Nutrition, Digestion, & Absorption
Globally, undernutrition is widespread, leading to impaired growth, defective immune system, and reduced work capacity. By contrast, in developed countries, and increasingly in developing countries, there is excessive food consumption (especially of fat), leading to obesity, and the development of diabetes, cardiovascular disease, and some cancers. Worldwide, there are more overweight and obese people than undernourished people. Deficiencies of vitamin A, iron, and iodine pose major health concerns in many countries, and deficiencies of other vitamins and minerals are a major cause of ill health.
Excessive secretion of gastric acid, associated with Helicobacter pylori infection, can result in the development of gastric and duodenal ulcers; small changes in the composition of bile can result in crystallization of cholesterol as gallstones; failure of exocrine pancreatic secretion (as in cystic fibrosis) leads to undernutrition and steatorrhea. Lactose intolerance is the result of lactase deficiency, leading to diarrhea and intestinal discomfort when lactose is consumed.
The digestion of carbohydrates is by hydrolysis to liberate oligosaccharides, then free mono- and disaccharides. The increase in blood glucose after a test dose of a carbohydrate compared with that after an equivalent amount of glucose is known as the glycemic index. Glucose and galactose have an index of 1 (or 100%), as do lactose, maltose, isomaltose, and trehalose, which give rise to these monosaccharides on hydrolysis. Fructose and the sugar alcohols are absorbed less rapidly and have a lower glycemic index, as does sucrose.
Amylases Catalyze the Hydrolysis of Starch

• The hydrolysis of starch is catalyzed by salivary and pancreatic amylases, which catalyze random hydrolysis of $\alpha(1 \rightarrow 4)$ glycoside bonds, yielding dextrins, then a mixture of glucose, maltose, and maltotriose and small branched dextrins (from the branch points in amylopectin).
Disaccharidases Are Brush Border Enzymes

- The disaccharidases, maltase, sucrase-isomaltase (a bifunctional enzyme catalyzing hydrolysis of sucrose and isomaltose), lactase, and trehalase are located on the brush border of the intestinal mucosal cells, where the resultant monosaccharides and those arising from the diet are absorbed.
- Congenital deficiency of lactase occurs rarely in infants, leading to lactose intolerance and failure to thrive when fed on breast milk or normal infant formula.
- Congenital deficiency of sucrase isomaltase occurs among the Inuit, leading to sucrose intolerance, with persistent diarrhea and failure to thrive when the diet contains sucrose.
There Are Two Separate Mechanisms for the Absorption of Monosaccharides in the Small Intestine

• Glucose and galactose are absorbed by a sodium-dependent process. They are carried by the same transport protein (SGLT 1) and compete with each other for intestinal absorption.

• Other monosaccharides are absorbed by carrier-mediated diffusion. Because they are not actively transported, fructose and sugar alcohols are only absorbed down their concentration gradient, and after a moderately high intake, some may remain in the intestinal lumen, acting as a substrate for bacterial fermentation. Large intakes of fructose and sugar alcohols can lead to osmotic diarrhea.
Transport of glucose, fructose, and galactose across the intestinal epithelium.
DIGESTION & ABSORPTION OF LIPIDS

• The major lipids in the diet are triacylglycerols and, to a lesser extent, phospholipids. These are hydrophobic molecules and have to be hydrolyzed and emulsified to very small droplets (micelles, 4-6 nm in diameter) before they can be absorbed.

• The fat-soluble vitamins, A, D, E, and K, and a variety of other lipids (including cholesterol and carotenes) are absorbed dissolved in the lipid micelles. Absorption of carotenes and fat-soluble vitamins is impaired on a very low fat diet.
Digestion and absorption of triacylglycerols.
DIGESTION & ABSORPTION OF PROTEINS

- Native proteins are resistant to digestion because few peptide bonds are accessible to the proteolytic enzymes without prior denaturation of dietary proteins (by heat in cooking and by the action of gastric acid).
several Groups of Enzymes Catalyze the Digestion of proteins

- There are two main classes of proteolytic digestive enzymes
- *(proteases)*: with different specificities for the amino acids forming the peptide bond to be hydrolyzed.
- **Endopeptidases**: hydrolyze peptide bonds between specific amino acids throughout the molecule.
• **Exopeptidases** catalyze the hydrolysis of peptide bonds, one at a time, from the ends of peptides.

• **Carboxypeptidases**, secreted in the pancreatic juice, release amino acids from the free carboxyl terminal;

• **Aminopeptidases**, secreted by the intestinal mucosal cells, release amino acids from the amino terminal.

• **Dipeptidases and tripeptidases** in the brush border of intestinal mucosal cells catalyze the hydrolysis of di- and tripeptides, which are not substrates for amino- and carboxypeptidases.
Free Amino Acids & Small peptides Are Absorbed by Different Mechanisms

• The end product of the action of endopeptidases and exopeptidases is a mixture of free amino acids, di- and tripeptides, and oligopeptides, all of which are absorbed.

• Free amino acids are absorbed across the intestinal mucosa by sodium-dependent active transport. There are several different amino acid transporters, with specificity for the nature of the amino acid sidechain (large or small, neutral, acidic, or basic).
DIGESTION & ABSORPTION OF VITAMINS & MINERALS

• Vitamins and minerals are released from food during digestion, although this is not complete, and the availability of vitamins and minerals depends on the type of food and, especially for minerals, the presence of chelating compounds.

