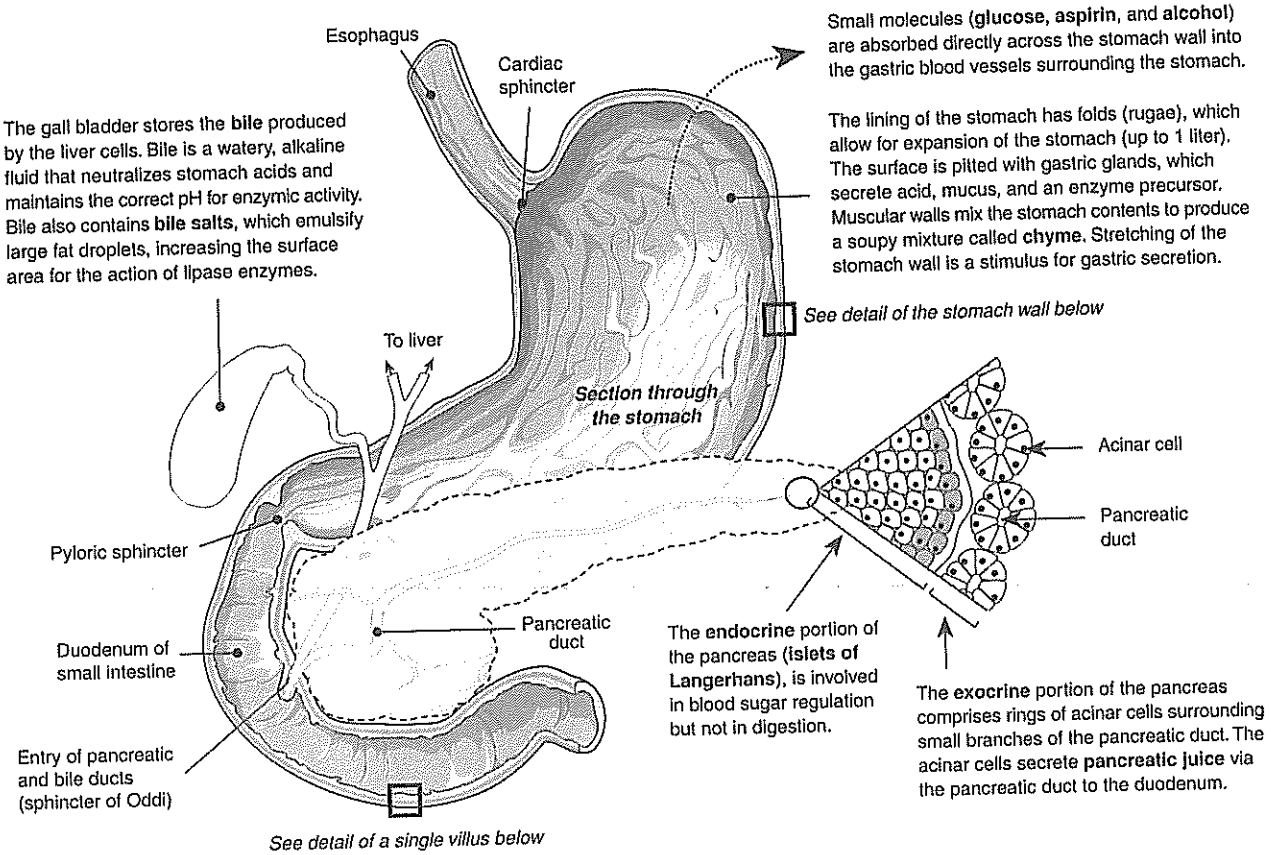
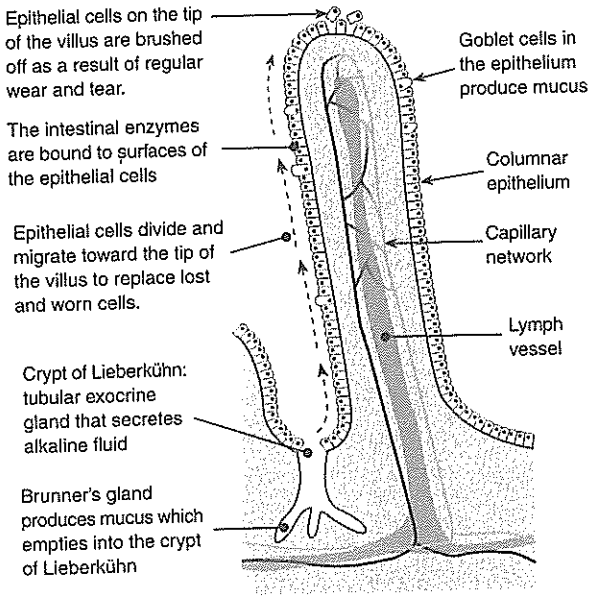
Stomach and Small Intestine

Digestion in the gut depends on both the physical movement of the food and its enzymatic breakdown into constituent components. Most digestion occurs in the stomach and small intestine. The digestive enzymes involved may be bound to the surfaces of the intestinal epithelial cells or occur as components of the secretions of digestive glands (e.g. pancreas). The structure and functions of the stomach and small intestines, and their enzymic secretions are shown on this and the next page.

