In order to grow, maintain itself, and reproduce, every animal requires both raw materials and energy. These materials and the energy used in their metabolism come from food, but what actually constitutes a food item varies greatly between animals, ranging from individual molecules absorbed across the general body surface to living prey swallowed whole. Regardless of its origin, which can be plant, animal, or inorganic sources, food is used as material for production of new tissue, for the repair of existing tissue, and for reproduction. Food also serves as an energy source for ongoing processes, such as movement and metabolism.

The chemical energy contained within food ultimately is derived from the sun (see Figure 3-3). Chlorophyll-containing plants are photosynthetic, autotrophic (self-nourishing) organisms that harness radiant energy to synthesize complex carbon compounds from simple precursors—CO₂ and H₂O. These compounds are repositories of chemical energy that can be released and utilized through coupled reactions to drive energy-consuming processes in living tissue. Almost all organisms are heterotrophic, depending on energy-yielding carbon compounds derived from the ingestion of other plants or animals, and ultimately on the photosynthesizers, which gather in the sun's energy. The exception of the relatively recently discovered "deep-sea vent" invertebrates, deriving their nutrition from mineral-rich vent waters, only highlights the normal dependency of animal life on the energy of the sun.

The flow of energy from the sun through a photosynthetic autotroph to a molecule of ATP in a heterotrophic animal is shown in Figure 15-1. Monosaccharides such as glucose are synthesized by green plants from CO₂ and H₂O. These elementary carbon compounds occur at the beginning of the food chain, which represents a series of organisms linked together by the fact that each "link" of the chain serves as a food item for the next. Each group of organisms represents a trophic level. In a short food chain with only two trophic levels, green plants are eaten by a large heterotroph, such as an elephant. This heterotroph, having no natural predators except humans, is at the end of that food chain until it dies and is consumed by bacteria and carrion-eating scavengers. In a longer chain, a representative succession would be phytoplankton > zooplankton > small fish > medium fish > large fish, and the nutrient flow is generally more complex (see Figure 3-3).

Usable material and free energy are lost in passing from one trophic level to another in a food chain. The grain produced in a 1-hectare (ha; 2.47-acre) field of wheat contains more material and energy directly available for human consumption than it does if that same grain is used as cattle feed, converted to beef, and then consumed by humans. For example, a 1-ha grain field produces on average 5 times more protein than does a hectare devoted to beef production, while a hectare of legumes produces 10 times more. A cow must be fed more than 20 kg of plant protein to produce just 1 kg of protein for human consumption. Humans are at the top trophic level of that food chain. At each level of feeding, digestion, and incorporation along the food chain, there is considerable energy loss due to the energetic cost of tissue maintenance and of food digestion and reassembly into new molecules to be incorporated into tissue. Consequently, a shorter food chain generally conserves greater amounts of photosynthetically captured energy for the top consumer than a long one does, if the efficiency of transfer from each trophic level to the next one is approximately equal.

We will now consider how various animals acquire food items.

FEEDING METHODS

Obtaining food adequate in both quantity and quality occupies much of the routine behavior of most animals. Certainly an animal’s physiology and morphology are the result of natural selection that favors effective acquisition of energy from food while avoiding becoming someone else’s meal. The complexity and sophistication of the nervous and muscular systems, for example, attest to the power of the selective forces acting on the organism. As these vary, so do the variety of methods by which animals feed. Sessile (non-mobile) bottom-dwelling species commonly resort to surface absorption, filter feeding, or trapping. Mobile
INTEGRATION OF PHYSIOLOGICAL SYSTEMS

Figure 15-1 Two trophic levels occur in this generalized flow diagram of chemical energy through a food chain. The flowchart begins with the photosynthetic formation of high-energy-content molecules (sugars) from low-energy-content raw materials (CO₂ and H₂O) in plants. Oxidation of carbon compounds yields free energy coupled to the synthesis of high-energy compounds, such as ATP, used as common energy currency in metabolism. Chemical energy content is at its peak following the photosynthetic production of sugars. When the plant material is consumed by a heterotroph, some chemical energy is converted to heat and thus is lost as a direct source of energy for driving biological processes. This food chain has only two trophic levels, but most food chains have many more intervening levels.

Animals follow a more active sequence, which in the extreme of many carnivores (meat eaters) includes searching, stalking, pouncing, capturing, and killing.

Food Absorption through Exterior Body Surfaces
The feeding method that is least dependent on specialized capture and digestive organs involves absorption of nutrients directly across the body wall. Certain protozoans, endoparasites (animals that live within other animals), and aquatic invertebrates are able to take up nutrient molecules from the surrounding medium directly through their soft body wall. Endoparasites such as parasitic protozoans, tapeworms, flukes, and certain mollusks and crustaceans are surrounded by host tissues or by alimentary canal fluids, both of which are high in nutrients. Tapeworms, which may be many meters long, lack even a rudimentary digestive system. Tapeworms evolved from a primitive flatworm that lacked a body cavity (i.e., was acoelomic). However, some endoparasites appear to have secondarily lost the digestive apparatus present in their ancestors. For example, parasitic crustaceans, which belong to the cirripeds (barnacle group), lack an alimentary canal, but they appear to have evolved from nonparasitic ancestors possessing a gut.

Some free-living protozoans and invertebrates derive part of their nutrients by direct surface uptake from the surrounding medium. Small molecules such as amino acids are taken up from dilute solution by transport mechanisms (described in Chapter 4), against what can often be a huge concentration gradient. In some of these organisms, larger molecules or particles are taken up by a bulk process such as phagocytosis, which is described next.