• The fat-soluble vitamins are absorbed in the lipid micelles that are the result of fat digestion;

• water-soluble vitamins and most mineral salts are absorbed from the small intestine either by active transport or by carrier-mediated diffusion followed by binding to intracellular proteins to achieve concentrative uptake.

• Vitamin B12 absorption requires a specific transport protein, intrinsic factor

• calcium absorption is dependent on vitamin D; zinc absorption probably requires a zinc-binding ligand secreted by the exocrine pancreas,
Calcium Absorption Is Dependent on Vitamin D

- In addition to its role in regulating calcium homeostasis,
- vitamin D is required for the intestinal absorption of calcium.
- Synthesis of the intracellular calcium-binding protein, calbindin, required for calcium absorption, is induced by vitamin D. Vitamin D also acts to recruit calcium transporters to the cell surface, so increasing calcium absorption rapidly—a process that is independent of new protein synthesis.
Iron Absorption Is Limited and Strictly Controlled, but Enhanced by Vitamin C and Alcohol

• Although iron deficiency is a common problem in both developed and developing countries, about 10% of the population are genetically at risk of iron overload (hemochromatosis), and in order to reduce the risk of adverse effects of nonenzymic generation of free radicals by iron salts, absorption is strictly regulated. Inorganic iron is transported into the mucosal cell by a proton-linked divalent metal ion transporter, and accumulated intracellularly by binding to ferritin. Iron leaves the mucosal cell via a transport protein ferroportin, but only if there is free transferrinin plasma to bind to. Once transferrin is saturated with iron, any that has accumulated in the mucosal cells is lost when the cells are shed.
Absorption of iron.
NETROGEN BALANCE: OVER- & UNDERNUTRITION

• After the provision of water, the body’s first requirement is for metabolic fuels—fats, carbohydrates, and amino acids from proteins
• Food intake in excess of energy expenditure leads to obesity, while intake less than expenditure leads to emaciation and wasting, marasmus, and kwashiorkor.
• Both obesity and severe undernutrition are associated with increased mortality.
• The body mass index = weight (in kg)/height² (in m) is commonly used as a way of expressing relative obesity; a desirable range is between 20 and 25.
Energy requirements Are Estimated by Measurement of Energy Expenditure

- Energy expenditure can be determined directly by measuring heat output from the body, but is normally estimated indirectly from the consumption of oxygen. There is an energy expenditure of $\sim 20$ kJ/L of oxygen consumed, regardless of whether the fuel being metabolized is carbohydrate, fat, or protein.
- Measurement of the ratio of the volume of carbon dioxide produced: volume of oxygen consumed (respiratory quotient, RQ) is an indication of the mixture of metabolic fuels being oxidized.
• Basal metabolic rate (BMR) is the energy expenditure by the body when at rest, but not asleep, under controlled conditions of thermal neutrality, measured about 12 hours after the last meal, and depends on weight, age, and gender.
• Total energy expenditure depends on the BMR, the energy required for physical activity, and the energy cost of synthesizing reserves in the fed state. It is therefore possible to estimate an individual’s energy requirement from body weight, age, gender, and level of physical activity.
Ten percent of the Energy Yield of a Meal May Be Expended in Forming reserves

- There is a considerable increase in metabolic rate after a meal
- *(diet-induced thermogenesis).* A small part of this is the
- energy cost of secreting digestive enzymes and of active transport of the products of digestion; the major part is the result of
- synthesizing reserves of glycogen, triacylglycerol, and protein.
There Are Two Extreme Forms of Undernutrition

- Marasmus can occur in both adults and children and occurs in vulnerable groups of all populations.
- Kwashiorkor affects only children and has been reported only in developing countries. The distinguishing feature of kwashiorkor is that there is fluid retention, leading to edema, and fatty infiltration of the liver.
- Marasmus is a state of extreme emaciation; it is the outcome of prolonged negative energy balance.
Kwashiorkor Affects Undernourished Children

• In addition to the wasting of muscle tissue, loss of intestinal mucosa and impaired immune responses seen in marasmus, children with kwashiorkor show a number of characteristic features. The defining feature is edema, associated with a decreased concentration of plasma proteins.

• In addition, there is enlargement of the liver as a result of accumulation of fat.
• Very commonly, an infection precipitates kwashiorkor.
• Superimposed on general food deficiency, there is probably a
  deficiency of antioxidant nutrients such as zinc, copper, carotene, and vitamins C and E. The respiratory burst in response to infection leads to the production of oxygen and halogen-free radicals as part of the cytotoxic action of stimulated macrophages. This added oxidant stress triggers the development of kwashiorkor.
protein requirements Can Be Determined by Measuring nitrogen Balance
There Is a Loss of Body protein in response to Trauma & Infection

• One of the metabolic reactions to a major trauma, such as a burn, a broken limb, or surgery, is an increase in the net catabolism of tissue proteins, both in response to cytokines and glucocorticoid hormones, and as a result of excessive utilization of threonine and cysteine in the synthesis of acute-phase proteins. As much as 6% to 7% of the total body protein may be lost over 10 days.

• Prolonged bed rest results in considerable loss of protein because of atrophy of muscles. Protein catabolism may be increased in response to cytokines, and without the stimulus of exercise it is not completely replaced. Lost protein is replaced during positive nitrogen balance.
The requirement is not just for protein, but for specific amino acid.

Two amino acids, cysteine and tyrosine, can be synthesized in the body, but only from essential amino acid precursors—cysteine from methionine and tyrosine from phenylalanine. The dietary intakes of cysteine and tyrosine thus affect the requirements for methionine and phenylalanine.