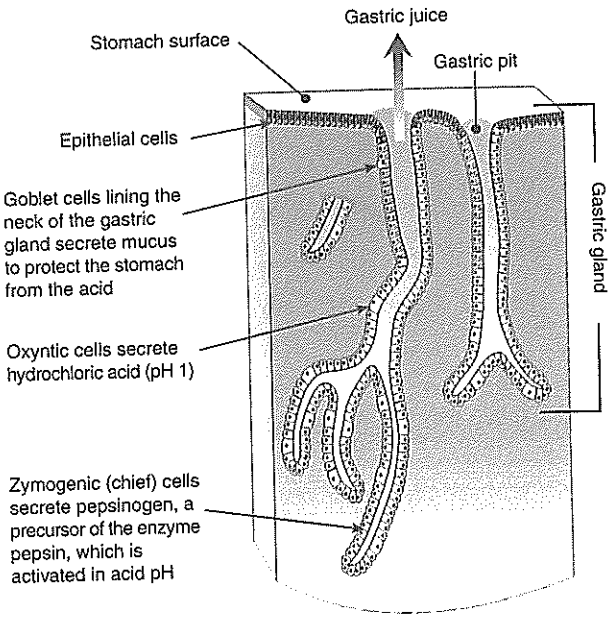
The Stomach and Organs of the Small Intestine



Detail of a Single Villus From Intestinal Wall



Detail of the Stomach Wall



1. Describe the two important roles of gut movements: _____

_____

_____

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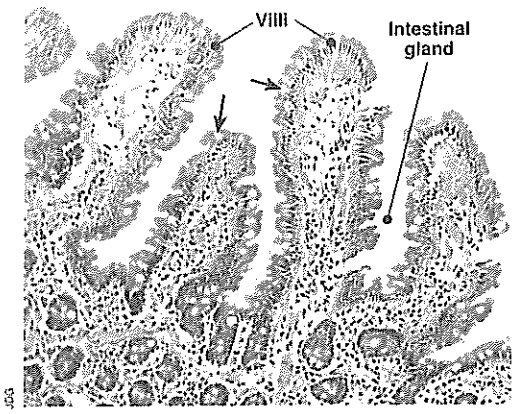
Related activities: The Human Digestive Tract, The Large Intestine
Web links: Acid Secretion in the Stomach, Interactive Digestion Quiz



Intestinal villi and microvilli

The photograph (left) shows a section through the ileum with the **intestinal villi** and **intestinal glands** (crypts of Lieberkühn) indicated. The intestinal glands secrete mucus and alkaline fluid. **Epithelial cells** lining the surface of the villi are regularly worn off and replaced by new cells migrating from the base of the intestinal glands. Each epithelial cell has many **microvilli** (microscopic projections called the brush border) which further increase the intestinal surface area.

Enzymes bound to the microvilli surfaces of the epithelial cells (peptidases, maltase, lactase, and sucrase) break down small peptides and carbohydrate molecules into their constituent parts. The breakdown products (monosaccharides, amino acids) are then absorbed into the underlying blood and lymph vessels. **Mucous cells** (white spots arrowed) produce mucus to protect the epithelial cells from enzymatic digestion. The **blood vessels** transport nutrients to the liver. **Lymph vessels** transport the products of fat digestion.

Enzyme secretions of the gut and their role in digestion

Secretion and source	Site of action	Active enzyme	Substrate and products	Control of secretion
Gastric juice: stomach	Stomach	Pepsin	Protein → peptides	Reflex stimulation, stretching of the stomach wall, and the hormone **gastrin**.
Pancreatic juice: pancreas (exocrine region only)	Duodenum	Pancreatic amylase Trypsin Chymotrypsin Pancreatic lipase	Starch → maltose Protein → peptides Protein → peptides Fats → fatty acids + glycerol	Control of pancreatic secretions is via release of the hormones **secretin** and **cholecystokinin**.
Intestinal juice and enzymes: small intestine	Small intestine	Maltase Peptidases	Maltose → glucose Polypeptides → amino acids	Reflex action and contact with intestinal wall.

2. Discuss the digestive and storage role of the stomach in humans, identifying important structures and secretions:

3. Identify two sites for enzyme secretion in the gut, give an example of an enzyme produced there, and state its role:

   (a) Site: _____ Enzyme: _____

   Enzyme's role: _____

   (b) Site: _____ Enzyme: _____

   Enzyme's role: _____

4. (a) Suggest why the pH of the gut secretions varies at different regions in the gut: _____

   (b) Explain why it is necessary for protein-digesting enzymes (e.g. trypsin, chymotrypsin, and pepsin) to be secreted in an inactive form and then activated after release:

5. Explain why alcohol exerts its effects more rapidly when the stomach is empty (rather than full): _____

6. Explain the role of sphincter muscles in the digestive tract: _____

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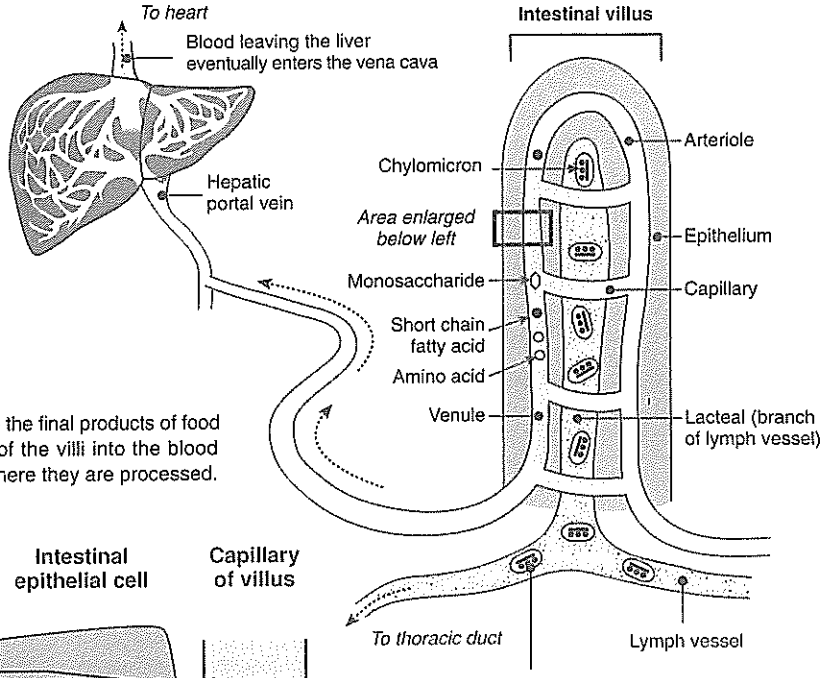
Absorption and Transport