Endocytosis
Endocytosis represents a more active form of “feeding” than passive absorption directly across the body wall. Like direct nutrient absorption, however, it occurs at the local cellular rather than tissue or organismal level. Endocytosis includes two processes, phagocytosis (“cell eating”) and pinocytosis (“cell drinking”). In phagocytosis, pseudopod-like protuberances extend out and envelope relatively large nutrient particles. Pinocytosis occurs when a smaller particle binds to the cell surface and the plasma membrane invaginates (folds inward) under it, forming an endocytic cavity. Whether captured by phagocytosis or pinocytosis, the morsel is then engulfed in a membrane-enclosed vesicle that pinches off from the bottom of the cavity.
The vesicle (or food vacuole in Protozoa) fuses with lysosomes, organelles containing intracellular digestive enzymes, whereafter it is called a secondary vacuole. After digestion, the contents of the vacuole pass through the vacuole wall into the cytoplasm. The remaining undigested material is excreted externally by exocytosis, essentially a reverse process of pinocytosis. Feeding by pinocytosis and phagocytosis is familiar in protozoans such as *Paramecium*, but also occurs in the lining of the alimentary canals and other tissues of many multicellular animals.

**Filter Feeding**

Many aquatic animals use filter feeding, also called suspension feeding, to capture food. Food items (usually phytoplankton or zooplankton) are carried to specialized entrapment devices either on the body surface or within it. Most marine filter feeders are small, sessile animals, such as sponges, brachiopods, lamellibranchs, and tunicates. Food items are carried along on water currents that either occur naturally or are generated by the movements of body parts of the filter-feeding animal itself, such as cilia or flagella. Brachiopods respond behaviorally to currents, rotating on their pedal stalks to present the most efficient hydrodynamic orientation for capturing the water current. A number of other sessile animals located in moving water make use of Bernoulli’s effect (i.e., a drop in fluid pressure as fluid velocity increases) to increase the rate of water flowing through the entrapment sites, at no energy cost to themselves. An example of such passively assisted filter feeding is seen in sponges (Figure 15-2). The flow of water across the large terminal opening causes a drop in pressure (Bernoulli’s effect) outside the osculum. As a result, water is drawn out of the sponge through the osculum, and is drawn in through the numerous ostia (mouth-like openings) in the body wall. The drop in pressure is facilitated by the shape of the sponge’s exterior, which causes the water over the osculum to flow with greater velocity than the water flowing past the ostia. Food particles, swept into the ostia of the sponge along with the water, are engulfed by choanocytes, the flagellated cells lining the body cavity. The flagella of the choanocytes also create internal water currents within spongocoel, the hollow water-filled interior. Some sponges living in moving water “pump” a volume of water equivalent to up to 20,000 times their body volume per day.

**Mucus**, a sticky mixture of mucopolysaccharides, often plays an important role in filter feeding. Waterborne microorganisms and food particles are trapped in a layer of mucus that covers a ciliated epithelium. The mucus is then transported to the oral parts by beating cilia. The cilia propel water through sessile animals not only to capture suspended food but also to aid in respiration. This is of greatest importance in still water. In mollusks such as the mussel, *Mytilus*, the cilia on the surface of the ctenidium draw a stream of water through the inhalant siphon, passing the water between the gill filaments (Figure 15-3). These cilia are also responsible for keeping mucus traveling down along the filaments (i.e., 90° to the water flow) to the tip of the gill, where it travels in a special groove under ciliary power toward the mouth in a rope-like string of mucus. Sand and other indigestible particles are sorted out and rejected (presumably on the basis of texture), passing out with the water leaving the exhalant siphon.

Non-sessile animals filter-feed by various mechanisms. A number of fishes are planktivorous, using modified gill...
rakers to strain food out of the flow of water passing through the mouth and over the gills. Juveniles of the paddlefish, *Polyodon spathula*, swim rapidly and continuously both to ventilate their gills and to filter out food items (see Chapter 16). Filter feeding is also very common in amphibian larvae. In *Xenopus laevis*, the South African clawed toad, the branchial chamber contains gills bearing branchial filter plates that entrap suspended organic material. The material becomes entrapped in mucus, which is then swept by cilia into the esophagus to be swallowed. In *Xenopus*, branchial respiration and food ingestion may present functional conflicts. As the gill filter plates load up with suspended food items, the resistance to water flow through the gills rises sharply. Indeed, in larval *Xenopus*, gill ventilation decreases in proportion to food density in inspired water, presumably maintaining a constant rate of food ingestion. Increased cutaneous and pulmonary respiration apparently can compensate for the lack of branchial gas exchange when optimal conditions for filter feeding result in reduced branchial water flow.

The largest filter feeders are the baleen whales, such as the right whale. Horny *baleen plates* bear a fringe of parallel filaments of hair-like keratin that hang down from the upper and lower jaws and act as strainers analogous to the gill rakers of fishes or larval amphibians (Figure 15-4A). These whales swim with jaws open into schools of pelagic crustaceans such as krill, engulfing vast numbers suspended in tons of water. As the jaws close, the water is squeezed back out through the baleen strainers with the help of the large tongue, and the crustaceans, left behind inside the mouth, are swallowed. Clearly, filter feeding can be a very effective form of food capture and can support an animal of huge dimensions.

Birds such as flamingos also use filter feeding to capture small animals and other morsels they find in the muddy bottoms of their freshwater habitat (Figure 15-4B). The flamingo and the right whale exhibit remarkable convergent evolution: they both have a deep-sided lower jaw, a recurved rostrum, fibrous-fringe filters suspended from the upper jaw, and a large, fleshy tongue. Both feed by filling the mouth cavity with water, and then using the tongue as a piston to force water out through the filters, trapping and retaining waterborne food particles.

**Fluid Feeding**

Fluid feeding involves a variety of structures and mechanisms, including piercing and sucking, and cutting and licking.

