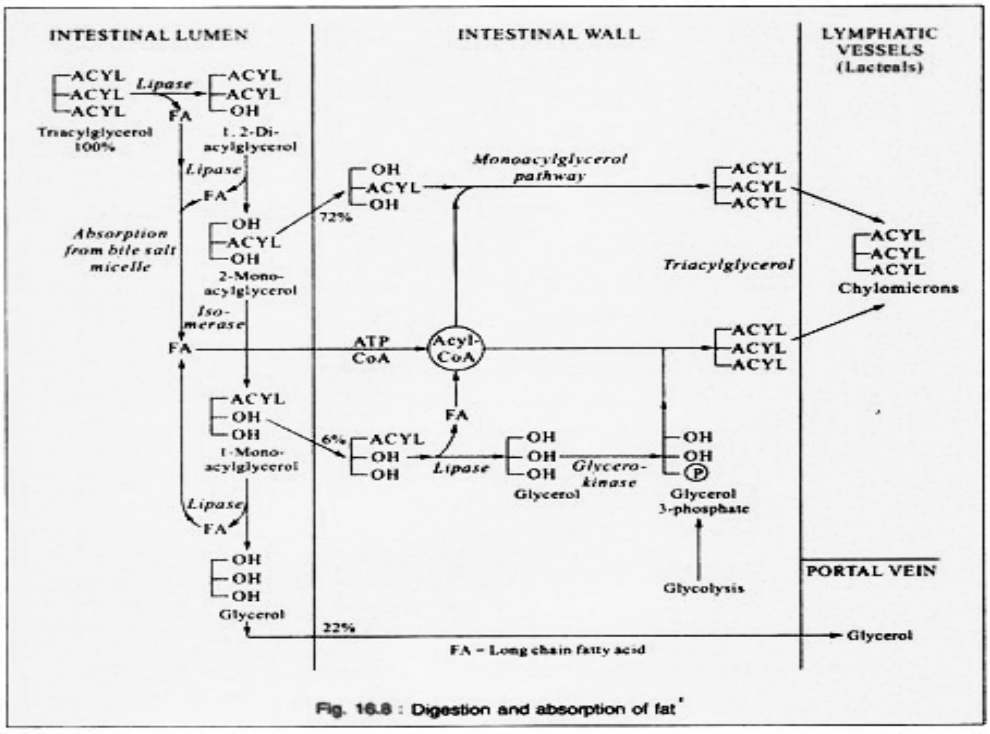
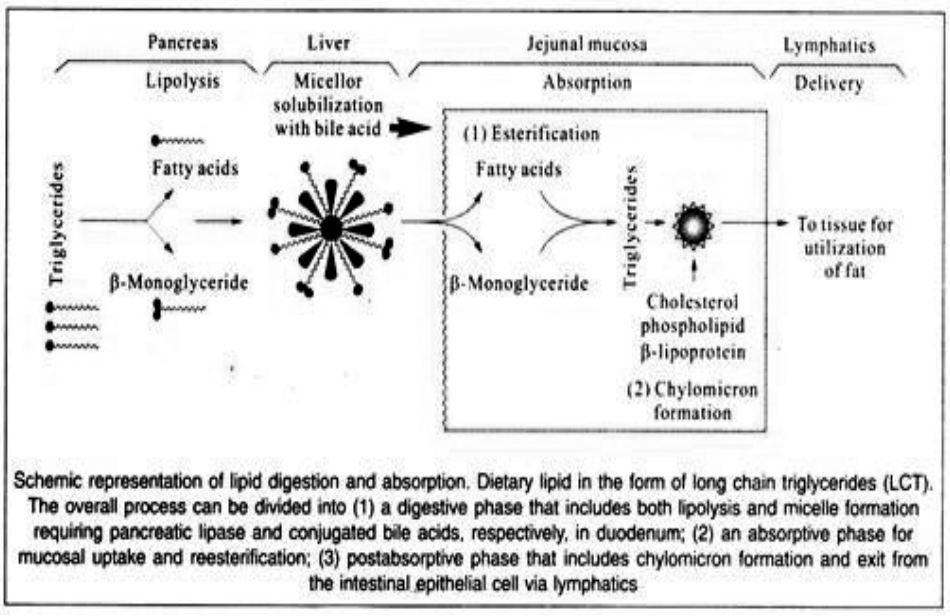


Fig. 16.8 : Digestion and absorption of fat

Fig.7.1 : Digestion and absorption of fat



Schemic representation of lipid digestion and absorption. Dietary lipid in the form of long chain triglycerides (LCT). The overall process can be divided into (1) a digestive phase that includes both lipolysis and micelle formation requiring pancreatic lipase and conjugated bile acids, respectively, in duodenum; (2) an absorptive phase for mucosal uptake and reesterification; (3) postabsorptive phase that includes chylomicron formation and exit from the intestinal epithelial cell via lymphatics

Absorption of Phospholipids

Phospholipids are split by phospholipases and their acryl chains are incorporated into chylomicrons, choline, the hydrophilic component, may be transported directly to the liver via the hepatic portal vein.

Absorption of Cholesterol :

It is absorbed into the lymphatics and recovered mainly as cholesteryl esters.

Chyluria :

In this abnormality, the patient excretes milky urine because of the presence of an abnormal connection between the urinary tract and the lymphatic drainage system of the intestine, a so-called “chylous fistula”.

What are dietary fats?

Dietary fat may have a bad reputation, but fat isn’t always a bad thing. Your body actually needs fat for energy and to process certain vitamins and minerals.

Unfortunately, added sugars and refined carbohydrates are often used to replace fat in processed foods. That adds up to a lot of extra calories with little to no nutritional value.

There’s one bad fat that you should avoid, i.e. trans fats. They have no nutritional value and are harmful to your health. They’re often found in fried foods, processed snacks, and baked goods.

Two other types of dietary fat are saturated and unsaturated fat. Rather than trying to cut fat, you’ll be better off learning more about these two types of fat and how they affect your body.

What is saturated fat?

Fats that are tightly packed are called saturated fats. There are some exceptions, but most are solid at room temperature.

Sources of saturated fat include:

- Red meat
- Some pork and chicken products
- Dairy products including butter, shortening, and cheese

A diet high in saturated fat may raise your low-density lipoprotein (LDL) cholesterol levels. This will raise your risk of heart disease and type 2 diabetes.

What is unsaturated fat?

Unsaturated fats are loosely packed. They tend to be liquid at room temperature.

Replacing saturated fat with unsaturated fat can improve your health. Unsaturated fat comes from plants. It's found in:

- vegetable oils
- olives
- nuts and seeds
- some fish

There are two main types of unsaturated fat:

Monounsaturated fats

Monounsaturated fats can help improve your cholesterol levels and lower your risk of cardiovascular disease. It may also help you control your insulin levels and blood sugar.

Foods that contain monounsaturated fats include:

- olive oil
- peanut oil
- canola oil
- avocados
- most nuts
- most seeds

Polyunsaturated fats

Your body needs polyunsaturated fats to function. This type of fat helps with muscle movement and blood clotting. Since your body doesn't

make it, you have to get it in your diet. Polyunsaturated fats can be further divided into two types: omega-3 and omega-6 fatty acids. Omega-3 fatty acids may be beneficial to the heart. Omega-3 fatty acids can be found in:

- fatty fish, such as sardines, tuna, salmon, trout, mackerel, and herring
- ground flax and flaxseed oil
- non-hydrogenated soybean oil
- safflower oil
- sunflower oil
- canola oil
- walnuts
- sunflower seeds
- chia seeds
- hemp seeds

Omega-6 fatty acids may also help protect against cardiovascular disease. But there's debate about the inflammatory role of omega-6. Most Americans consume more than enough of them.

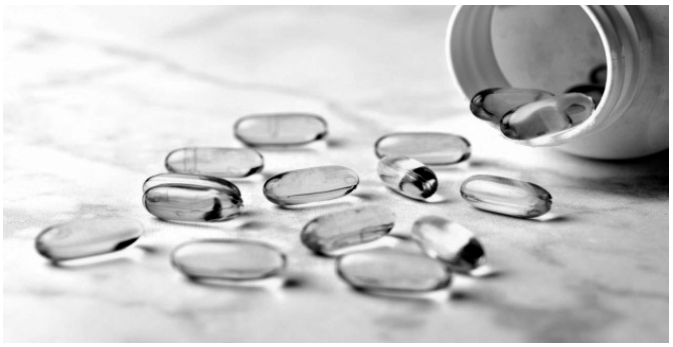
Omega-6 fatty acids can be found in:

- safflower oil
- soybean oil
- sunflower oil
- walnut oil
- corn oil

Recent research reveals that there's not enough evidence that saturated fat raises the risk of cardiovascular disease. But choosing polyunsaturated fats in place of saturated fat can reduce the risk. That's not the case if you replace saturated fat with sugar and processed carbohydrates. Some oils may have more health benefits than others. Canola oil, although considered an unsaturated fat, is typically genetically modified and refined, bleached and deodorized. This process may cause negative health effects. Eating oils in moderation and varying your intake of types of oils is recommended.

Science-Based Benefits of Omega-3 Fatty Acids

Omega-3 fatty acids are incredibly important. They have many powerful health benefits for your body and brain. In fact, few nutrients have been studied as thoroughly as omega-3 fatty acids. Here are 17 health benefits of omega-3 fatty acids that are supported by science.



Omega-3s Can Fight Depression and Anxiety.

Depression is one of the most common mental disorders in the world. Symptoms include sadness, lethargy and a general loss of interest in life. Anxiety, also a common disorder, is characterized by constant worry and nervousness Interestingly, studies indicate that people who consume omega-3s regularly are less likely to be depressed. What's more, when people with depression or anxiety start taking omega-3 supplements, their symptoms improve. There are three types of omega-3 fatty acids: ALA, EPA and DHA. Of the three, EPA appears to be the best at fighting depression .One study even found EPA as effective against depression as a common antidepressant drug.

Omega-3s Can Improve Eye Health

DHA, a type of omega-3, is a major structural component of the retina of your eye . When you don't get enough DHA, vision problems may arise. Interestingly, getting enough omega-3 is linked to a reduced risk of macular degeneration, one of the world's leading causes of permanent eye damage and blindness.

Omega-3s Can Promote Brain Health During Pregnancy and Early Life

Omega-3s are crucial for brain growth and development in infants. DHA accounts for 40% of the polyunsaturated fatty acids in your brain and 60% in the retina of your eye. Therefore, it's no surprise that infants fed a DHA-fortified formula have better eyesight than infants fed a formula without it. Getting enough omega-3s during pregnancy is associated with numerous benefits for your child, including.

- Higher intelligence
- Better communication and social skills
- Fewer behavioral problems
- Decreased risk of developmental delay
- Decreased risk of ADHD, autism and cerebral palsy

Omega-3s Can Improve Risk Factors for Heart Disease

Heart attacks and strokes are the world's leading causes of death. Decades ago, researchers observed that fish-eating communities had very

low rates of these diseases. This was later linked to omega-3 consumption. Since then, omega-3 fatty acids have been tied to numerous benefits for heart health.These benefits address:

- **Triglycerides :** Omega-3s can cause a major reduction in triglycerides, usually in the range of 15–30%
- **Blood pressure :** Omega-3s can reduce blood pressure levels in people with high blood pressure.
- **"Good" HDL cholesterol :** Omega-3s can raise "good" HDL cholesterol levels.
- **Blood clots :** Omega-3s can keep blood platelets from clumping together. This helps prevent the formation of harmful blood clots.
- **Plaque :** By keeping your arteries smooth and free from damage, omega-3s help prevent the plaque that can restrict and harden your arteries.
- **Inflammation :** Omega-3s reduce the production of some substances released during your body's inflammatory response. For some people, omega-3s can also lower "bad" LDL cholesterol. However, evidence is mixed — some studies find increases in LDL.

Despite these beneficial effects on heart disease risk factors, there is no convincing evidence that omega-3 supplements can prevent heart attacks or strokes.

Omega-3s Can Reduce Symptoms of ADHD in Children

Attention deficit hyperactivity disorder (ADHD) is a behavioural disorder characterized by inattention, hyperactivity and impulse. Several studies note that children with ADHD have lower blood levels of omega-3 fatty acids than their healthy peers. What's more, numerous studies observe that omega-3 supplements can reduce the symptoms of ADHD.