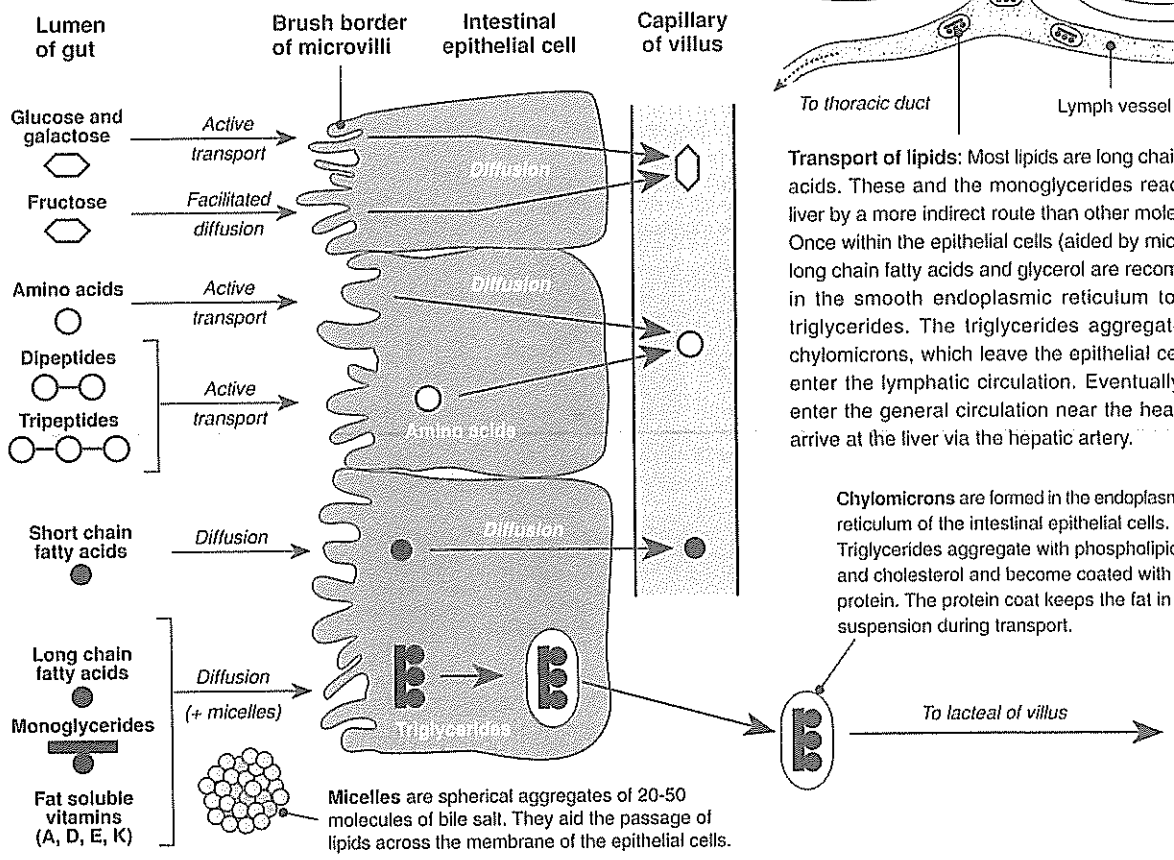
All the chemical and physical processes of digestion from the mouth to the small intestine are aimed at the breakdown of food molecules into forms that can pass through intestinal lining into the underlying blood and lymph vessels. These breakdown products include monosaccharides, amino acids, fatty acids, glycerol, and glycerides. Passage of these molecules from the gut into the blood or lymph is called **absorption**. After absorption, nutrients are transported directly or indirectly to the liver for storage or processing. Some of the features of nutrient absorption and transport are shown below. For simplicity, all nutrients are shown in the lumen of the intestine, even though some nutrients are digested on the epithelial cell surfaces.

The Hepatic Portal System

The liver obtains oxygenated blood from the hepatic artery, but it also receives deoxygenated blood containing newly absorbed nutrients via the hepatic portal vein. The **hepatic portal system** refers to all the blood flow from the digestive organs that passes through the liver before returning to the heart. Hepatic portal blood is rich in nutrients: the liver monitors and processes this load before the blood passes into general circulation.



Absorption: Most of the simple molecules that are the final products of food breakdown are absorbed by the epithelial cells of the villi into the blood vessels and are transported directly to the liver where they are processed.



Transport of lipids: Most lipids are long chain fatty acids. These and the monoglycerides reach the liver by a more indirect route than other molecules. Once within the epithelial cells (aided by micelles), long chain fatty acids and glycerol are recombined in the smooth endoplasmic reticulum to form triglycerides. The triglycerides aggregate into chylomicrons, which leave the epithelial cell and enter the lymphatic circulation. Eventually they enter the general circulation near the heart and arrive at the liver via the hepatic artery.

Chylomicrons are formed in the endoplasmic reticulum of the intestinal epithelial cells. Triglycerides aggregate with phospholipids and cholesterol and become coated with protein. The protein coat keeps the fat in suspension during transport.

Micelles are spherical aggregates of 20-50 molecules of bile salt. They aid the passage of lipids across the membrane of the epithelial cells.