**Piercing and sucking**

Feeding by piercing a prey or food item and sucking fluids from it occurs among the platyhelminths, nematodes, annelids, and arthropods. Leeches, among the annelids, are true bloodsuckers, using an anticoagulant in their saliva to prevent clotting in their prey's blood. In fact, the anticoagulants in leeches have been chemically isolated and are being used clinically. Leeches themselves are still used for medicinal purposes to reduce swelling by removing extracellular fluid following cosmetic and other forms of surgery. Some free-living flatworms seize their invertebrate prey by wrapping themselves around it. They then penetrate the body wall with a protrusible pharynx that sucks out the victim's body fluids and viscera. Penetration by the pharynx and liquefaction of the victim's tissues are facilitated by proteolytic enzymes secreted by the muscular pharynx.

Large numbers of arthropods feed by piercing and sucking. Most familiar and irksome of these to humans are mosquitoes, fleas, bedbugs, and lice, which can be vectors of disease. The majority of sucking arthropods victimize animal hosts. However, especially among the Hemiptera (true bugs) are species that pierce and suck plants, from which they draw sap. Sucking insects generally possess fine piercing mouthparts in the form of a proboscis (Figure 15-5A). Often, the two maxillae are shaped so that they make up two canals that run to the tip of the proboscis (Figure 15-5B and C). One of these, the dorsal canal, is the passage for blood or sap sucked from the host. The other, the ventral canal, carries saliva, containing anticoagulants or enzymes, from the salivary glands into the host. Sucking occurs by the action of a muscular pharynx. After feeding, most insects are able to fold the proboscis back out of the way.

![Figure 15-4](image-url)
Cutting and licking
Numerous invertebrates and a few vertebrates feed by cutting the body wall of a prey item and then licking, or sponging the body fluids that leak from the cut. The blackfly and related biting flies have mouthparts with a sharpened mandible for cutting, and a large, sponge-like labium for transferring the body fluid (usually blood) to the esophagus. Among the chordates, a few phyletically ancient fishes (lampreys, hagfishes) use rasp-like mouths to make large, circular flesh wounds on the host. They feed on the blood created from these wounds. Vampire bats use their teeth to make puncture wounds in cattle, from which they lick oozing blood. The saliva of these bats contains an anticoagulant, as well as an analgesic to prevent the host from feeling the effects of the bite, at least until the bat has finished feeding.

Seizing of Prey
Predators use various types of mouthparts and other appendages to capture and masticate animals and plants. Often toxins are used to further immobilize items of prey.

Jaws, teeth, and beaks
Although no true teeth occur among the invertebrates, various invertebrates have beak-like or tooth-like chitinous structures for biting or feeding. Invertebrates such as the preying mantis and the lobster also have anterior limbs modified for prey capture (Figure 15-6). Spiders and their relatives have needle-like mouthparts for injection of venom, while cephalopods like the octopus have a sharp, tearing beak. Among the vertebrates, hagfishes, sharks, bony fishes, amphibians, and reptiles have pointed teeth, mounted on the jaws or palate, that aid in holding, tearing, and swallowing prey.

The teeth of non-mammalian vertebrates are usually non-differentiated, with a single tooth type found throughout the mouth. One notable exception is found among the poisonous snakes, such as vipers, cobras, and rattlesnakes, which have modified teeth, called fangs, that they use to inject venom (Figure 15-7). These fangs either are equipped with a groove that guides the venom or are hollow, very much like a syringe. In rattlesnakes, the fangs fold back against the roof of the mouth, but extend perpendicularly when the mouth is opened to strike at prey. A snake’s jaws are held together with an elastic ligament that allows them...
Rattlesnakes have modified teeth, known as fangs, which they use to inject venom into their prey. These side views of a rattlesnake skull show (A) a non-striking position, with the jaws only partially open and the hinged fangs folded into the roof of the mouth, and (B) a striking position, in which the jaws are open wide and the fangs extended. The extraordinary flexibility of the lower jaws allows the snake to swallow prey whole after injecting it with deadly venom. [Adapted from Parker, 1963.]

to spread apart during swallowing. This enables the snake to swallow animals larger than the diameter of its head (see Figure 15-7). Swallowing prey whole is relatively common, and very evident in prey capture and consumption in snakes.

Mammals use their teeth for seizing and masticating their prey. Their teeth have developed very different shapes during evolution (Figure 15-8). Chisel-like incisors are used for gnawing, especially by rodents and rabbits. In the elephants (and before them, mammoths), the incisors are modified into a pair of tusks. Pointed, dagger-like canines are used by the carnivores, insectivores, and primates for piercing and tearing food. In some groups, like the wild pigs

Figure 15-7 Rattlesnakes have modified teeth, known as fangs, which they use to inject venom into their prey. These side views of a rattlesnake skull show (A) a non-striking position, with the jaws only partially open and the hinged fangs folded into the roof of the mouth, and (B) a striking position, in which the jaws are open wide and the fangs extended. The extraordinary flexibility of the lower jaws allows the snake to swallow prey whole after injecting it with deadly venom. [Adapted from Parker, 1963.]

Figure 15-8 Mammalian dentition is specialized for food type. (A) Teeth of a generalized placental mammal, showing the major divisions of denticion. (B) Squirrel, showing incisors enlarged for gnawing. (C) African lion, with carnassial teeth modified for shearing bone and tendon. (D) Ox, with extensive molars for grinding plant material. [Adapted from Romer, 1962; Cornwall, 1956.]
and walruses, the canines are elongated as tusks, which are used for prying and fighting. Most complex and interesting in their form are the molars of some herbivorous groups such as cattle, including oxen, pigs, hippopotamuses, and horses and zebras. These teeth, which are used in a side-to-side grinding motion, are composed of folded layers of enamel, cement, and dentine, all of which differ in hardness and in rate of wearing. Because the softer dentine wears rather quickly, the harder enamel and cement layers form ridges that enhance the effectiveness of the molars for chewing grass and other tough vegetation. Many mammals, such as the cats (the domestic cat and the great cats, such as the lion) use limbs equipped with sharp claws to supplement the teeth as food-capturing structures.