Omega-3s help improve inattention and task completion. They also decrease hyperactivity, impulsiveness, restlessness and aggression. Recently, researchers observed that fish oil supplements were one of the most promising treatments for ADHD.

Omega-3s Can Reduce Symptoms of Metabolic Syndrome

Metabolic syndrome is a collection of conditions. It includes central obesity — also known as belly fat — as well as high blood pressure, insulin resistance, high triglycerides and low "good" HDL cholesterol levels. It is a major public health concern because it increases your risk of many other illnesses, including heart disease and diabetes. Omega-3 fatty acids can improve insulin resistance, inflammation and heart disease risk factors in people with metabolic syndrome.

Omega-3s Can Fight Inflammation

Inflammation is a natural response to infections and damage in your body. Therefore, it is vital for your health. However, inflammation sometimes persists for a long time, even without an infection or injury. This is called chronic-or long-term-inflammation. Long-term inflammation can contribute to almost every chronic Western illness, including heart disease and cancer . Notably, omega-3 fatty acids can reduce the production of molecules and substances linked to inflammation, such as inflammatory eicosanoids and cytokines. Studies have consistently observed a connection between higher omega-3 intake and reduced inflammation.

Omega-3s Can Fight Autoimmune Diseases

In autoimmune diseases, your immune system mistakes healthy cells for foreign cells and starts attacking them. Type 1 diabetes is one prime example, in which your immune system attacks the insulin-producing cells in your pancreas.

Omega-3s can combat some of these diseases and may be especially important during early life. Studies show that getting enough omega-3s during your first year of life is linked to a reduced risk of many autoimmune diseases, including type 1 diabetes, autoimmune diabetes and multiple sclerosis. Omega-3s also help treat lupus, rheumatoid arthritis, ulcerative colitis, Crohn's disease and psoriasis.

Omega-3s Can Improve Mental Disorders

Low omega-3 levels have been reported in people with psychiatric disorders. Studies suggest that omega-3 supplements can reduce the frequency of mood swings and relapses in people with both schizophrenia and bipolar disorder. Supplementing with omega-3 fatty acids may also decrease violent behavior .

Omega-3s Can Fight Age-Related Mental Decline and Alzheimer's Disease

A decline in brain function is one of the unavoidable consequences of aging. Several studies link higher omega-3 intake to decreased age-related mental decline and a reduced risk of Alzheimer's disease. One review of controlled studies suggests that omega-3 supplements may be beneficial at disease onset, when the symptoms of AD are very mild. Keep in mind that more research is needed on omega-3s and brain health.

1. Omega-3s May Help Prevent Cancer

Cancer is one of the leading causes of death in the Western world, and omega-3 fatty acids have long been claimed to reduce the risk of certain cancers. Interestingly, studies show that people who consume the most omega-3s have up to a 55% lower risk of colon cancer Additionally, omega-3 consumption is linked to a reduced

risk of prostate cancer in men and breast cancer in women. However, not all studies give the same results .

Omega-3s Can Reduce Asthma in Children

Asthma is a chronic lung disease with symptoms like coughing, shortness of breath and wheezing. Severe asthma attacks can be very dangerous. They are caused by inflammation and swelling in the airways of your lungs. Several studies associate omega-3 consumption with a lower risk of asthma in children and young adults .

Omega-3s Can Reduce Fat in Your Liver

Non-alcoholic fatty liver disease (NAFLD) is more common than you think. It has increased with the obesity epidemic to become the most common cause of chronic liver disease in the Western world. However, supplementing with omega-3 fatty acids effectively reduces liver fat and inflammation in people with NAFLD.

Omega-3s May Improve Bone and Joint Health

Osteoporosis and arthritis are two common disorders that affect your skeletal system. Studies indicate that omega-3s can improve bone strength by boosting the amount of calcium in your bones, which should lead to a reduced risk of osteoporosis. Omega-3s may also treat arthritis. Patients taking omega-3 supplements have reported reduced joint pain and increased grip strength.

Omega-3s Can Alleviate Menstrual Pain

Menstrual pain occurs in your lower abdomen and pelvis and often radiates to your lower back and thighs.It can significantly affect your quality of life. However, studies repeatedly prove that women who consume the most omega-3s have milder menstrual pain. One study even determined that an omega-3 supplement was more effective than ibuprofen in treating severe pain during menstruation.

Omega-3 Fatty Acids May Improve Sleep

Good sleep is one of the foundations of optimal health. Studies tie sleep deprivation to many diseases, including obesity, diabetes and depression. Low levels of omega-3 fatty acids are associated with sleep problems in children and obstructive sleep apnea in adults. Low levels of DHA are also linked to lower levels of the hormone melatonin, which helps you fall asleep. Studies in both children and adults reveal that supplementing with omega-3 increases the length and quality of sleep.

Omega-3 Fats Are Good For Your Skin

DHA is a structural component of your skin. It is responsible for the health of cell membranes, which make up a large part of your skin. A

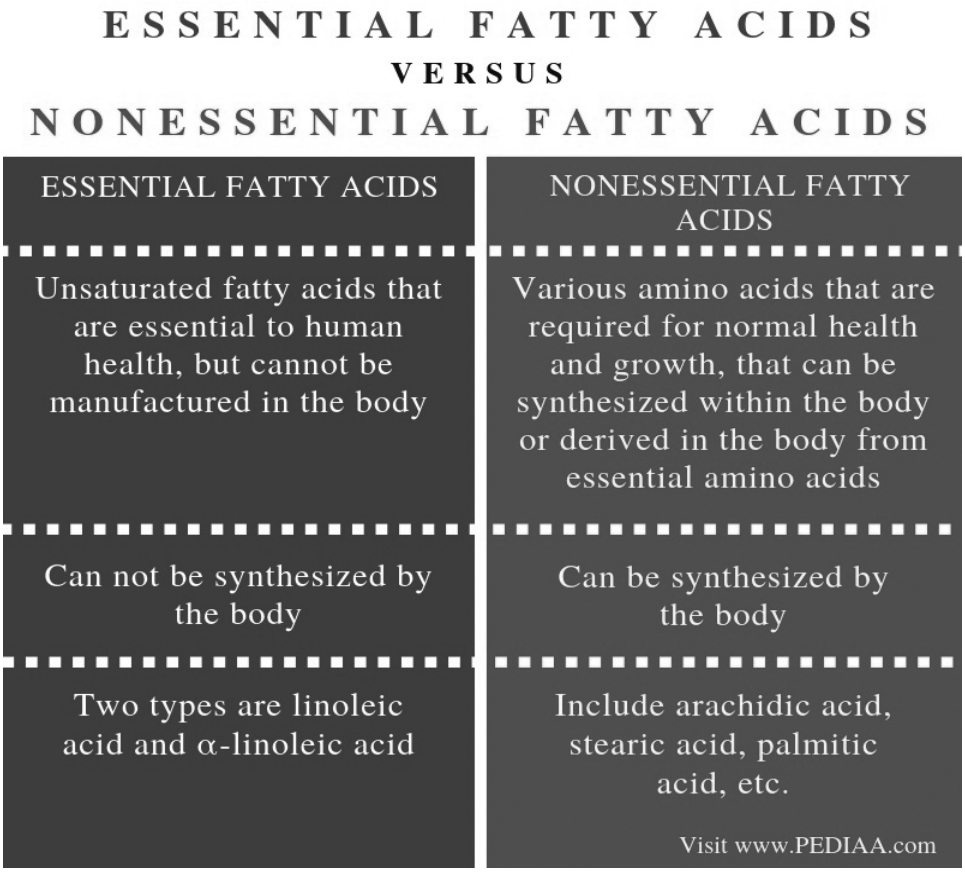
healthy cell membrane results in soft, moist, supple and wrinkle-free skin. EPA also benefits your skin in several ways, including

- Managing oil production and hydration of your skin.
- Preventing hyperkeratinisation of hair follicles, which appears as the little red bumps often seen on upper arms.
- Reducing premature aging of your skin.
- Reducing the risk of acne.

Omega-3s can also protect your skin from sun damage. EPA helps block the release of substances that eat away at the collagen in your skin after sun exposure .

7.23 ESSENTIAL AND NONESSENTIAL FATTY ACIDS

The **main difference** between essential and nonessential fatty acids is that **our body cannot produce essential fatty acids whereas our body can synthesize nonessential fatty acids through various biochemical reactions.** Essential and nonessential fatty acids are two types of fatty acids whose classification originates from the body's ability to synthesize fatty acids. Furthermore, the two types of essential fatty acids are linoleic acid and α-linoleic acid while there are various nonessential fatty acids including arachidic acid, stearic acid, and palmitic acid.



What are Essential Fatty Acids

Essential fatty acids are the type of fatty acids which cannot be synthesized by the body. That means; we need to include essential fatty acids in our diet. The two essential fatty acids in the human body are linoleic acid (LA) and α-linolenic acid (ALA). Both of them are short-chained polyunsaturated fatty acids with 18 carbon-long hydrocarbon chains. Here, the linoleic acid is an omega-6 fatty acid. It contains two double-bonds that are set apart by two single bonds. The main sources of linoleic acid are nuts and fatty seeds like poppy, sesame, hemp, and flaxseed.

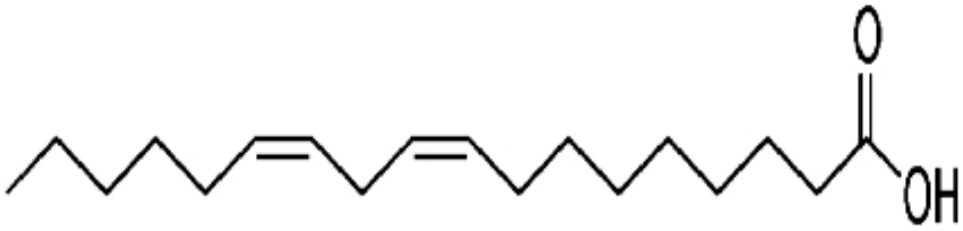


Fig. 1 : Linoleic Acid

On the other hand, α-linolenic acid is an omega-3 fatty acid. It contains three double-bonds separated by three single bonds. The main sources of α-linoleic acid are walnuts, seeds like chia, hemp, and flaxseed, and vegetable oils.

What are Nonessential Fatty Acids

Nonessential fatty acids are the other type of fatty acids the body can synthesize, either through various biochemical reactions or converting the essential amino acids such as alanine, asparagine, aspartic acid, cystine, glutamic acid, glutamine, glycine, proline, serine, and tyrosine. Therefore, their presence in the diet is not essential.

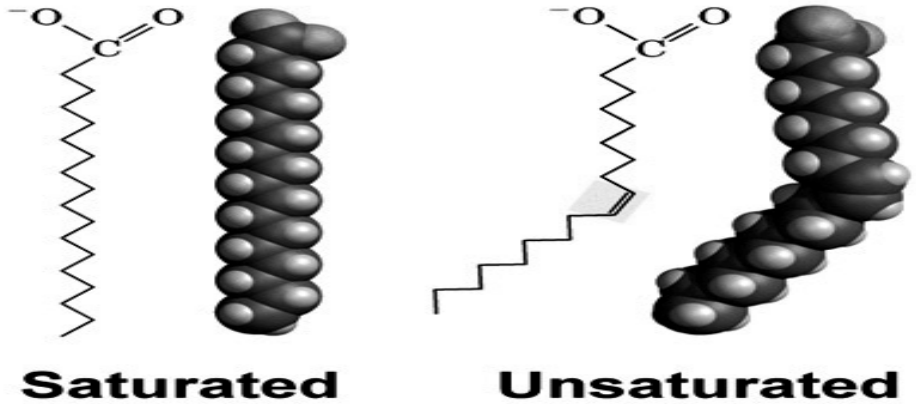


Fig. 2 : Saturated and Unsaturated Fatty acids

Nonessential fatty acids are either saturated fat or unsaturated fat. The fatty acid chain of the saturated fat only contains single bonds between carbon atoms. Saturated fat is bad fat since it can lead to atherosclerosis and heart disease. It exists as a soild in the room temperature and most of the animal fat is saturated. On the other hand, unsaturated fatty acids contain at least one single double bond in the hydrocarbon chain. It is good fat since it can increase the HDL levels in the body. Generally, unsaturated fat occurs as liquids in the room temperature. Most plant fats are unsaturated.