1. State the function of the following in fat digestion:

   (a) Micelles: _____

   (b) Chylomicrons: _____

2. Explain why it is important that venous blood from the gut is transported first to the liver via the hepatic portal circulation:

   _____

   _____

Related activities: Stomach and Small Intestine, Transport System in Humans, The Liver's Homeostatic Role

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The Liver's Role in Digestion

The liver is a large organ, weighing about 1.4 kg, and is well supplied with blood. It carries out several hundred different functions and has a pivotal role in maintaining homeostasis. Its role in the digestion of food centers around the production of the alkaline fluid, **bile**, which is secreted at a rate of 0.8-1.0 liter per day. It is also responsible for processing absorbed nutrients, which arrive at the liver via the hepatic portal system. These functions are summarized below.

Digestive Functions of the Liver

The production and secretion of bile is regulated through nervous and hormonal mechanisms.

The **vagus nerve** stimulates bile production

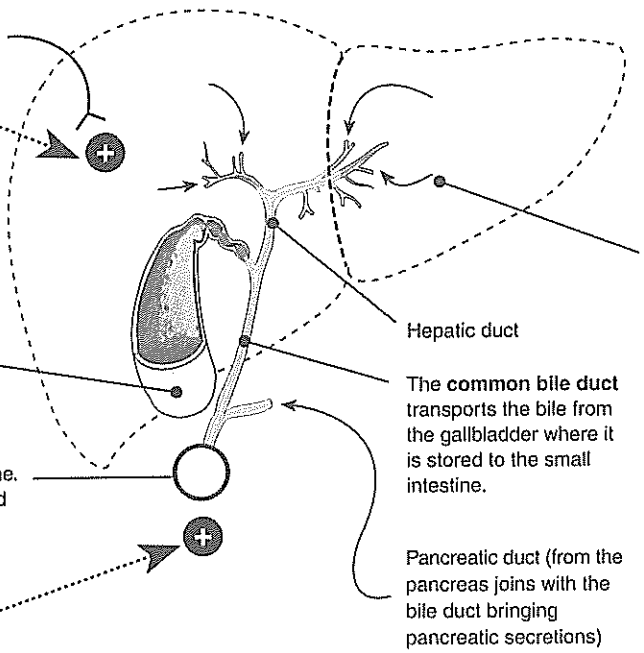
The hormone **secretin** stimulates bile production

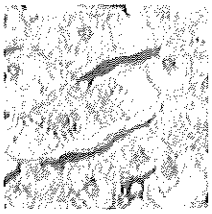
Secretin and CCK are released into the blood from the intestinal mucosa in response to food (especially fat) in the small intenstine.

Gallbladder stores bile, releasing it into the small intestine when required.

Sphincter of Oddi relaxes to release bile into the small intestine. Sphincter relaxation is stimulated by the hormone CCK.

The hormone **cholecystokinin (CCK)** stimulates the release of bile into the small intestine.





Cords of individual liver cells

Bile is produced by the liver cells and flows from small ductules into larger bile ducts. Bile is a greenish alkaline fluid (pH 7.6–8.6), consisting of water and bile salts, cholesterol, lecithin, bile pigments, and several ions. The bile salts emulsify (break up) fats in the small intestine for easier digestion and absorption. The high pH neutralizes the acid entering the small intestine from the stomach. Bile is also partly an excretory product; the breakdown of red blood cells in the liver produces the principal bile pigment, **bilirubin**. Bacteria act on the bile pigments, giving the brownish color to feces.

1. Identify the source of bile: _____

2. Describe the two main functions of bile in digestion:

   (a) _____

   (b) _____

3. Describe the two primary functions of the liver related to processing the products of digestion arriving from the gut:

   (a) _____

   (b) _____

4. Describe the role of the gall bladder in digestion: _____

   _____

5. Explain in what way bile is an excretory product as well as a digestive secretion: _____

   _____

6. Identify the two principal hormones controlling the production and release of bile, and describe the effect of each:

   (a) Hormone 1: _____ Effect: _____

   _____

   (b) Hormone 2: _____ Effect: _____

   _____

7. Describe the stimulus for hormonal stimulation of bile secretion: _____

   _____

Related activities: The Control of Digestion, The Liver's Homeostatic Role

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Infection and Gut Function

Cholera is an acute intestinal infection caused by the bacterium *Vibrio cholerae*. The bacterium produces an **enterotoxin** which binds to membrane receptors on the small intestine, opening the ion channels and increasing permeability of the mucosal epithelium to chloride ions. According to the principles of osmosis, water follows the salt across the membrane resulting in copious, painless, watery **diarrhea** that can lead to severe dehydration, kidney failure, and death within hours if left untreated. Cholera can be prevented by hygienic disposal of human feces, provision of an adequate supply of safe drinking water, safe food handling and preparation (e.g. preventing contamination of food and water), and effective general hygiene (e.g. hand washing with soap). Once contracted, the only treatment for cholera is the administration of **oral rehydration solutions (ORS)** to prevent dehydration or death. In severe cases the rehydration solution is administered intravenously, and the patient may be prescribed antibiotics to reduce the infection time. With prompt and appropriate ORS treatment, the fatality rate from cholera infection is less than 1%.

Development of Oral Rehydration Solutions

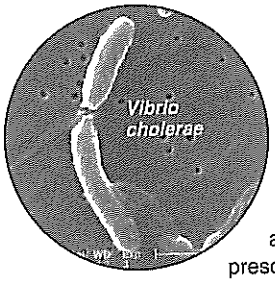
Many scientific disciplines have been involved in developing modern ORS. Key discoveries include:

1950s: Physiologists first noted that glucose and sodium were transported together across the intestinal epithelium.

1960s: The first ORS formulations were developed to treat severe diarrhea. In addition to electrolytes, they also contained glucose, which had been proven to increase water reabsorption.

The discovery that the cholera enterotoxin was responsible for fluid loss (diarrhea) by interfering with membrane cAMP activity and G-proteins.