Instead of teeth, birds have horny beaks, in a multitude of shapes and sizes, evolved to adapt to each species' unique food sources and methods of obtaining them. For instance, beaks may have finely serrated edges, sharp, hook-like upper bills, or sharp, wood-pecking points (Figure 15-9). Seed-eating birds eat their food whole (perhaps after removing the outer hull), but may grind the swallowed seed in a muscular crop or gizzard containing pebbles that act like "millstones." Raptorial birds (hawks, eagles), endowed with excellent vision and flight mobility, capture prey with their talons as well as their beaks.

**Toxins**

A large number of animals from different phyla use toxins either to subdue prey or to fend off predators. Most of these toxins act at synapses in the nervous system. Surprisingly simple animals can use sophisticated arrays of venom-producing cells. Among the coelenterates (hydras, jellyfish, anemones, corals) for example, there is extensive use of nematocysts (stinging cells). Concentrated in large numbers on the tentacles, the nematocysts inject paralytic toxins into prey and immobilize it while the tentacles carry it to the mouth (Figure 15-10). Many nemertine worms paralyze their prey by injecting venom through a stiletto-like proboscis. Venoms are also used by annelids, gastropod mollusks (including one species of octopus), and a wide variety of arthropods.

Among the last group, scorpions and spiders are most notorious for their toxins, which are usually highly specific chemicals that bind to specific receptor types. After grabbing its prey with its large chelae (pincer-like organs), a scorpion will arch its tail and then plunge its sting into its prey (Figure 15-11). The scorpion then injects the victim with a poison containing a neurotoxin that interferes with the proper firing of nerve impulses. Spider poisons also contain neurotoxins. The venom from the black widow spider contains a substance that induces massive release of

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**Figure 15-9** Bird beaks are adapted to suit herbivory, omnivory, and carnivory. [Adapted from Marshall and Hughes, 1980.]
neurotransmitter at the motor endplate in muscle. A neurotoxin, \textit{\textalpha;-bungarotoxin} (see Spotlight 6-3), found in the venom of the cobra-like krait, binds to nicotinic acetylcholine (ACh) receptors, thereby blocking neuromuscular transmission in vertebrates. The venoms of various species of rattlesnake contain hemolytic (blood cell-destroying) substances.

Toxins, although highly effective, are generally expensive to produce. Usually carefully measured doses of toxins are delivered during a bite or sting. Toxins also must be specially stored before administration to avoid self-poisoning. Toxins are generally proteins and, as such, are rendered harmless by the proteolytic enzymes of the predator’s digestive system when it ingests its poisoned prey.

\textbf{Herbivory and Grazing to Collect Food}

Herbivores often have mouth parts specialized for feeding on plant material. Many gastropods use a rasp-like structure termed a radula to scrape algae from rock surfaces or to rasp through vegetation (Figure 15-12). Vertebrate herbivores have bony plates (some fish and reptiles) or teeth primarily in the form of molars with wide flat surfaces mod-
ified for grinding plant material. Plants (especially some grasses) contain relatively large amounts of silicates, and can be tremendously abrasive. Consequently, the molars of herbivores often are coated in especially tough enamel to resist wear. Alternatively, some herbivores such as small rodents (microtines) have continuously growing, rootless teeth.

**OVERVIEW OF ALIMENTARY SYSTEMS**

Alimentary systems play an essential role in providing nourishment through digesting and absorbing food, and removing from the body indigestible materials and toxic by-products of digestion. The most primitive "alimentary system" is the plasma membrane of unicellular organisms, in which microscopic food particles are engulfed, undigested, by endocytosis directly into the cell itself. Once in the cell, food particles undergo intracellular digestion by acids and enzymes. More complex multicellular animals rely primarily on extracellular digestion carried out by true alimentary systems.

From an anatomical perspective, there are myriad designs of alimentary systems. However, from a physiological perspective, alimentary systems fall into one of three categories on the basis of how they process food in a "reactor," or site of chemical digestion. So-called batch reactors are blind tubes or cavities that receive food and eliminate wastes in a pulsed fashion; that is, one batch is processed and eliminated before the next one is brought in (Figure 15-13, left). Coelenterates, for example, have a blind tube or cavity, the coelenteron, which opens only at a "mouth" that serves also for the expulsion of undigested remains. In all phyla higher than the flatworms, ingested material passes through a hollow, tubular cavity—the alimentary canal—extending through the organism and open at both ends. Processing goes on continuously, rather than in pulses, with new food being ingested while older food is still being processed. Some alimentary canals can be modeled as ideal continuous-flow, stirred-tank reactors, in which food is continually added and mixed into a homogeneous mass, and the products of digestion are continuously eliminated, overflowing from the reactor (Figure 15-13, middle). An example of such a reactor is the forestomach of ruminants. The third way of processing food is in a plug-flow reactor, in which a bolus (a discrete plug or collection) of food is progressively digested as it winds its way through a long, tube-like digestive reactor (Figure 15-13, right). Unlike the stirred-tank reactor, its composition varies according to its position along the reactor tube. The small intestine of many vertebrates functions as a plug-flow reactor. It is important to recognize that many animals combine features of both continuous- and plug-flow reactors. As you will see below, in many animals chemical digestion begins in the stomach, configured as a continuous-flow, stirred-tank reactor, and then continues on into the small intestine, configured as a plug-flow reactor.
It is critically important that the design of the alimentary canal and the reactors it contains matches well with the quality of the food that the animal routinely eats. A high-quality food can release maximum amounts of energy with minimal time spent in the digestive reactor, whatever its type (Figure 15-14). A lower-quality food, on the other hand, requires a longer period of digestion to release its energy. This in turn requires longer periods spent in the reactor and longer transit times through the alimentary canal. As also indicated in Fig. 15-14, the amount of energy spent in capturing a particular food must also be factored into consideration of food quality.