Similarities between essential and nonessential fatty acids

- Essential and nonessential fatty acids are the two types of fatty acids classified based on the ability of the body to produce them.
- Both consist of long hydrocarbon chains with a terminal carboxylic group.
- Also, both have a role in the formation of triglycerides.

Difference between essential and nonessential fatty acids

Essential fatty acids refer to unsaturated fatty acids that are essential to human health, but cannot be manufactured in the body while nonessential fatty acids refer to any of various amino acids that are required for normal health and growth, that can be synthesized within the body or derived in the body from essential amino acids. So, this is the fundamental difference between essential and nonessential fatty acids.

Ability of the Body to Synthesize

Simply, the difference between essential and nonessential fatty acid is that our body cannot synthesize essential fatty acids, but it can synthesize nonessential fatty acids. For **examples**, the two types of essential fatty acids are linoleic acid and α-linoleic acid while some nonessential fatty acids include arachidic acid, stearic acid, palmitic acid, etc. The two types of essential fatty acids are linoleic acid and α-linolenic acid. They have to be included in the diet. On the other hand, our body can produce nonessential fatty acids through metabolic reactions. These fatty acids are either saturated or unsaturated fats. Therefore, the main difference between essential and nonessential fatty acids is the ability of the body to synthesize them.

Tips for making sure your diet is balanced

Your body needs fat. The goal isn't to cut out fats completely, but to eat healthier fats whenever you can.

Limit these foods	Replace them with these foods
butter, stick margarine, and cream cheese	oil-based dressings and spreads
sour cream and ice cream	low-fat plain or Greek yogurt
whole milk	skim or low-fat milk or plant milk (soy, almond, flax, hemp)
pizza, processed meats, fatty meats, fried chicken, or other skin-on chicken dishes	lean cuts of meat, poultry, seafood, and fish
desserts, baked goods, and processed snacks	Whole grains, fruits, vegetables, and nuts

Note :

When cooking :

- Sauté with olive oil instead of butter, lard, or shortening.
- Bake with canola, olive, sunflower, or avocado oil.
- Bake, broil, or grill seafood and poultry instead of frying.

When you go grocery shopping, read nutrition labels carefully. Many foods contain both saturated and trans fat. Be cautious when buying reduced-fat products. The fats are often replaced with something worse.

The bottom line

Healthy eating starts with a diet rich in the following:

- whole grains
- beans and legumes
- vegetables
- fruits

Eating too much fat can contribute to weight gain. This can raise your risk of heart disease and other chronic health problems. But fats are part of a healthy diet. The trick is to favour the healthier fats over the less healthy fats.

To cut down on your total fat intake, it’s important to replace fats with healthy options rather than processed foods. If you have high cholesterol, high triglycerides, or high blood pressure, talk to your doctor.

7.24 SUMMARY

Dietary fiber consists of non-starch polysaccharides and other plant components such as cellulose, resistant starch, resistant dextrins, inulin, lignins, chitins, pectins, beta-glucans, and oligosaccharides. Different fibers have different effects, suggesting that a variety of dietary fibers contribute to overall health. Some fibers contribute through one primary mechanism Fermentable fibers-such as resistant starch and insulin – feed the bacteria and micro biota of the large intestine, and is metabolized to yield short-chain fatty acids, which have diverse roles in gastrointestinal health.

Omega-3 supplements may help prevent and treat depression and anxiety. EPA seems to be the most effective at fighting depression. Getting enough omega-3s during pregnancy and early life is crucial for your child's development. Supplementing is linked to higher intelligence and a lower risk of several diseases.

- Omega-3s can have numerous benefits for people with metabolic syndrome. They can reduce insulin resistance, fight inflammation and improve several heart disease risk factors. Omega-3 fatty acids can help fight several autoimmune diseases, including type 1 diabetes, rheumatoid arthritis, ulcerative colitis, Crohn's disease and psoriasis.
- Omega-3 fats may prevent age-related mental decline and Alzheimer's disease. But Omega-3 intake may decrease the risk of some types of cancer, including colon, prostate and breast cancer. Omega-3 intake has been associated with a lower risk of asthma in both children and young adults.
- Omega-3 fatty acids reduce liver fat in people with non-alcoholic fatty liver disease. Omega-3 fatty acids can reduce menstrual pain and may even be more effective than ibuprofen, an anti-inflammatory drug. Omega-3 fatty acids — especially DHA — may improve the length and quality of your sleep. Omega-3s can help keep your skin healthy, preventing premature aging and safeguarding against sun damage.

7.25 Terminal Question

Q.1. Write note on Dietary Fibres.

Answer: ----------

Q.2. What are soluble and insoluble dietary fibres?

Answer: ----------

Q.3. Define chylomicrons.

Answer: ----------

Q.4. Enumerate physiochemical properties of dietary fibres.

Answer: ----------

Q.5. What are vegetable gums? Give examples.

Answer: ----------

Q.6. What are various sources of vegetable oils?

Answer: ----------

7.26 FURTHER READINGS

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UNIT-8 DRUG-NUTRIENT INTERACTIONS

Structure

8.1 INTRODUCTION

The drug-nutrient interaction is a reaction between a medicine and one or more nutrients. The dietary supplement is a vitamin, mineral, or herb that you take to improve your health or wellness. However, when taken with prescription or over-the-counter medicines, dietary supplements can cause side effects. Supplements can affect the way a medicine acts, or the way that the body absorbs, uses, or gets rid of a medicine. Food can increase or decrease the amount of medicine your body absorbs. If your body cannot absorb as much of the medicine as it should, you will not get the full effect of the medicine.

Objectives

- Define to drug-nutrient and supplement interactions
- To discus about Alcohol and Nutrient Deficiency
- Drug administration with respect to food intake per package inserts recommendations
- To learn about pharmacodynamic interactions

8.2 DRUG-NUTRIENT INTERACTION

A drug-nutrient interaction is a reaction between a medicine and one or more nutrients. Nutrients are the vitamins and minerals that are in the food you eat. Vitamins and minerals nourish your body and help to keep you healthy and reduce your risk for chronic diseases. When a medicine interacts with a nutrient, it can keep the medicine from working properly. It can also decrease or increase the amount of a nutrient in your body. Food can increase or decrease the amount of medicine your body absorbs. If your body cannot absorb as much of the medicine as it should, you will not get the full effect of the medicine. If your body absorbs too much of the medicine, it can cause the medicine to have an effect that is too strong. Food and nutrients can also affect the rate at which your body processes or removes a medicine.

For example, eating foods high in vitamin K can keep warfarin (a blood thinner) from working properly. Foods high in vitamin K include broccoli and spinach. Foods high in tyramine, such as aged cheeses, can cause severe high blood pressure in people who take monoamine oxidase inhibitors (MAOIs).

There are several different ways a medicine can affect the amount of a nutrient in your body. Some medicines can make you feel less hungry or sick to your stomach, all of which affect how much food you eat. Some medicines can keep your body from absorbing or making certain nutrients. For example, chemicals in **grapefruit** can cause your body to absorb either too much or not enough medicine into your bloodstream.

8.3 DRUG-SUPPLEMENT INTERACTIONS

A dietary supplement is a vitamin, mineral, or herb that you take to improve your health or wellness. However, when taken with prescription or over-the-counter medicines, dietary supplements can cause side effects. Supplements can affect the way a medicine acts, or the way that the body absorbs, uses, or gets rid of a medicine. For example, St. John's wort, a popular dietary supplement, can affect many different medicines, including selective serotonin reuptake inhibitors (SSRIs). Taking St. John's wort while also taking an SSRI can lead to high levels of serotonin levels in your body (called serotonin syndrome).

What is drug-nutrient depletion?

Drug-nutrient depletion occurs when long-term use of a medicine affects the body's ability to create or maintain a healthy nutrient level. This can cause low levels of nutrients in your body. For example:

- Statins (cholesterol-lowering medicine) can cause coenzyme Q10 levels to be too low in your body

- Diuretics (water pills) can cause potassium levels to be too low in your body
- Acid reducers can decrease your body's levels of vitamin B12, calcium, magnesium, and other minerals
- Anticonvulsants (seizure medicine) can cause low levels of vitamin D. This depletion is usually a slow process, occurring over time.

Questions to Ask Your Doctor

- Am I at risk for a drug-nutrient interaction or drug-supplement interaction?
- Will any of my medications react poorly to other prescriptions, vitamins or supplements?
- How should my medicines be taken?
- Can we check my nutrient levels?
- Are there any supplements I should be taking?

8.4 ALCOHOL AND NUTRIENT DEFICIENCY

For people with an alcohol dependency, the toxic effects of the alcohol itself aren't the only health problems that develop. In the long term, alcoholism also leads to the development of deficiency in several different vitamins and minerals. This relationship between alcohol and vitamin deficiency has been the subject of several studies and has been realized as a dangerous symptom of an addiction to alcohol. Keep reading to find out which vitamins alcoholics are deficient in as they continue their destructive habit.

Why do deficiencies develop?

Nutrient deficiencies develop in people with alcoholism for several reasons: first is simply that some alcoholics neglect their food intake. They eat less food than they need, and instead get the bulk of their calories from alcohol; but since alcohol contains none of the micro-nutrients that are essential for health, inadequate food intake on its own can lead to nutritional deficiencies.

The second reason is that alcohol reduces the body's ability to extract nutrients from food because, over time, heavy consumption of alcohol damages the lining of the gastrointestinal tract, which interferes with nutrient absorption. As well as this, chronic alcoholism causes the body to excrete higher than normal amounts of certain nutrients.

For all alcoholics, therefore, there are serious risks of deficiency in multiple nutrients, and the risk is greater in people who eat less food as a result of drinking.

8.5 COMMON VITAMIN DEFICIENCIES IN ALCOHOLICS

People who use alcohol in excess, both short-term and long-term, are at risk of nutritional deficiencies, but the risk does increase with long-term alcohol use. Many of the symptoms of alcohol withdrawal are related to nutritional deficiency, but those symptoms are masked by the effects of alcohol consumption and are felt only once consumption ceases. The main vitamins that alcoholics tend to lack are vitamin A, vitamin B, and vitamin D.

Not all vitamins and minerals are at risk of deficiency due to alcohol—it depends on how readily available nutrients are in food, and how vulnerable they are to alcohol-induced damage. For example, **B-group vitamins are particularly vulnerable** and alcoholics have a high risk of deficiency in these vitamins. One of the most important is Thiamine, a B-group vitamin that is absolutely essential for human health. People who are long-term alcoholics have a risk of developing a degenerative brain disease that causes serious damage and eventually death and one of the most important factors leading to alcohol-induced brain disease is a B-group vitamin called thiamine. One common type of brain disease that can result is Wernicke-Korsakoff syndrome, which develops almost exclusively in chronic alcoholics, and causes psychosis, memory loss, and other disorders.

Other common deficiencies in alcoholics include:

- Vitamin C
- Magnesium
- Calcium
- Zinc
- Iron
- Potassium

All of these play important roles in human health, with symptoms such as depression, fatigue, insomnia, central nervous system problems, and hypoglycemia being possible results of deficiency. Vitamin A deficiencies are associated with alcoholism as well, which can increase the risk of infections and reduce eyesight. This can happen when vitamin A is improperly absorbed by the gut.

Alcohol doesn't just affect the body's ability to absorb nutrients from food. As well as this, there's also a risk of deficiency in vitamin D, a vitamin that promotes the health of several organs, including the heart, and is essential in maintaining bone tissue. However, this particular deficiency isn't caused by problems with eating or digestion, as this essential vitamin is created by skin cells during sun exposure. The vitamin D that's

produced by skin cells isn't in a form that the body can use—it has to be processed in the liver and kidneys before the body can make use of it.

But when someone drinks excessive amounts of alcohol, these organs, particularly the liver, are already overloaded by the alcohol they must metabolize and excrete. As a result, the ability of the liver and kidneys to metabolize vitamin D is severely impaired, and a deficiency develops, with consequences that can include fatigue, muscle pain and wasting, and loss of bone density, with osteoporosis an eventual risk.