Current: The development of low osmolarity solutions which use alternative carbohydrate sources such as rice, instead of sugars to minimize diarrheal effect.

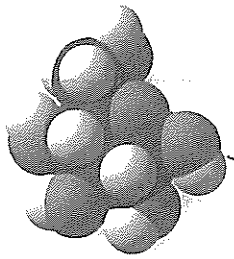


CDC

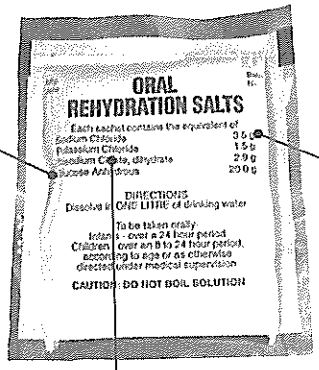
Administering ORS to a cholera patient

Oral Rehydration Solutions

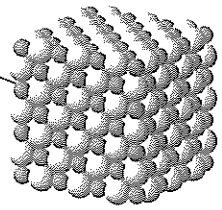
Diarrhea causes water and electrolytes to be lost from the body, causing dehydration and electrolyte imbalance. This in turn can alter osmotic gradients in the body, affecting hydration, blood pH, and nerve and muscle function. Drinking water alone to treat diarrhea is ineffective for two reasons: during bouts of diarrhea the large intenstine is losing rather than absorbing water, and secondly, electrolyte loss is not addressed. Instead, **oral rehydation solutions** (ORS) are prescribed. Modern ORS are simple and inexpensive, and can be administered with no medical training. They contain water and salts in specific ratios designed to replenish fluids and electrolytes. Carbohydrates, such as glucose or sucrose, are added to enhance electrolyte absorption in the intestinal tract. Although the presence of sugars can increase the rate of diarrhea, they still have an overall benefit because they increase fluid replacement and improve patient hydration.

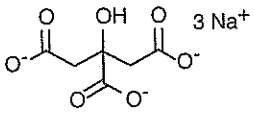


Carbohydrates, such as sucrose or glucose (above) increase water and electrolyte absorption.



*Sodium and potassium salts replace lost **electrolytes**. They are usually present as a chloride salt such as sodium chloride, NaCl (below).*





***Sodium bicarbonate** or **sodium citrate** (right) help maintain homeostatic blood pH and revert metabolic acidosis which occurs if blood pH falls below 7.35.*

1. Identify the pathogen that causes cholera: _____

2. Describe why severe diarrhea caused by cholera infection can be so dangerous if not treated quickly:

_____

_____

_____

3. Briefly describe why ORS are more effective in treating the symptoms of cholera than water alone:

_____

_____

4. Explain why a patient taking an ORS with glucose might feel that their symptoms were worsening and stop treatment:

_____

_____

5. Discuss some of the ethical issues associated with trialing new ORS formulations on humans: _____

_____

_____

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Related activities: Absorption and Transport, Passive Transport Processes

Malnutrition and Obesity

Malnutrition describes an imbalance between what someone eats and what is required to remain healthy. In economically developed areas of the world, most (but not all) forms of malnutrition are the result of poorly balanced nutrient intakes rather than a lack of food *per se*. Amongst the most common of these is **obesity**, as indicated by BMI values in excess of 30 (below). Although some genetic and hormonal causes are known, obesity is commonly the result of excessive energy intake, usually associated with a highly processed diet, high in fat and sugar. In addition, incidental physical activity is declining: we drive more, use labor-saving machines, and exercise less. Obesity is a risk factor in a number of chronic diseases, including hypertension, cardiovascular disease, and type 2 diabetes. Paradoxically, obesity in developed countries is more common in poorly educated, lower socio-economic groups than amongst the wealthy, who often have more options in terms of food choices.

Obesity and Malnutrition

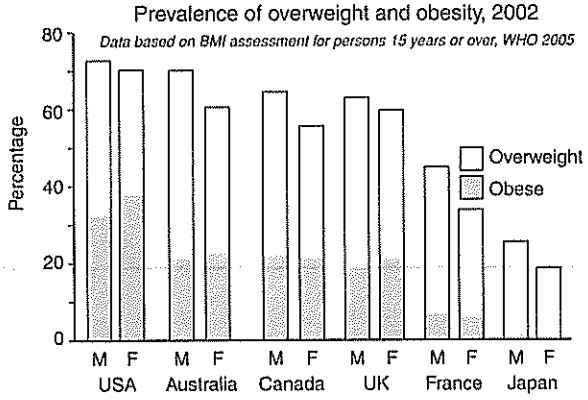
In adults, the exact level of obesity is determined by reference to the Body Mass Index (BMI). A score of 30+ on the BMI indicates mild obesity, while those with severe or morbid obesity have BMIs of 40+. Child obesity is based on BMI-for-age, and is assessed in relation to the weight of other children of a similar age and gender. Central or abdominal obesity, now classified as an independent risk factor for some serious diseases, refers to excessive fat around the abdomen. While the explanation for excessive body fat is simple (energy in exceeds energy out), a complex of biological and socio-economic factors are implicated in creating the problems of modern obesity.

Obesity Prevalance

In 2000, an estimated 20.4% of adult Americans were obese and a further 36.7% overweight, leaving fewer than half of adult Americans not at risk for health problems related to excess weight. The prevalence of obesity (BMI > 30) continues to be a health concern for adults, children, and adolescents in the US and other developed countries, as indicated by self reported BMI assessment data below.