A generalized alimentary canal, or digestive tract, is illustrated in (Figure 15-15). The lumen of this alimentary canal is topologically external to the body. Sphincters and other devices guard the entrance to and exit from the canal, preventing uncontrolled exchange between the lumen and the external environment. Ingested material is subjected to various mechanical, chemical, and bacterial treatments as it passes through this canal, and digestive juices (primarily enzymes and acids) are mixed with the ingested material at appropriate regions in the alimentary canal. As the ingested material is first mechanically broken down and then chemically digested, nutrients undergo absorption and are then transported into the circulatory system. Undigested, non-absorbed material is stored briefly until it, along with bacterial remains, is expelled as feces by the process of defecation.

The overall tubular organization of the alimentary canal is efficient because it allows ingested material to travel in one direction, passing through different regions that can then be specialized for particular digestive tasks. For example, the alimentary canal near the point of ingestion is often specialized for acid secretion, while more distant regions are alkaline. This regional specialization allows both acid and base secretion to occur at the same time and to permit different types of digestive action.

In general, alimentary canals can be divided on a structural and functional basis into four major divisions (see Figure 15-15): (1) headgut, (2) foregut, (3) midgut and (4) hindgut. These regions are specialized for (1) receiving ingested material, (2) conducting, storing, and digesting ingested material, (3) digesting and absorbing nutrients, and (4) absorbing water and defecating. Representative alimentary canals from the different invertebrate and vertebrate classes are illustrated in Figures 15-16 and 15-17, respectively.
Digestive systems of invertebrates show great variation, ranging from simple to highly complex. (A) Section through body wall of Hydra, a coelenterate. The epithelial lining of the coelenteron includes phagocytosing cells (called nutritive muscle cells) and gland cells that secrete digestive enzymes. (B) Digestive system of a polyclad flatworm. (C) Digestive system of a prosobranch gastropod mollusk. Arrows show ciliary currents and the rotation of the mucous mass. (D) Digestive system of the cockroach Periplaneta. The proventriculus (or gizzard) contains chitinous teeth for grinding food. (Part C from Rupert and Barnes, 1994; part D from Imms, 1949.)
Figure 15-17. The tube-like digestive system of vertebrates has a basic organizational plan, with common elements of esophagus, stomach, intestine, and colon. B, bladder; C, cecum; Cr, crop (gizzard); E, esophagus; G, gallbladder; L, liver; LI, large intestine; P, pancreas; PA, pyloric appendices; SG, spiral gut; SI, small intestine; St, stomach. [From Florey, 1966; adapted from Stempell, 1926.]
Headgut: Food Reception

The headgut is the anterior (cranial) region of the alimentary canal, providing an external opening for food entry (see Figure 15-15). It consists of organs and structures for feeding and swallowing, including the mouthparts, buccal cavity, pharynx, and associated structures such as bills, teeth, tongue, and salivary glands. Where a common pathway exists leading to both the alimentary canal and the pas sageway (e.g., the trachea) ending in the organ of internal gas exchange, there may be additional sphincter- or valve-like structures that control and divert the flow of ingested material and inspired water or air into their respective channels.

Other than in small-particle feeders such as coelenterates, flatworms, and sponges, the headgut of most metazoans has salivary glands, the secretions of which aid in ingestion and the mechanical (and often chemical) digestion of food. The primary function of the salivary secretion, saliva, is lubrication to assist swallowing. The lubrication is provided in many cases by a slippery mucous of which the chief constituent is a type of mucopolysaccharide named mucin. The saliva often contains additional agents, such as digestive enzymes, toxins, and anticoagulants (in blood-sucking animals such as vampire bats and leeches). (See Chapter 8 for a discussion of salivary glands.)

Tongues, an innovation of the chordates, assist in the mechanical digestion and swallowing of food. In some animals tongues are used to grasp food. They are also used in chemoreception, bearing gustatory receptors called taste buds (see Figure 7-16A). Snakes use their forked tongues to take olfactory samples from the air and the substratum, retracting the tongue to wipe the samples in Jacobson’s organ, which consists of a pair of richly innervated chemosensory pits located in the roof of the buccal cavity. Jacobson’s organs are found in other reptiles and some amphibians.

Foregut: Food Conduction, Storage, and Digestion

In most species the foregut consists of an esophagus, a tube that leads from the oral region to the digestive region of the alimentary canal, and a stomach (see Figure 15-15).

Esophagus

The esophagus conducts food from the headgut to the digestive areas, usually the stomach (see below). In chordates and some invertebrates, the esophagus conducts the bolus, or mass of chewed food mixed with saliva, by peristaltic movement (see Chapter 11) from the buccal cavity or pharynx. In some animals, this conducting region contains a sac-like expanded section, the crop, which is used to store food before digestion. The presence of a crop, generally found in animals that feed infrequently, allows quantities of food to be stored for digestion at a later time. Leeches, for example, feed very infrequently, with weeks or months between feeding periods. However, they ingest large quantities of blood at a “sitting,” storing the blood for many weeks and digesting it in small amounts between their rare feedings. In some animals crops are also used to ferment or digest foods for purposes other than their immediate digestion. Parent birds prepare food in this way to be regurgitated for their nestlings.