8.6 PREVENTING NUTRITIONAL DEFICIENCIES

For someone who has developed nutritional deficiencies as a result of alcoholism, or who is at risk, the best way by far to start repairing the damage is to stop drinking. But due to the nature of alcohol addiction, that's not always possible; so for someone who's unable to give up drinking in the present, it's important that they protect their future health as much as possible by getting enough to eat, and by supplementing with the vitamins and minerals they're likely to be lacking. A daily multivitamin supplement, plus extra supplementation with calcium, B vitamins, vitamin D, and other key nutrients, can make a huge difference in the long term and may help prevent serious alcohol-related diseases.

Things to consider

Don't take any herbal health products or supplements without talking to your family doctor first. This is especially the case if you take any other prescription or over-the-counter medicine. If you do use an herbal health product or supplement, read the directions on the label to learn how much to take and how often to take it. You should never take more than the recommended amount. If you have any questions about how much to take, ask your doctor.

8.7 ANTIDEPRESSANTS AND NUTRIENT INTERACTION

Monoamnine Oxidases

- Antidepressant activity of monoamine oxidase inhibitors (MAOIs) was initially noted in the 1950s. Although older monoamine oxidase inhibitors (MAOIs) are effective in the treatment of depressive disorders, they are under-utilized in clinical practice due to main concerns about interaction with tyramine-containing food (matured cheese, red vine, ripped bananas, yogurt, shrimp paste and salami) or so called cheese reaction, since they are capable of producing hypertensive crisis in patients taking MAOIs.
- The first-generation MAOIs such as phenelzine and isocarboxazid were largely nonselective inhibitors of both subtypes of MAO,

MAO (A) and MAO (B). These medications carried with them dietary restrictions. Tyramine is an indirectly acting sympathomimetic agent, is degraded by MAO but in the presence of MAOIs, it escapes degradation and reaches the systemic circulation where it is taken up by the adrenergic neuron, leading to a hypertensive crisis. However, MAOIs have been well established as an effective intervention for people with treatment-resistant depression, and transdermal formulations may provide a valuable therapeutic option and eliminate the drug-food interaction.

8.8 PSYCHOACTIVE DRUGS AND NUTRIENT DRUG INTERACTION

Food-drug interactions have been identified for many psychotropics. Most of the listed food-psychotropic interactions are pharmacokinetic, involving drug absorption, metabolism, and/or excretion.

8.8.1 PHARMACOKINETIC INTERACTIONS

Absorption

The presence of food in the stomach or small bowel affects the rate and/or extent of absorption for many drugs. This may be a significant factor for drugs such as buspirone, lurasidone, sertraline, vilazodone, and ziprasidone, all of which have potentially increased absorption in the presence of food. For other drugs, including certain hypnotics and anticonvulsants, the rate of absorption is slowed in the presence of food, so the speed of drug onset is slower. This can be used to advantage for drugs such as immediate-release trazodone, as slowed absorption can reduce the risk of orthostatic hypotension.

Since 1989, when the first interaction between drugs and grapefruit juice (GFJ) was serendipitously discovered, interactions with GFJ have been extensively studied, mostly by in vitro methods. Various compounds present in GFJ influence the activity of several enzymes and transporters, including CYP3A and p-glycoprotein; in vivo evidence exists for clinically relevant inhibition of CYP3A, but only in the GI tract with normal GFJ consumption. Drugs that should be avoided when GFJ is ingested include buspirone, mifepristone, pimozide, and ziprasidone. Drugs for which caution is advised with GFJ include carbamazepine and benzodiazepines.

In vivo evidence also supports altered activity of organic anion transporter proteins in the presence of GFJ, but the significance for psychotropics is not known. Even for CYP3A, clinically relevant interactions are limited to oral drugs significantly metabolized by 3A that undergo extensive first-pass metabolism at the gut wall. When these interactions do occur, CYP3A inhibition is irreversible, such that it would

take as long as three days for 3A activity in the intestine to return after GFJ consumption.

Metabolism

In vitro and animal studies have demonstrated that kale and other leafy green vegetables competitively inhibit the activities of many CYP enzymes, including CYP1A2, 2D6, 2C19, and 3A4, among others. Although the amount of kale that would have to be ingested to cause this inhibition is at least an order of magnitude more than would be usual, the potential for additive inhibition should be considered. For example, kale and fluvoxamine could significantly inhibit 1A2, and kale and fluoxetine (or other psychotropics) could significantly inhibit 2D6; kale and fluoxetine, vilazodone, or fluvoxamine could significantly inhibit 2C19. For CYP3A4, psychotropic inducers such as carbamazepine, phenobarbital, or St. John's wort could mitigate inhibitory effects of kale. Similarly, soy milk and miso have been reported to induce the activity of p-glycoprotein and CYP3A4, but the clinical significance of this is not known.

Excretion

It is well known that lithium has a very significant interaction with dietary sodium. The higher the sodium intake, the lower the lithium level. Initiation of a low-salt diet can result in lithium toxicity. In addition, good hydration is important for all patients, but particularly for those on lithium, to avoid renal injury.

Relatively less is known about the human multidrug and toxic compounds extrusion transporter 1 (hMATE1), which is a cation exporter that functions in the liver and kidneys to facilitate the excretion of xenobiotics and toxic drug metabolites. hMATE1 activity is inhibited by compounds present in food such as quercetin (present in red wine, dark-red or purple fruits, and green leafy vegetables) and isorhamnetin (present in almonds, pears, onions, and fennel). The significance of this inhibition for the metabolism of various psychotropics is not known.

8.8.2 PHARMACODYNAMIC INTERACTIONS

One of the most infamous of the pharmacodynamic food-drug interactions is the tyramine reaction. This occurs when foods with high tyramine content are ingested in the presence of a nonselective MAOI. Restricted foods include tap beer, red wine, sherry, liqueurs, aged cheeses, cured meats, fermented cabbage, soy sauce, yeast extracts, and broad-bean pods. Improperly stored or spoiled foods also are problematic. The mechanism of this interaction involves the release of excessive noradrenaline into the synaptic cleft and sympathetic overstimulation.

Table.8.1 : Drug administration with respect to food intake per package inserts recommendations

Therapeutic class[b]	Drugs	Directions
Miscellaneous	Pimozide	Food effect is not known
CNS stimulants	Amphetamine, dextroamphetamine	Food effect has not been studied; take with or without food
	Lisdexamfetamine	t_{max} prolonged by ≈ 1 hour after high-fat meal; take in the morning with or without food
	Methamphetamine	Take 30 minutes before meals
	Dexmethylphenidate	Take tablet or capsule formulation with or without food; no food effect study available for extended-release capsule
	Methylphenidate	Take in the morning with or without food
	Armodafinil	Food can potentially affect the onset and time course of pharmacological action; take with or without food
	Modafinil	Absorption may be delayed by ≈ 1 hour if taken with food; take with or without food
Anorexigenics	Diethylpropion	Take 1 hour before meals and in mid-evening, if desired, to overcome night hunger
	Phendimetrazine	Take 1 hour before meals
	Phentermine	Take with or without food
Anxiolytics	Diazepam	No recommendation
Hypnotics	Buspirone	Take in a consistent manner with regard to the timing of dosing; either always with or always without food
	Eszopiclone, ramelteon, zaleplon, zolpidem	Effects on sleep latency may be reduced if taken with or immediately after a high-fat/heavy meal; for faster onset of sleep, do not take with or immediately after a meal
Anti-manic agents	Lithium salts	During initial stabilization period, maintain consistent, adequate salt and fluid (2.5 - 3.5 L) intake
Miscellaneous	Acamprosate, atomoxetine	Take with or without food

NRIs, norepinephrine reuptake inhibitors; t_{max}, time to maximum drug concentration.
[a] Based on American Hospital Formulary Service Drug Information® classification. (Note: Psychotropic agents have multiple clinical, labeled, and off-label, indications.)
[b] Compiled from http://dailymed.nlm.nih.gov and American Hospital Formulary Service Drug Information® 2013.

Table 8.2 Summary of some significant Food-Drug Interactions

Drugs	Food	Drug-Food Interaction
WARFARIN	High-protein diet	raise serum albumin levels, decrease in international normalized ratio (INR)
	Vegetables containing vitamin k	interferes with the effectiveness and safety of warfarin therapy.
	Charbroiled	decrease warfarin activity
	Cooked onions	increase warfarin activity

Drugs	Food	Drug-Food Interaction
	Cranberry juice	elevated INR without bleeding in elderly patient
	Leafy green vegetables	thromboembolic complications may develop
	Charbroiled	decrease warfarin activity
Monoamnine Oxidases	Tyramine-containing food1	hypertensive crisis
Propranolol	Rich protein food	serum level may be increased
Celiprolol	Orange juice	the intestinal absorption is inhibited
Aces Inhibitors	Empty stomach	absorption is increased
Ca2 Channel	Grape fruit juice	increases the bioavailability
Antibiotics	with milk products2	that complex with some antibiotics and prevent their absorption. reduced bioavailability
Acetaminophen	Pectin	delays its absorption and onset
Nsaids	Alcohol	can increase risk of liver damage or stomach bleeding
	Beverages	the c_{max} and $auc_{0-alpha}$ significantly increased3
Theophyline	High-fat meal and	increase bioavailability

Drugs	Food	Drug-Food Interaction
	grape fruit juice	
	Caffeine	increases the risk of drug toxicity
Esomeprazole	High-fat meal	bioavailability was reduced
Cimetidine, Rupatadine	with food(any type)	increase bioavailability
Isoniazide	Plantsmedicinal herbsoleanolic acid	exerts synergistic effect
Cycloserine	High fat meals	decrease the serum concentration
Esomeprazole	High-fat meal	bioavailability was reduced
Cimetidine, Rupatadine	with food(any type)	increase bioavailability
Isoniazide	Plantsmedicinal herbsoleanolic acid	exerts synergistic effect
Cycloserine	High fat meals	decrease the serum concentration
Glimepiride	with breakfast	absolute bioavailability
Acarbose,	at start of each meal	maximum effectiveness
Mercaptopurine	Cow's milk4	reduce bioavailability
Tamoxifen	Sesame seeds	negatively interferes with tamoxifen in inducing regression of established mcf-7 tumor size but beneficially interacts with

Drugs	Food	Drug-Food Interaction
		tamoxifen on bone in ovariectomized athymic mice
Levothyroxine	Grapefruit juice	delay the absorption5
Glimepiride	with breakfast	absolute bioavailability

8.9 SUMMARY

A large number of drugs are introduced every year. Food-drug interactions can produce negative effects in safety and efficacy of drug therapy, as well in the nutritional status of the patient. Generally speaking, drug interactions are to be avoided, due to the possibility of poor or unexpected outcomes. Like food, drugs taken by mouth must be absorbed through the lining of the stomach or the small intestine. Consequently, the presence of food in the digestive tract may reduce absorption of a drug. Often, such interactions can be avoided by taking the drug 1 hour before or 2 hours after eating. Like drugs, foods are not tested as comprehensively so they may interact with prescription or over-the-counter drugs. One of the most infamous of the pharmacodynamic food-drug interactions is the tyramine reaction. This occurs when foods with high tyramine content are ingested in the presence of a no selective MAOI.

8.10 TERMINAL QUESTIONS

Q.1. What are Monoamine Oxidase inhibitors?

Answer:----------

Q.2. Explain the interaction of Psychoactive Drugs with Nutrients?

Answer:----------

Q.3. How alcohol effect drug nutrient interaction?

Answer:----------

Q.4. What do you understand by ADME of drug?

Answer:----------

Q.5. What do you understand by the term Drug Supplements?

Answer:----------

Q.6. Explain Drug Nutrient depletion?

Answer:----------

Q.7. What interactions might the supplement cause with medicines I am taking?

Answer:----------

8.11 FURTHER READINGS

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UNIT-9 NUTRITIONAL STATUS

Structure

9.1 INTRODUCTION

Nutritional status is the requirement of health of person convinced by the diet, the level of nutrient containing in the body and moral metabolic integrity. Nutrition education is an essential component in improving dietary habits and food choices, in order to reverse the under nutrition and improve the nutritional diagnosis. Nutritional status is the condition of the body resulting from the nutrient content of the food we eat in relation to our nutritional needs, and from the ability of our bodies to digest, absorb and use those nutrients. The nutritional status depends on generally two factors as external factors like food safety, cultural and social economic factors and internal factor like age, sex, nutrition, behaviours and physical activity and disease of person. Biochemical assessment of nutritional status is done by interpretation of various clinical tests done in laboratories as part of clinical pathology. A nutrition assessment is an in-depth evaluation of both objective and subjective data related to an individual's food and nutrient intake, lifestyle, and medical history.