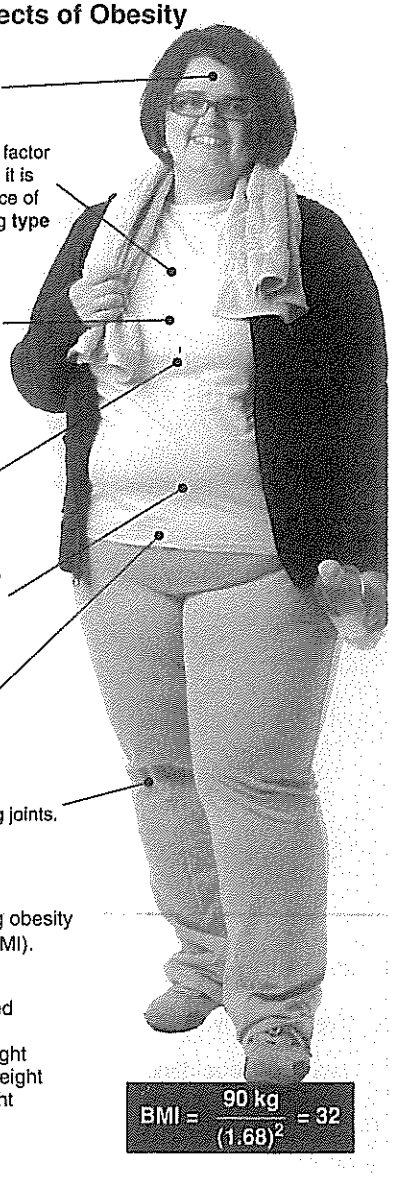
Prevalence of overweight and obesity, 2002

Data based on BMI assessment for persons 15 years or over, WHO 2005



Recent data show clear differences in the percentage of overweight and obese adults between Australia, Canada, the USA, and the UK (which are similar) and Japan and France, where obesity is much less common. These differences are attributable largely to customary dietary differences between these nations.

Health Effects of Obesity



Obesity more than doubles the risk of hypertension and stroke.

Obesity is a major independent risk factor for cardiovascular disease because it is associated with increased prevalence of cardiovascular risk factors, including **type 2 diabetes** and **high blood lipids**.

The heaviness of the chest wall and a higher-than-normal oxygen requirement in obese people restricts normal physical activity and increases respiratory problems.

Obesity is associated with high bile cholesterol levels, gallstones and gall bladder disease.

Obesity is clearly associated with higher risk of certain types of cancers, including rectal, colon and breast cancer. Cancer survival rates are also lower among obese patients.

Obesity in premenopausal women is associated with irregular menstrual cycles and infertility.

Obese people are at higher risk of osteoarthritis in their weight-bearing joints.

Body Mass Index

A common method of assessing obesity is the **body mass index** (BMI).

$$\text{BMI} = \frac{\text{weight of body (in kg)}}{\text{height (in metres) squared}}$$

A BMI of: 17 to 20 = underweight
20 to 25 = normal weight
25 to 30 = overweight
over 30 = obesity

$$\text{BMI} = \frac{90\ \text{kg}}{(1.68)^2} = 32$$

1. (a) Explain why obesity is regarded as a form of malnutrition: _____

   _____

   (b) Describe the two basic energy factors that determine how a person's weight will change: _____

   _____

2. Using the BMI, calculate the minimum and maximum weight at which a 1.85 m tall man would be considered:

   (a) Overweight: _____ (b) Obese: _____

3. BMI is routinely used to assess healthy weight. Explain why BMI might sometimes not be a reliable in this respect:

   _____

Related activities: Deficiency Diseases, Cardiovascular Disease, Type 2 Diabetes

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Deficiency Diseases

Malnutrition is the general term for nutritional disorders resulting from not having enough food (**starvation**) or not enough of the right food (**deficiency**). Children are the most at risk from malnutrition because they are growing rapidly and are more susceptible to disease. Malnutrition is a key factor in the deaths of 6 million children each year and, in developing countries, dietary deficiencies are a major problem. In these countries, malnutrition usually presents as energy and protein deficiencies. Specific vitamin and mineral deficiencies in adults are associated with specific disorders, e.g. **scurvy** (vitamin C), **rickets** (vitamin D), **pellagra** (niacin), **pernicious anemia** (vitamin B_{12}), or **anemia** (iron). Deficiency diseases are rare in developed countries and are usually limited to people with very restricted diets, intestinal disorders, or drug and alcohol problems, although some deficiencies, e.g. iron deficient anemia, are much more common than others. The ideas on what constitutes a balanced diet have changed somewhat in the last decade. Previous recommendations emphasized a reduced fat intake, but more recent advice emphasizes the benefits of 'healthy fats' and whole grains in preference to highly processed food of any kind.

Vitamin Deficiencies

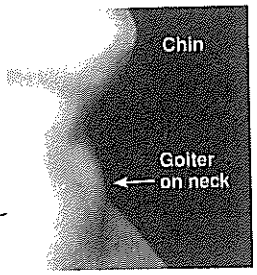
Vitamin A (found in animal livers, eggs, and dairy products) is essential for the production of light-absorbing pigments in the eye and for the formation of cell structures. Symptoms of **vitamin A deficiency** include loss of night vision, inflammation of the eye, corneal damage, and the presence of Bitot's spots (foamy patches on the white of the eye, arrowed).

Vitamin C Deficiency causes a disease known as scurvy, once the scourge of sailors but now rare in developed countries. Inadequate vitamin C intake disturbs the body's normal production of collagen, a protein in connective tissue that holds body structures together. This results in poor wound healing, rupture of small blood vessels (visible bleeding in the skin), swollen gums, and loose teeth.

Vitamin B_{12} (found primarily in meat, but also in eggs and dairy products) is required for nucleic acid and protein metabolism, and for the maturation of red blood cells. It is essential for proper growth and for the proper nervous system function. Deficiency results in pernicious anemia, poor appetite, weight loss, growth failure, fatigue, brain damage, nervousness, muscle tics, depression, spinal cord degeneration, and lack of balance.