Stomach

In vertebrates and some invertebrates digestion takes place primarily in the stomach and the midgut. The stomach serves as a storage site for food, and in many species begins the initial stages of digestion. In most vertebrates, for example, the stomach initiates protein digestion by secreting the enzyme pepsinogen (later converted to pepsin) and hydrochloric acid, which provides the highly acidic environment required for pepsin activation. Contraction of the muscular walls of the stomach also provides mechanical mixing of food, saliva, and stomach secretions.

Stomachs are classified as monogastric or digastric, according to the number of chambers they possess. A monogastric stomach consists of a single strong muscular tube or sac. Vertebrates that are carnivorous or omnivorous characteristically have a monogastric stomach (Figure 15-18). Instead of a stomach, some invertebrates, such as insects (see Figure 15-16D), have outpouchings termed gastric ceca (singular, cecum), which are lined with enzyme-secreting cells, as well as phagocytic cells that engulf partially digested food and continue the process of digestion. In these alimentary systems the processes of digestion and absorption are completed in the ceca, and the remainder of the alimentary canal is concerned primarily with water and electrolyte balance and defecation.

Some birds have a tough, muscular gizzard, or crop, or both (see Figure 15-17). Sand, pebbles, or stones are swallowed and then lodge in the gizzard, where they aid in the grinding of seeds and grains. The proventriculus of insects and the stomach of decapod crustaceans, comparable to the bird’s gizzard, contain grinding apparatuses for chewing swallowed food. Some fish such as mullets also have gizzards. On the other hand, some fish and larval toads lack stomachs altogether, with material from the esophagus entering into what is functionally the midgut.

Multichambered digastric stomachs (Figure 15-19) are found in the mammalian suborder Ruminantia (deer, elk, giraffe, bison, sheep, cattle, etc.). Somewhat similar digastric stomachs occur outside this suborder, in particular in the suborder Tylopoda (camel, llama, alpaca, vicuña). Microorganisms in the first division of the stomach carry out fermentation, the anaerobic conversion of organic compounds to simpler compounds, yielding energy as ATP. All of the above-named groups carry out rumination, in which partially digested food is regurgitated (transported back to the mouth) for remastication (additional chewing). This process allows the ruminant (a gazelle on the open savanna, for example) to swallow food hastily while grazing and then to chew it more thoroughly later when at rest in a place of relative safety from predators. After the regurgitated food is chewed, it is swallowed again. This time it passes into the second division of the digastric stomach and...
begins the second stage of digestion. In this stage hydrolysis takes place with the assistance of digestive enzymes secreted by the stomach lining.

The digastric stomach of the Ruminantia (see Figure 15-19) has four chambers, separated into two divisions. The first division consists of the **rumen** and **reticulum** chambers; the second division comprises the **omasum** and the **abomasum** (true stomach). The rumen and reticulum act as a fermentation vat that receives grazed vegetation. Bacteria and protozoans in these chambers thrive on the vegetation, causing extensive digestive breakdown by fermentation of carbohydrates to butyrate, lactate, acetate, and propionate. These products of fermentation, along with some peptides, amino acids, and short-chain fatty acids, are absorbed into the bloodstream from the rumen fluid. Symbiotic microorganisms grown in the rumen, along with undigested particles, are passed into the omasum (absent in the Tylopoda) and then into the abomasum. Only the latter secretes digestive enzymes and is homologous to the monogastric stomach of non-ruminants.

Fermentation in the stomach is not limited to ruminating animals. It is found in other animals in which the passage of food in the stomach is delayed, allowing the growth of symbiotic microorganisms in a zone anterior to the digestive stomach, as in the kangaroo and the crops of galliform (chicken-like) birds.

**Midgut: Chemical Digestion and Absorption**

In vertebrates, the **midgut** is the major site for the chemical digestion of proteins, fats, and carbohydrates. Once digested to their component molecules, these materials are then absorbed in the midgut and transported away from the alimentary canal in the blood. As food is ready to pass on from the vertebrate stomach, it is released into the midgut through the **pyloric sphincter**, which relaxes as the peristaltic movements of the stomach squeeze the acidic contents into the duodenum, the initial segment of the **small intestine** (see Figure 15-18A). Digestion continues in the small intestine, generally in an alkaline environment.

**General structure and function of the midgut**

Among the vertebrates, carnivores have shorter and simpler intestines than do herbivores, reflecting the shorter time required to digest meat than vegetation. For example, a tad-
pole, which is almost always herbivorous, has a longer intestine than the adult frog, which is carnivorous.

The vertebrate midgut or small intestine is typically divided into three distinct portions. The first, rather short, section is the duodenum, the lining of which secretes mucus and fluids and receives secretions carried by ducts from the liver and pancreas. Next is the jejunum, which also secretes fluid and is involved in digestion and absorption. The most posterior section, the ileum, acts primarily to absorb nutrients digested previously in the duodenum and jejunum, although some secretion occurs from the ileum.

As just noted, the secretory functions of the vertebrate duodenal epithelium are supplemented by secretions from the liver and pancreas. The cells of the liver produce bile salts, which are carried in the bile fluid to the duodenum through the bile duct. Bile fluid has two important functions. It emulsifies fats, and it helps neutralize acidity introduced into the duodenum from the stomach. The pancreas, an important exocrine organ described in Chapter 9, produces pancreatic juice, which contains many of the proteases, lipases, and carbohydrates essential for intestinal digestion in vertebrates. Pancreatic juice is released into the pancreatic duct and, like bile, is important in neutralizing gastric acid in the intestine.

The intestine of most animals contains large numbers of bacteria, protozoans, and fungi. These multiply, contributing enzymatically to digestion, and are usually, in turn, digested themselves. An important function of some intestinal symbionts is the synthesis of essential vitamins.