Objectives

- To know about nutrition assessment
- Define the biochemical assessment
- Reactive Oxygen Species and their role in metabolic activity
- Differential diagnosis of B_{12} and foliate

9.2 ANTHROPOMETRIC MEASUREMENTS

Anthropometric measurements are used to assess the size, shape and composition of the human body. Learn about common methods used to gather these measurements, such as BMI, waist-to-hip ratio, skin-fold test and bioelectrical impedance. This man weighs 250 pounds. So does this man.

Do you see a difference? Even though these two men share the same weight, their bodies are very different in shape, structure and composition.

9.2.1 DIFFERENT BODY COMPOSITION

Simply knowing how much someone weighs does not reveal much about their overall condition. To fully assess the status of the human body, we need to utilize various **anthropometric measurements**, which are systematic measurements of the size, shape and composition of the human body. This is a fairly easy term to recall if you remember that the prefix 'anthropo' refers to 'human' and 'metric' refers to 'measurement.' In this lesson, we will learn why athletes, health care professionals and researchers might be interested in anthropometric measurements and the methods they use to gather this information.

Purpose

Anthropometric measurements are useful in many fields. For example, athletes understand that body size and composition are important factors in sports performance. For example, a petite man with a low percentage of body fat will be more successful as a jockey in the Kentucky Derby than he would be as a defensive lineman in the National Football League. Sports coaches can also use these measurements to monitor an athlete's body to ensure they stay in peak physical shape.

Health care professionals rely on body measurements to evaluate a patient's overall health. For example, body mass index, or BMI, is a measurement of a person's weight-to-height ratio. Health care providers, insurance companies and government agencies use BMI to determine if a person is underweight, overweight or obese. A BMI of 30 or greater indicates obesity. Because obesity is linked to chronic diseases, like heart disease, diabetes and certain cancers, knowing this anthropometric measurement can be a lifesaver.

Anthropometric measurements can also be used when studying groups of people. This broader approach allows researchers to evaluate health trends and concerns in various populations. For example, **anthropometry**, which is the scientific study of human body measurements, has been used to assess the nutritional status of children in underdeveloped countries. These measurements can be used to determine the prevalence of undernutrition and evaluate the need for nutritional support.

9.2.2 ANTHROPOMETRY DEFINITION

Anthropometry is the science of obtaining systematic measurements of the human body. Anthropometry first developed in the 19th century as a method employed by physical anthropologists for the study of human variation and evolution in both living and extinct populations. In particular, such anthropometric measurements have been used historically as a means to associate racial, cultural, and psychological attributes with physical properties. Specifically, anthropomorphic measurements involve the size (e.g., height, weight, surface area, and volume), structure (e.g., sitting vs. standing height, shoulder and hip width, arm/leg length, and neck circumference), and composition (e.g., percentage of body fat, water content, and lean body mass) of humans.

9.2.3 ANTHROPOMETRIC TOOLS

To obtain anthropometric measurements, a variety of specialized tools (as depicted below) are used:

- Stadiometers: height
- Anthropometers: length and circumference of body segments
- Biocondylar calipers: bone diameter
- Skinfold calipers: skin thickness and subcutaneous fat
- Scales: weight

Although the majority of the instruments appear straight forward to use, a high level of training is required to achieve high validity and accuracy of measurements. Alphonse Bertillon (1853-1914) developed anthropometry.

Alphonse Bertillon was the son of the physician and founder of the Society of Anthropology of Paris, Louis-Adolphe Bertillon. Although the process of obtaining human measurements had originated in ancient civilizations, Alphonse Bertillon is credited as the father of anthropometrics based on his classification system known as the "anthropometric system" or "judicial anthropometry". Alphonse Bertillon began his career working for the Paris police force in the criminal records department. It was here that Bertillon recognized the recurring problem that it was becoming increasingly more difficult to identify repeat offenders, as the criminal records were stored alphabetically and many criminals were devising aliases in order to avoid deportation and harsher sentences. To address this issue, Bertillon devised a new classification system based on anthropomorphic measurements with the assumptions that bone density is fixed past the age of 20 years, and human dimensions are intrinsically highly variable. Bertillon obtained measurements of height, breadth, foot size, length and width of the head, length of the middle finger, and the length of the left forearm, as well as other

morphological and distinguishing characteristics of criminals in custody (as shown below). He then classified each individual as small, medium, or large, and added frontal and profile photography to each file. Such photography is still currently used today in the form of a "mug shot". After convincing the Paris criminology department to implement Bertillon's system, this method of classification was used to quickly and easily identify unknown individuals and repeat offenders. The use of this anthropometric system was subsequently termed "Bertillonage" and spread rapidly throughout the world during the late 1800s and early 1900s.

9.2.4 CURRENT APPLICATIONS OF ANTHROPOMETRY

While physical anthropologists and criminologists continue to use anthropometric measurements in the study of human evolution through the comparison of novel fossil remains to archived specimens and forensics, respectively, current applications have extended to:

- Industrial design and architecture (e.g., vehicle seating and cockpits)
- Clothing (e.g., military uniforms)
- Ergonomics (e.g., seating)
- Medicine (e.g., nutrition, aging, obesity, sports science, and diabetes)

In these industries, anthropometric data is invaluable to the optimization of various products and observing the changes which occur in response to various lifestyle, genetic, and ethic factors.

9.2.4.1 ERGONOMICS

Economics as it applies to anthropometric measurements is derived from the understanding that every aspect of human life involves activity (e.g., leisure, work, family, education, spirituality, and physical/exercise). As such, specific tools and equipment are required for each activity. Ergonomics is the industry centered around the design and creation of these instruments through the evaluation of human comfort, movement, and other anthropometric measurements. Typically, optimal design is created with an interdisciplinary team involving anthropologists, psychophysicists, and physiologists. Ergonomic designs are tested with a series of experiments which involves:

1. Obtaining anthropometric measurements to derive "ergonomic dimensions" of posture and movement.
2. Recording the subjective feelings of comfort that the individual experiences when using the equipment.
3. Evaluating the ability of the instrument to perform the desired activity.

Anthropometric measurements in the field of ergonomics are obtained in a variety of positions, including sitting, standing, lying down, as well as various derivatives of these poses (e.g., arms stretched out, hands on a table, arms raised above the head, etc.). In addition, due to the high degree of human variability by ethnicity and body composition, the use of multivariate statistics is often applied to various anthropometric measurements for the creation of an optimal design.

9.2.4.2 KINANTHROPOMETRY

Kinathropometry involves obtaining measurements of the human body for the application of human movement. Such measurements include body proportions, composition, somatotype, maturation, motor ability, cardiorespiratory capacity, and physical performance. Therefore, kinanthropometry is highly aligned with the related disciplines of physical education, sports science, pediatrics, physical anthropology, gerontology, and ergonomics.

9.2.4.3 MEDICAL SCIENCE

While early anthropometric measurements have been applied to the field of medicine since the early 17th century as a correlate of disease, recent medical applications involve radiological measurements, computerized tomography (CT), magnetic resonance imaging (MRI), 3D imaging, cosmetology, geriatrics, pediatrics, and bariatrics (obesity). In particular, radiology has been used since the late 1800's to obtain X-rays that can be used to assess bone density and other internal attributes (e.g., pulmonary function). Similarly, CT has been used to obtain cross-

sectional images of the human body to characterize bone mineral density, distinguish between cortical and trabecular bone density, and degenerative changes in the spine. MRI has been applied to obtain high quality images of the brain and other organs, and 3D imaging has permitted the quantitation of the various anatomical structures within the human body. The data generated from these imaging modalities has been used to improve human health and quality of life. In cosmetology, undesirable features caused by injury or aging can be corrected by using facial anthropometrics to identify disproportions and the necessary modifications can be calculated using 3D imaging and reconstruction software. Another medical application of anthropometry is breast cosmetology, which involves the assessment of breast density, volume, and asymmetry via mammography, 3D imaging, and other imaging techniques to determine the most appropriate surgical course of treatment.

9.2.4.4 PEDIATRICS

As mentioned above, anthropometrics has long been recognized as an indicator of human health. As such, anthropometrics is widely used to assess the growth and development of humans, both *in utero* and during childhood. The most important anthropometric measurements during this period include head circumference, weight, and length/height. Head circumference is particularly important as it is correlated with brain growth. In particular, pediatric head circumference measurements are used to identify severe and/or chronic malnutrition in children under the age of two, as well as potential growth abnormalities of the fetus. Weight is also used to assess the presence of malnutrition, and is plotted on established growth curves to monitor the child's growth over time. Length and height are used to assess the body mass index, creatinine height index, height for age, and basal energy expenditure. An extremely short height for age may indicate chronic malnutrition or other musculoskeletal abnormalities.

Quiz

1. **What anthropometric measurement(s) are typically used as an indication of sexual dimorphism in humans?**
   A. Stature
   B. Bertillon Classification
   C. Androgyny index
   D. Osteometry

Answer to Question #1

C is correct. The androgyny index is the shoulder to pelvis ratio which can be used to distinguish between males and females after puberty.

2. **Craniometry is a good anthropometric indicator of:**
   A. Nutritional status
   B. Age
   C. Human evolution
   D. All of the above

Answer to Question #2

D is correct. Cranial measurements can be used to assess all of these factors.

3. The novel design of the interior of a spaceship shuttle is an example of what anthropometric application?

A. Kinanthropometry
B. Ergonomics
C. Somatometry
D. Bertillonage

Answer to Question #3

B is correct. The design of a space shuttle interior involves the application of anthropometrics in the field of ergonomics.

9.3 BIOCHEMICAL ASSESSMENT OF NUTRITIONAL STATUS

Biochemical assessment of nutritional status is done by interpretation of various clinical tests done in laboratories as part of clinical pathology.

Why are labs ordered?

- to confirm a clinical impression or to make a diagnose
- to rule out a disease or diagnosis
- to provide prognostic information
- to provide therapeutic guidelines
- to screen for a disease

Remember though :

Some values do not necessarily correlate with clinical or dietary findings
-results can vary between labs
-results of one reading should be interpreted with caution
-many factors can affect lab values

Measurements are used to determine changes in:

-serum proteins
-blood forming nutrients
-vitamins (fat and water soluble)
-minerals
-disease related values
-enzymes: reported in ranges (normal/healthy people)

9.3.1 LIMITATIONS OF LAB VALUES

1. Technical problems
2. Pathological conditions
3. Medications
4. Lack of specificity
5. Often reflect immediate, rather than usual intake.
6. No single/group of tests caassess or monitor nutritional status
7. Need A, C, D also
8. Hydration is very important

Haematology

-Platelet Count
-WBC
-RBC
-Hematocrit

RBC Count

-RBC/Erythrocyte count
-#RBC in peripheral circulation
-Differential: other types RBC

WBC Count

-Helps to Dx certain types of infections or diseases
-WBC/leukocyte count
-Differential

Protein Status

-Primary compound upon which body structures are based
-if protein used for energy=loss of function
-loss of somatic and visceral proteins=malnutrition
-Evaluation of protein status is very important

Serum Albumin

-about 60% of total serum protein, large body pool
-indicates depleted protein stores
-Half life (14-20 days)
-responds to nutritional intervention
-not a good indictor of early protein depletion
-value <3.0=protein malnutrition
-highly correlated (AMC/AMA)
-dehydration can falsely increase

Serum Pre-Albumin

-trasnport portein that is made in the liver
-short half life (2-3 days)
-responds quickly to nutritional intervention
-sensitive indicator of protein status
-can return to normal with adequate energy intake

Serum Retinol Binding Protein (RBP)

-Early and sensitve index of developing protein deficiency when used with prealbumin
-responds quickly to nutritional deprivation and repletion
-good indicator of recent change
-small body pool
-short half-life (12 hours)

Serum Iron

-estimates total iron stores
-decrease in iron deficiency
-decrease in infections, MI, maliganncy
-increase in iron posisoning, prenicious anemia, liver disease and iron overload

Iron deficiency occurs in stages:

1. decrease storage (serum ferritin)
2. increase transport (serum trasnferrin)
3. decrease Hemoglobin and Hematorcrit

*No single test exists to reliably assess iron status..need several indicators to determine this.