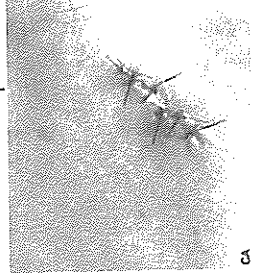
Lack of vitamin D in children produces the disease rickets. In adults a similar disease is called osteomalacia. Suffers typically show skeletal deformities (e.g. bowed legs) because inadequate amounts of phosphorus and calcium are incorporated into the bones. Vitamin D is produced by the skin when exposed to sunlight and it is vital for the absorption of calcium from the diet.

Common Mineral Deficiencies

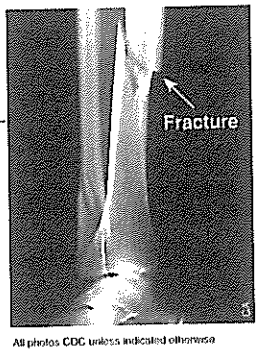


Iodine
Iodine is essential for the production of thyroid hormones, which control growth, metabolic rate, and development. Shortage of iodine in the diet may lead to **goiter** (enlargement of the thyroid). Iodine deficiency is also responsible for some cases of thyroid underactivity.

Iron
Anemia results from lower than normal levels of hemoglobin in red blood cells. Iron from the diet is required to produce hemoglobin. People most at risk include women during **pregnancy** and those with an inadequate dietary intake. Symptoms include fatigue, fainting, breathlessness, and heart palpitations.



Zinc
Zinc is found in red meat, poultry, fish, whole grain cereals and breads, legumes, and nuts. It is important for enzyme activity, production of insulin, making of sperm, and perception of taste. A deficiency in zinc causes growth retardation, a delay in puberty, muscular weakness, dry skin, and a delay in wound healing.



Calcium
Calcium is required for enzyme function, formation of bones and teeth, blood clotting, and muscular contraction. Calcium deficiency causes poor bone growth and structure, increasing the tendency of bones to fracture and break. It also results in muscular spasms and poor blood clotting.

All photos CDC unless indicated otherwise

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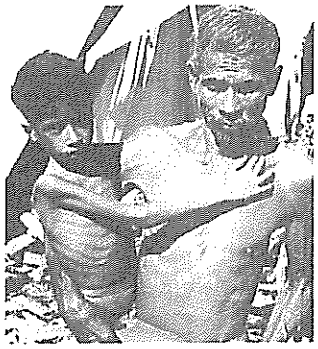
Related activities: The Human Diet, Malnutrition and Obesity

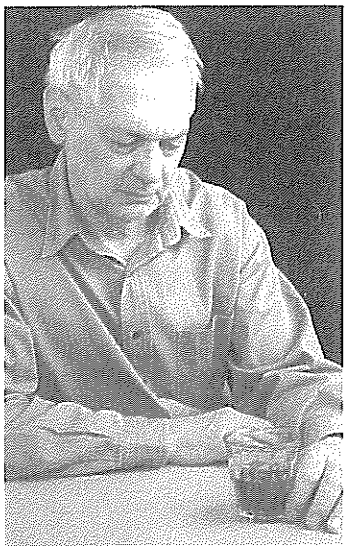
Protein and Energy Deficiencies



Marasmus is the most common form of deficiency disease. It is a severe protein and energy malnutrition that usually occurs in famine or starvation conditions. Children suffering from marasmus are stunted and extremely emaciated. They have loose folds of skin on the limbs and buttocks, due to the loss of fat and muscle tissue. Sufferers have no resistance to disease and common infections are typically fatal.

Kwashiorkor is a severe type of protein-energy deficiency in young children (1-3 years old), occurring mainly in poor rural areas in the tropics. Kwashiorkor occurs when a child is suddenly weaned on to a diet that is low in calories, protein, and certain essential micronutrients. Children have stunted growth, low resistance to infection, oedema (accumulation of fluid in the tissues), and are inactive, apathetic and weak.

Alcohol Abuse and Nutritional Deficiency



Common nutrient deficiencies in alcoholics

- Thiamin (vit. B_1)
- Riboflavin (vit. B_2)
- Vitamin B_{12}
- Folate (folic acid)
- Viamin A
- Vitamin C
- Vitamin D
- Vitamin K
- Iron
- Calcium
- Magnesium
- Zinc

People who regularly consume excessive alcohol are at increased risk of nutritional deficiencies. Even when food intake is adequate, alcohol interferes with the metabolism of food by affecting digestion, storage, utilization, and excretion of nutrients. Alcohol damages the cells lining the small intestine and impairs absorption of nutrients. For example, alcohol inhibits fat absorption, impairs the digestion of proteins, and interferes with glucose metabolism.

1. Using examples, distinguish between **malnutrition** and **starvation**: _____

2. Suggest why young children, pregnant women, and athletes are among the most susceptible to dietary deficiencies:

3. (a) Explain why a lack of iron leads to the symptoms of anemia (fatigue and breathlessness): _____

   (b) Explain why iron deficiency is relatively more common in women of child-bearing age than in men: _____

4. Using the example of **iodine**, explain how artificial dietary supplementation can be achieved and discuss its benefits:

5. Suggest why a zinc deficiency is associated with muscular weakness and a delay in puberty: _____

6. Explain why alcoholics are likely to be deficient in fat soluble vitamins (A, D, K) even when food intake is adequate:

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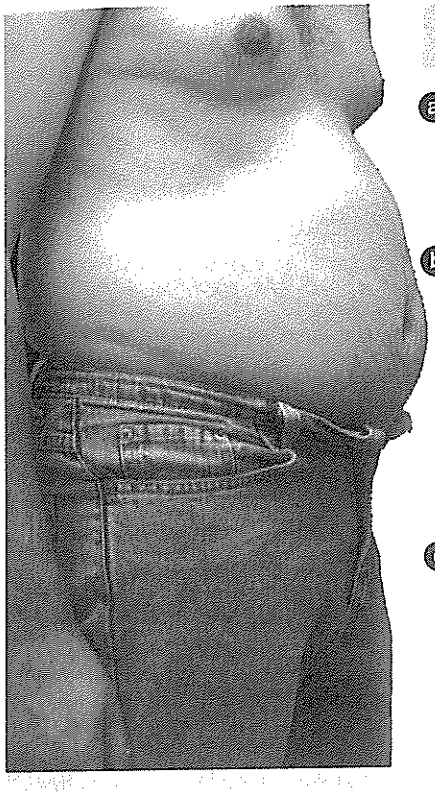
Type 2 Diabetes Mellitus

Diabetes is a general term for a range of disorders sharing two common symptoms: production of large amounts of urine and excessive thirst. **Diabetes mellitus** is the most common form of diabetes and is characterized by **hyperglycemia** (high blood sugar). **Type 1** is characterized by a complete lack of insulin production and usually begins in childhood, while **type 2** is more typically a disease of older, overweight people whose cells develop a resistance to insulin uptake. Both types are chronic, incurable conditions and are managed differently. Type 1 is treated primarily with insulin injection, whereas type 2 sufferers manage their disease through diet and exercise in an attempt to limit the disease's long term detrimental effects.



Symptoms of Type 2 Diabetes Mellitus

(a) Symptoms may be mild at first. The body's cells do not respond appropriately to the insulin that is present and blood glucose levels become elevated. Normal blood glucose level is 60-110 mg dL^{-1}. In diabetics, fasting blood glucose level is 126 mg dL^{-1} or higher.

(b) Symptoms occur with varying degrees of severity:

- Cells are starved of fuel. This can lead to increased appetite and overeating and may contribute to an existing obesity problem.
- Urine production increases to rid the body of the excess glucose. Glucose is present in the urine and patients are frequently very thirsty.
- The body's inability to use glucose properly leads to muscle weakness and fatigue, irritability, frequent infections, and poor wound healing.

(c) Uncontrolled elevated blood glucose eventually results in damage to the blood vessels and leads to:

- coronary artery disease
- peripheral vascular disease
- retinal damage, blurred vision and blindness
- kidney damage and renal failure
- persistent ulcers and gangrene

Risk Factors

Obesity: BMI greater than 27. Distribution of weight is also important.

Age: Risk increases with age, although the incidence of type 2 diabetes is increasingly reported in obese children.

Sedentary lifestyle: Inactivity increases risk through its effects on bodyweight.

Family history: There is a strong genetic link for type 2 diabetes. Those with a family history of the disease are at greater risk.

Ethnicity: Certain ethnic groups are at higher risk of developing of type 2 diabetes.

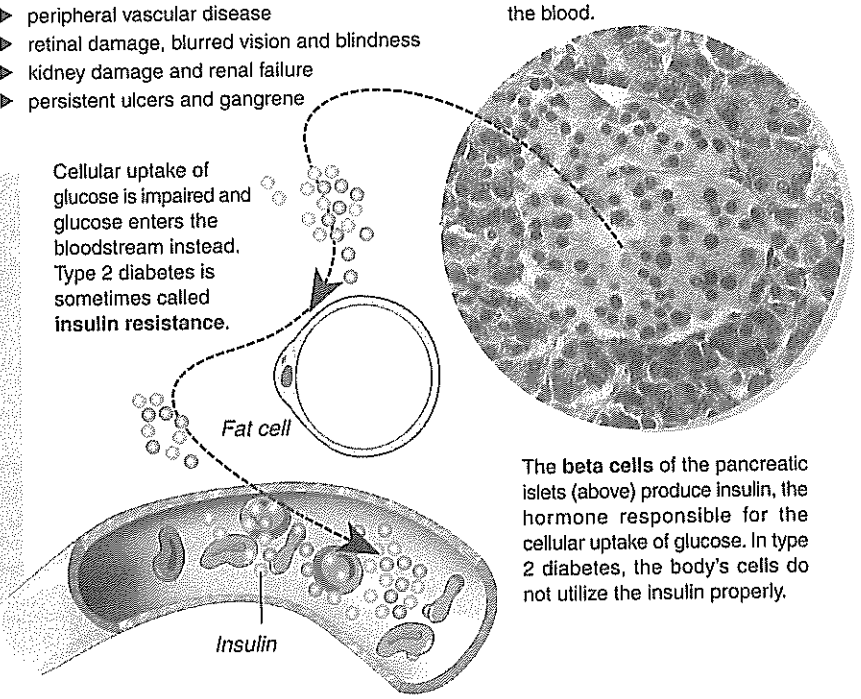
High blood pressure: Up to 60% of people with undiagnosed diabetes have high blood pressure.

High blood lipids: More than 40% of people with diabetes have abnormally high levels of cholesterol and similar lipids in the blood.

Treating Type 2 Diabetes

Diabetes is not curable but can be managed to minimize the health effects:

- Regularly check blood glucose level
- Manage diet to reduce fluctuations in blood glucose level
- Take regular exercise
- Reduce weight
- Reduce blood pressure
- Reduce or stop smoking
- Take prescribed anti-diabetic drugs
- In time, insulin therapy may be required



The **beta cells** of the pancreatic islets (above) produce insulin, the hormone responsible for the cellular uptake of glucose. In type 2 diabetes, the body's cells do not utilize the insulin properly.

1. Distinguish between type 1 and type 2 diabetes, relating the differences to the different methods of treatment:

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2. Explain what dietary advice you would give to a person diagnosed with type 2 diabetes: _____

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3. Explain why the increase in type 2 diabetes is considered epidemic in the developed world: _____

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Web links: Cellular Mechanisms of Diabetes