The midgut region varies greatly not only in structure, but also in function in different animal groups. In many invertebrates, especially those with extensive ceca and diverticula (blind outpouchings of the alimentary canal), the intestine serves no digestive function. In some air-breathing fishes (e.g., the weather loach, Misgurnus anguillicaudatus), the midgut is modified into a gas exchange organ where O₂ from gulped air is exchanged with CO₂ from the cells, with residual gas then being expelled out the anus.

**Intestinal epithelium**

The vertebrate small intestine has adaptations at every anatomical level, from its gross anatomy to the organelles of individual cells, all designed to amplify the surface area available for absorption of nutrients. In humans, the lumen of the small intestine has a gross cylindrical surface area of only about 0.4 m², or about 7–8 pages of this book. However, because of the enormous elaboration of absorptive surfaces provided by this hierarchy of structures, the true area is increased at least 500 times, to a total of 200 to 300 m², or about the size of a doubles tennis court. Since the rate of absorption is generally proportional to the area of the apical surface membrane of the cells lining the epithelium, this huge increase in surface area greatly aids absorption of digested substances from the fluid within the intestine. We will now examine this remarkable system of valleys and peaks, peninsulas and inlets.

The general organization of the vertebrate small intestine is shown in Figure 15-20A. The outermost layer is the serosa, which is the same tissue that covers the visceral organs of the abdomen. The serosa overlies an outer layer of...
longitudinal smooth muscle, while an inner layer of circular smooth muscle surrounds the epithelial layer, which consists of the submucosa (a layer of fibrous connective tissue) and the mucosa (or mucous membrane). Projecting into and encircling the lumen of the small intestine are numerous folds of the mucosa, variously called the folds of Kerckring or the circular folds (Figure 15-20A and B). In addition to increasing surface area, these folds serve to slow the progress of food through the intestine, allowing more time for digestion. At the next anatomical level are the finger-like villi (Figure 15-20B and C), which line the folds, standing about 1 mm tall. Each villus sits in a circular depression known as the crypt of Lieberkühn (see Figure 15-20C). Within each villus is a network of blood vessels—arterioles, capillaries and venules—and a network of lymph vessels, the largest of which is the central lacteal. Nutrients taken up from the intestine are transferred into these blood and lymph vessels for transport to other tissues; the central lacteal can, in addition, take up larger particles.

The villi are lined with the actual absorptive surface of the small intestine, the cells of the digestive epithelium (Figure 15-21). The epithelium consists of goblet cells interspersed among columnar absorptive cells (Figure 15-21A). The absorptive cells proliferate at the base of the villus and steadily migrate toward its tip, where they are sloughed off at the rate of about $2 \times 10^{10}$ cells per day in the human intestine, meaning that the entire midgut lining is replaced every few days.

The next level in the hierarchy of absorptive adaptations is found at the apical surface of each absorptive cell, where there are striated structures called microvilli, which collectively form the brush border (Figure 15-21B and D). There are up to several thousand microvilli per cell (about $2 \times 10^3$ per square millimeter); each standing 0.5 to 1.5 μm tall and about 0.1 μm wide. The membrane of the microvillus is continuous with the plasma membrane of the epithelium and contains actin filaments that form cross-bridge links with myosin filaments present at the base of each microvillus (Figure 15-21C). Intermittent actin-myosin interaction produces rhythmic motions of the microvilli, which might help mix and exchange the intestinal chyme (semifluid mass of partially digested food) near the absorptive surface.

The surfaces of the microvilli are covered by the glycocalyx, a meshwork up to 0.3 μm thick comprising acid mucopolysaccharides and glycoproteins (Figure 15-21C). Water and mucus are trapped within the interstices of the glycocalyx. The mucus is secreted by the mucous (goblet)
cells, named for their shape, that occur among the absorptive cells (see Figure 15-21A).

Adjacent absorptive cells are held together by desmosomes (Chapter 4). Near the apex, the zonula occludens encircles each cell, making a tight junction with its neighbors (Figure 15-21B). The tight junctions are especially tight in this epithelium, so that the apical membranes of the absorptive cells effectively form a continuous sheet of apical membrane, without breaks between cells. Because of the virtual impermeability of the tight junctions, all nutrients must pass across this membrane and through the absorptive cell cytoplasm to get from the lumen to the blood and lymph vessels within the villi. Little, if any, paracellular passage occurs.

**Hindgut: Water and Ion Absorption and Defecation**

The hindgut serves to store the remnants of digested food (see Figure 15-15). From this material is absorbed inorganic ions and excess water for return to the blood. In vertebrates, this function is carried out primarily in the latter portion of the small intestine and in the large intestine. In some insects, the feces within the rectum are rendered almost dry by a specialized mechanism for removing water from the rectal contents (Chapter 14). The hindgut also functions as the major site for bacterial digestion of intestinal contents through the action of the bacterial flora found in herbivorous reptiles, birds, and most herbivorous mammals.

In many species it is the hindgut that consolidates undigested material and bacteria growing in the hindgut into feces. The feces pass into the cloaca or rectum and are then expelled through the anus in the process of defecation (see below).

The hindgut is also the site of hindgut fermentation in many animals (Figure 15-22). The colon acts as a modified plug-flow reactor in most large animals that are hindgut fermenters (e.g., horses, zebras, tapirs, sirensians, elephants, rhinos, and marsupial wombats). In smaller hindgut fermenters the tremendously enlarged cecum acts as a continuous-flow, stirred-tank reactor (rabbits, many rodents, hyraxes, howler monkeys, koalas, and brushtail and ringtail opossums).

The hindgut terminates in a cloaca in many vertebrates, including hagfish, lungfish, Latimeria, elasmobranchs, adult amphibians, reptiles, birds, and a few mammals (monotremes, marsupials, some Insectivora, a few rodents). The cloaca aids in urinary ion and water resorption in those species in which the ureters terminate in the cloaca rather than in external genitalia.