Haemoglobin (Hgb)

-oxygen carrying pigment found in RBC's
-used as screening tool for IDA
-decrease levels seen in all types of anemia
-does not become abnormal until late stages of anemia
-changes in blood volume can cause value to change

Hematocrit (HCT)

-packed cell volume
-% RBC making up entire volume of whole blood
-expressed as a percentage
-example: HCT of 46= 46ml of RBC in 100 ml of whole blood
-decrease levels due to hemorrhage, over hydration, and IDA and increase levels seen in dehydration

Serum Trasnferrin

-transports iron in blood
-iron levels can be measured by the amount of iron bound to trasnferrin
-used with other tests to diagnose malnutrition
-can be normal or elevated in iron deficiency

Total Iron Binding Capacity (TIBC)

-Capacity of transferrin to bind to iron
-increase level=iron deficiency, blood loss, pregnancy
-decrease level=infection, uremia, cancer, malnutrition

Serum Ferritin

-most sensitive test for iron deficiency
-very good indicator of iron stores
-decreased level seen in early iron deficiency
-level can increase during infection, viral hepatitis, CRF, inflammation
-in iron overload level is greatly increased

MCH (mean corpuscular hemoglobin)

-average weight of hemogolbin in red blood cells
-calculated by Hgb/RBC
-can help identify anemias
-increase macrocytic anemia
-decrease microcytic anemia

MCHC (mean corpuscular hemoglobin concentration)

-average concentration or % of Hgb in single RBC
-decrease levels=hypochromic cells
-increase levels in IDA and chronic blood loss (hemorrhage)

MCV (means corpuscular volume)

-average volume (size) of a single RBC
-used to identify anemia
-macrocytic vs. microcytic

Macrocytic Anemia

-RBC are abnormally large
-Higher MCV values seen with:
1.folate and B12 deficiency
2.chronic liver disease, alcoholism, during chemotherapy.

Microcytic Anemia

-RBC are abnormally small
-Lower MCV levels seen with:
1. iron deficiency, blood loss, low dietary intake

Electrolytes : Sodium (Na)

-major extracellular cation
-important in acid-base balance
-important in fluid balance
-important in transmission of nerve impulses
-increase dehydration, severe vomiting, diarrhea, sodium retention, burns
-decrease fluid losses, burns, renal disease
-Serum levels NOT related to dietary intake

Electrolytes: Potassium (K)

-major intracellular cation
-important in acid-base and fluid balance
-important in transmission of nerve impulses and in renal and glucose function
-increase (hyperkalemia) renal failure, Addison disease, severe burns
-decrease (hypokalemia) use of diureetics, vomiting, diarrhea, eating disorders
-NOT an accurate index of K nutritional status

Electrolytes : Phosphate (P)

-usually correlated with calcium
-used to monitor patients with renal disease
-if the BUN and creatinine are normal..high values probably due to endocrine or bone problems

Electrolytes : Chloride (Cl)

-works with sodium to regulate acid-base balance
-increase dehydration, renal insufficiency
-decrease severe vomiting, diarrhea, burns, diabetic ketoacidosis
-NOT related to nutritional status

9.3.2 OTHER BLOOD CHEMISTRY TESTS

Cholesterol

-used to assess risk of heart disease
-need a lipid profile for good evaluation of risk
-need to also look at HDL, LDL, TG

Blood chemistry: BUN (blood urea nitrogen)

-urea end product of protein metabolism
-Azotemia usually indicates renal disease
-increase levels seen in high protein intake, dehyrdation, GI bleeding, urinary tract blockage, chronic gout
-decrease levels: liver failure
-decrease levels normal in growth (infancy/pregnancy)

Blood chemistry : creatinine

-by product of muscle breakdown
-evaluates renal funciton
-more sensitive than BUN
-high levels seen when 50% or more of kidneys' nephrons destroyed
-not influenced by dietary intake of protein

Blood chemistry : calcium

-used to diagnose neuromuscular and skeletal disorders, arrhythmia, blood clotting, acid-base balance
-does NOT reflect dietary calcium intake

Blood chemistry : glucose

glucose: used in diagnosis and management of diabetes mellitus
-glycosylated hemoglobin-index of long term glucose control

Blood chemistry : CO_2

-used in assessment of acid-base balance (exchange of oxygen and co2)
-always think HCO3 (bicarbonate)
-increase levels (metabolic alkalosis)
-decrease levels (metabolic acidosis) diabetic ketoacidosis

Uric Acid

-end product of purine metabolism
-increase levels:gout, renal failure, anorexia, diuretic use, acute arthritis

Blood Chemistry : Serum Amylase

-used to diagnose pancreatitis and perforated gastric ulcer
-high levels 4-12 hours after onset
-low levels in pancreatic cancer, cirrhosis, hepatisis

Blood Chemistry : Billirubin

-reddish
-major pigment of bile
-produced by breakdown of Hgb
-increase obstructed bile duct, RBC destruction, jaundice, liver disease
-used to elevate liver function

Blood Chemistry : Enzyme : LDH/LD

-found in cells of many organs
-released into blood when cell damage occurs
-12-24 hours after MI

Blood Chemistry Enzyme: SGPT (ALT)

-highest concentration in liver
-less in skeletal muscle, kidney, and myocardium (heart muscle)

-increase levels with injury to liver
-increase levels (lesser degree) in MI, acute pancreatitis
-decrease levels in chronic renal dialysis

Blood Chemistry Enzyme : ALP

-found in liver, bone, placenta, intestine
-useful in detecting disease of these organs
-increase levels with liver disease and in time of growth
-decrease levels are not significant

Blood Chemistry Enzyme : CPK

-found mainly in heart muscle
-increase levels 2-4 hrs after MI
-peaks at 12-24 hours
-returns to normal in 48 hours

Three isomers of CPK are measured

1. CPK1- Brain
2. CPK2- Cardiac (MI)
3. CPK3- Skeletal Muscle

Blood Chemistry Enzyme: SGOT (AST)

-found in high concentration in the myocardium, liver, skeletal muscle, kidneys and pancreas
-increase levels within 8-12 hours of injury
-peaks at 24-36 hours
-returns to normal in 4-6 days
-increase levels MI, liver disease, prancreaitis, musculoskeletal injury, exposure to drugs toxic to the liver

Routine Urin Analysis

color, pH, specific gravity, presence of glucose, protein, blood, ketones, acetone, cells, bacteria, crystals

Specific tests

-creatinine
-nitrogen balance
-osmolarity

-Color

-colorless with diabetes insipidus and milky in severe infection

Specific gravity

-a measure of the concetrating ablitly of the kidney
-increase SG= concentrate urine
-decrease SG= dilute urine

Glucose

-not normal in urine
-listed at +1 to +4
-can help diagnose DM

Osmolarity

-dilution/concentration of urine particles
-number particles present
-increase= high protein diets
-decrease= renal problems

Protein

-not normal in urine
-listed at +1 to +4
-can help diagnose kidney disease and other problems

Ketones

-not normal in urine
-listed as +1 to +4
-if increase usually indicative of diabetic acidosis

pH

-reflects acid-base balance
-useful in assessing kidney stone formation
-low=acid and high=basic

Crystals

Evaluation of mineral content of kidney stones
-600-2500 ml/day

Amylase

high in pranceatitis and perforated stomach ulcer

RBC/WBC

infection of kidney or bladder

Hemoccult (Guaiac)

-a test to detect blood in stools
-fat in stools can indicate malabsorption

9.3.3 NUTRITIONAL ASSESSMENT

A Nutritional Assessment can be defined as a structured way to establish the nutritional status and energy requirements by objective measurements and whereby, accompanied by objective parameters and in relation to specific disease indications, an adequate

(nutritional) treatment can be developed for the patient. All this happens preferably in a multidisciplinary setting.

Nutritional status

The definition of nutritional status is: the condition of the body as a result of the intake, absorption and use of nutrition, as well as the influence of disease-related factors.

How to measure?

There is no golden standard for identifying malnourished patients or patients at risk. Therefore, multiple parameters are used to constitute a representation of the nutritional status of a patient.

Goals

- Timely identification of malnourished patients or patients at risk, so that the dietician can start her nutritional treatment as soon as possible;
- To determine the quantity of malnutrition, so an adequate assessment of the individual nutritional need is possible
- Çollecting data for diagnostic purposes;
- Monitoring changes in the nutritional status during a nutritional intervention;
- Collecting data for scientific research;
- Monitoring the patient's nutritional status during hospitalisation;
- Improving the Nutritional Assessment method.

9.4 REACTIVE OXYGEN SPECIES

Reactive oxygen species (**ROS**) are chemically reactive chemical species containing oxygen. Examples include peroxides, superoxide, hydroxyl radical, singlet oxygen, and alpha-oxygen.

The reduction of molecular oxygen (O_2) produces superoxide ($^{\bullet}O^{-}_{2}$) and is the precursor of most other reactive oxygen species:

$$O_2 + e^- \rightarrow {}^{\bullet}O^{-2}$$

Dismutation of superoxide produces hydrogen peroxide (H_2O_2):

$$2\ H^+ + {}^{\bullet}O^{-}_{2} + {}^{\bullet}O^{-}_{2} \rightarrow H_2O_2 + O_2$$

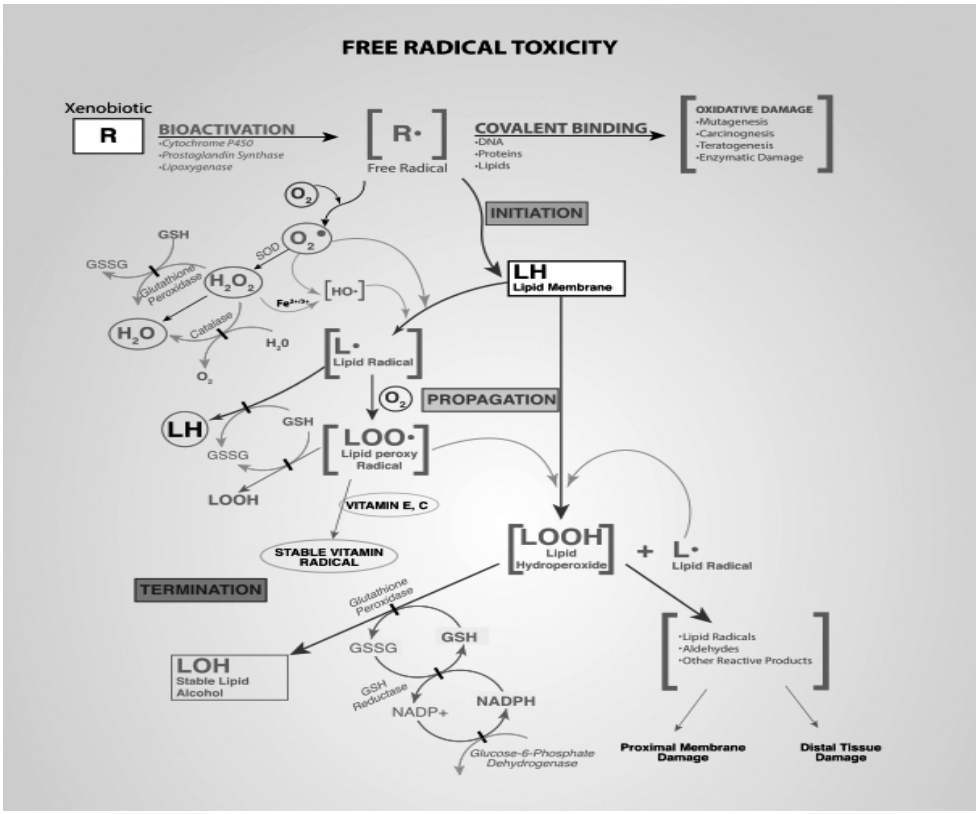
Hydrogen peroxide in turn may be partially reduced to hydroxyl radical ($^{\bullet}OH$) or fully reduced to water:

$$H_2O_2 + e^- \rightarrow HO^- + {}^{\bullet}OH$$

$$2\ H^+ + 2\ e^- + H_2O_2 \rightarrow 2\ H_2O$$

In a biological context, ROS are formed as a natural byproduct of the normal metabolism of oxygen and have important roles in cell signaling and homeostasis. However, during times of environmental stress (e.g., UV or heat exposure), ROS levels can increase dramatically. This may result in significant damage to cell structures. Cumulatively, this is known as oxidative stress. The production of ROS is strongly influenced by stress factor responses in plants, these factors that increase ROS production include drought, salinity, chilling, nutrient deficiency, metal toxicity and UV-B radiation. ROS are also generated by exogenous sources such as ionizing radiation.

Sources of ROS production



Free radical mechanisms in tissue injury. Free radical toxicity induced by xenobiotic and the subsequent detoxification by cellular enzymes (termination).

9.4.1 ENDOGENOUS SOURCES

ROS are produced during a variety of biochemical reactions within the cell and within organelles such as mitochondria, peroxisomes, and

endoplasmic reticulum. Mitochondria convert energy for the cell into a usable form, adenosine triphosphate (ATP). The process of ATP production in the mitochondria, called oxidative phosphorylation, involves the transport of protons (hydrogen ions) across the inner mitochondrial membrane by means of the electron transport chain. In the electron transport chain, electrons are passed through a series of proteins via oxidation-reduction reactions, with each acceptor protein along the chain having a greater reduction potential than the previous. The last destination for an electron along this chain is an oxygen molecule. In normal conditions, the oxygen is reduced to produce water; however, in about 0.1–2% of electrons passing through the chain (this number derives from studies in isolated mitochondria, though the exact rate in live organisms is yet to be fully agreed upon), oxygen is instead prematurely and incompletely reduced to give the superoxide radical ($^{\bullet}O^{-}_{2}$), most well documented for Complex I and Complex III.

Another source of ROS production is the electron transfer reactions catalyzed by the mitochondrial P450 systems in steroidogenic tissues. These P450 systems are dependent on the transfer of electrons from NADPH to P450. During this process, some electrons "leak" and react with O_2 producing superoxide. To cope with this natural source of ROS, the steroidogenic tissues, ovary and testsis, have a large concentration of antioxidants such as vitamin C (ascorbate) and β-carotene and anti-oxidant enzymes.

If too much damage is present in mitochondria, a cell undergoes apoptosis or programmed cell death. ROS are produced in immune cell signaling via the NOX pathway. Phagocytic cells such as neutrophils, eosinophils, and mononuclear phagocytes produce ROS when stimulated.

9.4.2 EXOGENOUS SOURCES

The formation of ROS can be stimulated by a variety of agents such as pollutants, heavy metals, tobacco, smoke, drugs, xenobiotics, or radiation.

Ionizing radiation can generate damaging intermediates through the interaction with water, a process termed radiolysis. Since water comprises 55–60% of the human body, the probability of radiolysis is quite high under the presence of ionizing radiation. In the process, water loses an electron and becomes highly reactive. Then through a three-step chain reaction, water is sequentially converted to hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide (H_2O_2), superoxide radical ($^{\bullet}O^{-}_{2}$), and ultimately oxygen (O_2).

The hydroxyl radical is extremely reactive and immediately removes electrons from any molecule in its path, turning that molecule into a free radical and thus propagating a chain reaction. However, hydrogen peroxide is actually more damaging to DNA than the hydroxyl

radical, since the lower reactivity of hydrogen peroxide provides enough time for the molecule to travel into the nucleus of the cell, subsequently reacting with macromolecules such as DNA.

9.4.3 ANTIOXIDANT ENZYMES

9.4.3.1 SUPEROXIDE DISMUTASE

Superoxide dismutases (SOD) are a class of enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide. As such, they are an important antioxidant defense in nearly all cells exposed to oxygen. In mammals and most chordates, three forms of superoxide dismutase are present. SOD1 is located primarily in the cytoplasm, SOD2 in the mitochondria and SOD3 is extracellular. The first is a dimer (consists of two units), while the others are tetramers (four subunits). SOD1 and SOD3 contain copper and zinc ions, while SOD2 has a manganese ion in its reactive centre. The genes are located on chromosomes 21, 6, and 4, respectively (21q22.1, 6q25.3 and 4p15.3-p15.1).

The SOD-catalysed dismutation of superoxide may be written with the following half-reactions:

$$M^{(n+1)+} - SOD + O^{-2} \rightarrow M^{n+} - SOD + O_2$$

$$M^{n+} - SOD + O^{-2} + 2H^{+} \rightarrow M^{(n+1)+} - SOD + H_2O_2.$$

where M = Cu (n = 1); Mn (n = 2); Fe (n = 2); Ni (n = 2). In this reaction the oxidation state of the metal cation oscillates between n and n + 1.

Catalase, which is concentrated in peroxisomes located next to mitochondria, reacts with the hydrogen peroxide to catalyze the formation of water and oxygen. Glutathione peroxidase reduces hydrogen peroxide by transferring the energy of the reactive peroxides to a very small sulfur-containing protein called glutathione. The sulfur contained in these enzymes acts as the reactive center, carrying reactive electrons from the peroxide to the glutathione. Peroxiredoxins also degrade H_2O_2, within the mitochondria, cytosol, and nucleus.

$$2\ H_2O_2 \rightarrow 2\ H_2O + O_2 \qquad \textit{(catalase)}$$

$$2GSH + H_2O_2 \rightarrow GS{-}SG + 2H_2O \qquad \textit{(glutathione peroxidase)}$$

9.4.3.2 SINGLET OXYGEN

Another type of reactive oxygen species is singlet oxygen ($^1O_2$) which is produced for example as byproduct of photosynthesis in plants. In the presence of light and oxygen, photosensitizers such as chlorophyll may convert triplet ($^3O_2$) to singlet oxygen.

Singlet oxygen is highly reactive, especially with organic compounds that contain double bonds. The resulting damage caused by

singlet oxygen reduces the photosynthetic efficiency of chloroplasts. In plants exposed to excess light, the increased production of singlet oxygen can result in cell death. Various substances such as carotenoids, tocopherols and plastoquinones contained in chloroplasts quench singlet oxygen and protect against its toxic effects. In addition to direct toxicity, singlet oxygen acts a signaling molecule. Oxidized products of β-carotene arising from the presence of singlet oxygen act as second messengers that can either protect against singlet oxygen induced toxicity or initiate programmed cell death. Levels of jasmonate play a key role in the decision between cell acclimation or cell death in response to elevated levels of this reactive oxygen species.

9.4.3.3 DAMAGING EFFECTS

Effects of ROS on cell metabolism are well documented in a variety of species. These include not only roles in apoptosis (programmed cell death) but also positive effects such as the induction of host defence genes and mobilization of ion transport systems. This implicates them in control of cellular function. In particular, platelets involved in wound repair and blood homeostasis release ROS to recruit additional platelets to sites of injury. These also provide a link to the adaptive immune system via the recruitment of leukocytes.

Reactive oxygen species are implicated in cellular activity to a variety of inflammatory responses including cardiovascular disease. They may also be involved in hearing impairment via cochlear damage induced by elevated sound levels, in ototoxicity of drugs such as cisplatin, and in congenital deafness in both animals and humans. ROS are also implicated in mediation of apoptosis or programmed cell death and ischaemic injury. Specific examples include stroke and heart attack.

In general, harmful effects of reactive oxygen species on the cell are most often:

1. Damage of DNA or RNA
2. oxidations of polyunsaturated fatty acids in lipids (lipid peroxidation)
3. oxidations of amino acids in proteins
4. oxidative deactivation of specific enzymes by oxidation of co-factors

9.5 BIOCHEMICAL PARAMETERS

In a full nutritional assessment it can be useful to screen the following biochemical parameters: albumin, prealbumin, CRP, transferrin, hemoglobin, urea and creatine, lymphocytes and point deficiencies.

Albumin

As a measure in a nutritional assessment, albumin is useful because a fast diminishing albumin concentration is a sign for an inflammatory reaction. An increasing albumin level can be interpreted as an improvement; the patient becomes anabolic. The albumin level only increases when the inflammation decreases. Nutrition has no influence on that.

Creatinine

In certain cases creatinine can be used to get an impression of the quantity of muscle mass. When the kidney works well, a decreased creatinine can indicate decreased muscle mass. Creatinine arises by the conversion of creatine to creatinine in the muscle mass.

CRP (C-Reactive protein)

An increased CRP is a result of inflammation. CRP can increase up to a thousand times as a reaction to inflammation, sepsis or infection. It can be used to monitor stress response during the acute fase.

Hemoglobin

This parameter can be used to determine the response to illness. During illness Hb decreases very fast.

Lymphocytes

The total lymphocytes count is not a sensitive index for malnutrition, because it reacts very slowly to recovery from malnutrition. The total amount of lymphocytes can increase in case of inflammation, radiation therapy and chemotherapy.

Point deficiencies

Screening on point deficiencies with the aid of medical and food questionnaires. Only in case of severe deficiencies this is shown in the blood.

Prealbumin

This is a sensitive indicator for protein-deficiency. Prealbumin increases with nutritional therapy, even when the disease condition is not getting better. It decreases fast in case of a low energy intake, even if protein intake is adequate. However it also decreases in case of inflammation and is dependent on the level of hydration. Careful interpretation of prealbumin values in the clinical setting is advised.

Transferrin

Transferrin is produced in the liver. It is a transport protein for iron and zinc, and can also be used as an indicator for the iron status in the body. In iron-deficiency, the serum transferrin increases. In illness,

transferrin is low because the liver produces less transferrin. Anaemia and nephrosis also influence transferrin.

Urea

The liver produces urea if amino acids break down. The urea production is more after a protein rich meal and when endogenous catabolism is increased (in case of infections, internal bleedings, intoxication, fever and after tissue damage).

9.6 GLYCOSYLATED HEMOGLOBIN (HBA1C)

Glycated hemoglobin (**A1C**, **hemoglobin A1c**, **HbA1c**, or less commonly HgbA1c, haemoglobin A1c, HbA_{1c}, Hb1c, etc.) is a form of hemoglobin (abbreviated Hb) that is chemically linked to a sugar. The usual sugar is glucose. The formation of the sugar-Hb linkage indicates the presence of excessive sugar in the bloodstream, often indicative of diabetes. A1c is of particular interest because it is easy to detect. The process by which sugars attach to Hb is called glycation. HbA_c is a measure of the beta-N-1-deoxy fructosyl component of hemoglobin.

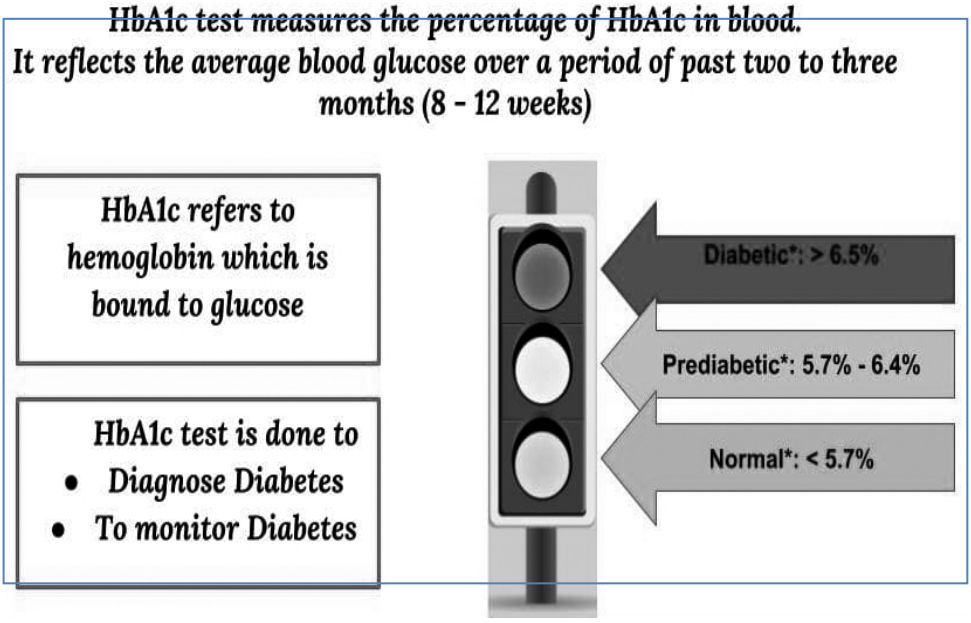


Fig. Glycosylated hemoglobin (HbA1c) Test

It is measured primarily to determine the three-month average blood sugar level and can be used as a diagnostic test for diabetes mellitus and as an assessment test for glycemic control in people with diabetes.The test is limited to a three-month average because the average lifespan of a red blood cell is four months. Since individual red blood cells have varying lifespans, the test is used as a limited measure of three months. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way. In

diabetes, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, neuropathy, and retinopathy.

Terminology

Glycated hemoglobin is preferred over glycosylated hemoglobin to reflect the correct (nonenyzmatic) process. Early literature often used *glycosylated* as it was unclear which process was involved until further research was performed. The terms are still sometimes used interchangeably in English language literature.

The naming of HbA_c derives from Hemoglobin type A being separated on cation exchange chromatography. The first fraction to separate, probably considered to be pure Hemoglobin A, was designated HbA_0, and the following fractions were designated HbA_{1a}, HbA_{1b}, and HbA_{1c}, in their order of elution. There have subsequently been more sub fractions with improved separation techniques.

History

Hemoglobin A1c was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column. It was first characterized as a glycorotein by Bookchin and Gallop in 1968. Its increase in diabetes was first described in 1969 by Samuel Rahbar *et al.* The reactions leading to its formation were characterized by Bunn and his coworkers in 1975.

The use of hemoglobin A1c for monitoring the degree of control of glucose metabolism in diabetic patients was proposed in 1976 by Anthony Cerami, Ronald Koenig and coworkers.

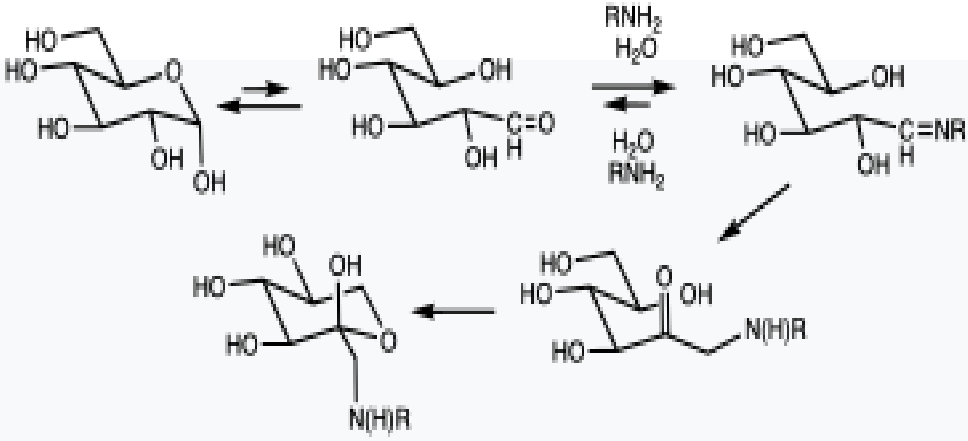
Damage mechanisms

Glycated hemoglobin causes an increase of highly reactive free radicals inside blood cells. Radicals alter blood cell membrane properties. This leads to blood cell aggregation and increased blood viscosity, which results in impaired blood flow.

Another way glycated Hb causes damage is via inflammation, which results in atherosclerotic plaque (atheroma) formation. Free-radical build-up promotes the excitation of Fe^{2+}-Hb through Fe^{3+}-Hb into abnormal ferryl Hb (Fe^{4+}-Hb). Fe^{4+} is unstable and reacts with specific amino acids in Hb to regain its Fe^{3+} oxidation state. Hb molecules clump together via cross-linking reactions,and these Hb clumps (multimers) promote cell damage and the release of Fe^{4+}-Hb into the matrix of innermost layers (subendothelium) of arteries and veins. This results in increased permeability of interior surface (endothelium) of blood vessels and production of pro-inflammatory monocyte adhesion proteins, which promote macrophage accumulation in blood vessel surfaces, ultimately leading to harmful plaques in these vessels.

Highly glycated Hb-AGEs go through vascular smooth muscle layer and inactivate acetylcholine-induced endothelium-dependent relaxation, possibly through binding to nitric oxide (NO), preventing its normal function. NO is a potent vasodilator and also inhibits formation of plaque-promoting LDLs (i.e. "bad cholesterol") oxidized form.

This overall degradation of blood cells also releases heme from them. Loose heme can cause oxidation of endothelial and LDL proteins, which results in plaques.



Glycation pathway via Amadori Rearrangement (in HbA1c, R is typically N-terminal valine).

Principle in medical diagnostics

Glycation of proteins is a frequent occurrence, but in the case of hemoglobin, a nonenzymatic condensation reaction occurs between glucose and the N-end of the beta chain. This reaction produces a Schiff base (R-N=CHR', R = beta chain, CHR'= glucose-derived), which is itself converted to 1-deoxyfructose. This second conversion is an example of an Amadori rearrangement. When blood glucose levels are high, glucose molecules attach to the hemoglobin in red blood cells. The longer hyperglycemia occurs in blood, the more glucose binds to hemoglobin in the red blood cells and the higher the glycated hemoglobin.

Once a hemoglobin molecule is glycated, it remains that way. A buildup of glycated hemoglobin within the red cell, therefore, reflects the average level of glucose to which the cell has been exposed during its life-cycle. Measuring glycated hemoglobin assesses the effectiveness of therapy by monitoring long-term serum glucose regulation.

A1c is a weighted average of blood glucose levels during the life of the red blood cells (117 days for men and 106 days in women). Therefore, glucose levels on days nearer to the test contribute substantially more to the level of A1c than the levels in days further from the test.

This is also supported by data from clinical practice showing that HbA1c levels improved significantly after 20 days from start or intensification of glucose-lowering treatment.

Measurement

Several techniques are used to measure hemoglobin A1c. Laboratories use high-performance liquid chromatography (the HbA_{1c} result is calculated as a ratio to total hemoglobin using a chromatogram); immunoassay; enzymatic assay; capillary electrophoresis; or boronate affinity chromatography. Point of care (e.g., doctor's office) devices use immunoassay ororonate affinity chromatography.

In the United States, HbA_{1c} testing laboratories are certified by the National Glycohemoglobin Standardization Program to standardize them against the results of the 1993 Diabetes Control and Complications Trial (DCCT). An additional percentage scale, Mono S has previously been in use by Sweden and KO500 is in use in Japan.

Indications and use

Glycated hemoglobin testing is recommended for both checking the blood sugar control in people who might be prediabetic and monitoring blood sugar control in patients with more elevated levels, termed diabetes mellitus. For a single blood sample, it provides far more revealing information on glycemic behavior than a fasting blood sugar value. However, fasting blood sugar tests are crucial in making treatment decisions. The American Diabetes Association guidelines are similar to others in advising that the glycated hemoglobin test be performed at least twice a year in patients with diabetes who are meeting treatment goals (and who have stable glycemic control) and quarterly in patients with diabetes whose therapy has changed or who are not meeting glycemic goals.

Glycated hemoglobin measurement is not appropriate where a change in diet or treatment has been made within 6 weeks. Likewise, the test assumes a normal red blood cell aging process and mix of hemoglobin subtypes (predominantly HbA in normal adults). Hence, people with recent blood loss, hemolytic anemia, or genetic differences in the hemoglobin molecule (hemoglobinopathy) such as sickle-cell disease and other conditions, as well as those who have donated blood recently, are not suitable for this test.

Due to glycated hemoglobin's variability (as shown in the table above), additional measures should be checked in patients at or near recommended goals. People with HbA_{1c} values at 64 mmol/mol or less should be provided additional testing to determine whether the HbA_{1c} values are due to averaging out high blood glucose (hyperglycemia) with low blood glucose (hypoglycemia) or the HbA_{1c} is more reflective of an elevated blood glucose that does not vary much throughout the day. Devices such as continuous blood glucose monitoring allow people with diabetes to determine their blood glucose levels on a continuous basis, testing every few minutes. Concentrations of hemoglobin A1 (HbA1) are increased, both in diabetic patients and in

patients with renal failure, when measured by ion-exchange chromatography. The thiobarbituric acid method (a chemical method specific for the detection of glycation) shows that patients with renal failure have values for glycated hemoglobin similar to those observed in normal subjects, suggesting that the high values in these patients are a result of binding of something other than glucose to hemoglobin.

9.7 DIFFERENTIAL DIAGNOSIS OF VITAMIN 12 AND FOLIATE

A diagnosis of vitamin B12 or folate deficiency anaemia can often be made by a General protection based on your symptoms and the results of blood tests.

Blood tests

Different types of blood tests can be carried out to help identify people with a possible vitamin B12 or folate deficiency.

These tests check:

- whether you have a lower level of haemoglobin (a substance that transports oxygen) than normal
- whether your red blood cells are larger than normal
- the level of vitamin B12 in your blood
- the level of folate in your blood

But some people can have problems with their normal levels of these vitamins, or may have low levels despite having no symptoms. This is why it's important for your symptoms to be taken into account when a diagnosis is made. A particular drawback of testing vitamin B12 levels is that the current widely used blood test only measures the total amount of vitamin B12 in your blood. This means it measures forms of vitamin B12 that are "active" and can be used by your body, as well as the "inactive" forms, which cannot. If a significant amount of the vitamin B12 in your blood is inactive, a blood test may show that you have normal B12 levels, even though your body cannot use much of it. There are some types of blood test that may help determine if the vitamin B12 in your blood can be used by your body, but these are not yet widely available.

Identifying the cause

If your symptoms and blood test results suggest a vitamin B12 or folate deficiency, your GP may arrange further tests.

If the cause can be identified, it'll help to determine the most appropriate treatment.

For example, you may have additional blood tests to check for a condition called pernicious anaemia.

This is an autoimmune condition, where your immune system produces antibodies to attack healthy cells, which means you're unable to absorb vitamin B12 from the food you eat.

Tests for pernicious anaemia are not always conclusive, but can often give your GP a good idea of whether you have the condition.

Referral to a specialist

You may be referred to a specialist for further tests or treatment.

This may include:

1. a specialist in treating blood conditions (a haematologist) – if you have vitamin B12 or folate deficiency anaemia and your GP is uncertain of the cause, you're pregnant or symptoms suggest your nervous system has been affected

2. a specialist in conditions that affect the digestive system (a gastroenterologist) – if your GP suspects you do not have enough vitamin B12 or folate because your digestive system is not absorbing it properly

3. a specialist in nutrition (a dietitian) – if your GP suspects you have a vitamin B12 or folate deficiency caused by a poor diet

4. A dietitian can devise a personalised eating plan for you to increase the amount of vitamin B12 or folate in your diet.

9.8 SUMMARY

The nutritional status depends on external and internal. Anthropometric measurements are used to assess the size, shape and composition of the human body. The purpose of nutritional screening is to rapidly identify patients at high nutritional risk. The purpose of nutritional assessment, however, is to define a patient's nutritional status, to define clinically relevant malnutrition and to monitor changes in nutritional status. Biochemical assessment of nutritional status is done by interpretation of various clinical tests done in laboratories as part of clinical pathology. Ergonomics is the industry centered around the design and creation of these instruments through the evaluation of human comfort, movement, and other anthropometric measurements. Reactive oxygen species (ROS) are chemically reactive chemical species containing oxygen. ROS are generated by exogenous sources such as ionizing radiation. **A diagnosis of vitamin B12 or folate deficiency anaemia can often be made by a GP based on your symptoms and the results of blood tests.**

9.8 TERMINAL QUESTION

Q.1. What is Anemia? Explain different types of Anaemia?

Answer: ----------

Q.2. What is the range of HBAC1 for diabetics? Explain.

Answer: ----------

Q.3. What is other name of Vitamin B12 ? How will you diagnose it?

Answer: ----------

Q.4. How reactive oxygen species are produced, show with help of chemical reactions?

Answer: ----------

Q.5. Write note on biochemical parameters in clinical pathology.

Answer: ----------

9.10 FURTHER READINGS

1. Satyanarayan, U. & Chakrapani, U. Biochemistry. Books and Allied (P) Ltd, Kolkata,5th Edition, 2019.
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Rough Work

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