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**Figure 15-21** The lining of the mammalian small intestine has a complex microanatomy specialized for absorption and secretion. The luminal surface is shown in color. (A) A villus covered with the mucosal epithelium, which consists primarily of absorptive cells and occasional goblet cells. (B) An absorptive cell. The luminal, or apical, surface of the absorptive cell bears a brush border of microvilli. (C) The microvilli consist of evaginations of the surface membrane, enclosing bundles of actin filaments. (D) Scanning electron micrograph of a group of absorptive cells from the human small intestine, showing the brush border. [Parts A–C from "The Lining of the Small Intestine," by F. Moog. Copyright © 1981 by Scientific American, Inc. All rights reserved. Part D from Lodish et al., 1995.]
Dynamics of Gut Structure — Influence of Diet

Research over the past decade has changed our traditional view of the gut as a relatively static set of organs and tissues. In fact, we now know that gut size and structure are quite dynamic, responding to changes in both energy demand and food quality in most animals, be they carnivores or herbivores. Most responsive is overall gut size. House wrens (Troglodytes aedon), induced to increase food intake through exposure to combinations of lowered ambient temperature and enforced exercise over several months, responded by increasing the overall length of the small intestine by about one-fifth. Efficacy of nutrient uptake increases as a result. The mass of the empty stomach of the ground squirrel (Spermophilus tridecemlineatus) increases three- to fourfold within a few months after rousing from hibernation. Although reptiles have a much lower rate of metabolism than birds and mammals (see Chapter 16), some reptiles appear to remodel their gut in response to food intake much more rapidly than has been shown for birds and mammals, sometimes within a few hours or days. In the Burmese python (Python molurus), anterior small intestine mass increases by over 40% over fasting levels within 6 hours of a large meal (25% of body mass), and reaches double the fasting mass two days after a meal. These changes are due largely to proliferation of the mucosal rather than serosal layer. Associated with these morphological changes were increases in capacity for amino acid uptake that ranged from 10-24 times the fasting values.

Even when overall length and diameter are not affected by dietary changes, the "microstructure" in terms of villi may change, resulting in alterations in absorptive surface area. These changes can lead to an overall increase in nutrient absorption when an animal's energy demands are great, as well as aid in slowing the passage of digesting food, to enhance extraction of nutrients. This latter situation is particularly evident in cecal fermenters.

Dietary adjustments can similarly alter the cellular and macromolecular makeup of the gut. Research over the last few decades by investigators, including Jared Diamond and William Karasov, has shown that most intestinal membrane transporters are regulated by dietary levels of their substrates. Increasing substrate levels stimulates an increase in concentration and/or activity of transporters for glucose, fructose, some nonessential amino acids, and peptides. The proliferation of transporters appears to be matched to the level of nutrient intake so as to provide no more than the uptake capacity necessary.

It is important to emphasize that an expansion of gut surface area or nutrient transporter proteins carries with it significant metabolic cost in support of this new macro- or microstructure. Consequently, most changes in gut structure appear to be completely reversible, to reduce the metabolic cost of maintaining the gut during periods when food resources are scarce.

MOTILITY OF THE ALIMENTARY CANAL

The ability of the alimentary tract to contract and propel ingested material along its length, a characteristic called motility, is important to digestive function for:

1. Translocation of food along the entire length of the alimentary canal and the final expulsion of fecal material
2. Mechanical treatment by grinding and kneading to help mix in digestive juices and convert food to a soluble form
3. Mixing of the contents so that there is continual renewal of material in contact with the absorbing and secreting surfaces of the epithelial lining.

**Muscular and Ciliary Motility**

Motility can be achieved by two different mechanisms—muscular motility and ciliary motility. **Muscular motility**, in which transport is achieved by muscle contraction of the walls of the alimentary canal, is the only mechanism found in arthropods and chordates. In chordates, motility is achieved strictly by smooth muscle fibers, but in many arthropods motility is achieved by striated fiber contraction. Muscular mechanisms permit handling of harder and larger pieces of food. Ciliary motility, in which cilia lining the digestive tract generate currents of fluid within, is the only mechanism used to translocate food along the alimentary canals of annelids, lamellibranch mollusks, tunicates, and cephalochordates. However, ciliary motility is used in conjunction with muscular mechanisms in echinoderms and most mollusks.

**Peristalsis**

The alimentary musculature is made up of smooth muscle tissue in all animal groups other than arthropods, where it comprises striated muscle. The arrangement of the musculature in vertebrates consists of an inner circular layer and an outer longitudinal layer (Figure 15-23; see also Figure 15-20A). The contraction of the circular layer coordinated with relaxation of the longitudinal layer produces an active constriction with an elongation. Active shortening of the longitudinal layer with relaxation of the circular layer produces distension. Peristalsis occurs as a traveling wave of constriction produced by contraction of circular muscle and is preceded along its length by a simultaneous contraction of the longitudinal muscle and relaxation of the circular muscle (Figure 15-24). This pattern of contraction "pushes" the luminal contents in the direction of the peristaltic wave. Mixing of the luminal contents is achieved primarily by a process called segmentation, which consists of rhythmic contractions of the circular muscle layer that occur asynchronously along the intestine at various points without participation of the longitudinal muscle.

**Swallowing** in vertebrates involves the integrated movements of muscles in the tongue and pharynx, as well as peristaltic movements of the esophagus, which are under direct neural control of the medulla oblongata of the brain. These actions propel a bolus to the stomach. **Regurgitation** occurs when peristalsis takes place in the reverse direction,
Coordinated contraction of the gastrointestinal tract propels material through its lumen. (A) Peristalsis occurs as a traveling wave of contraction of circular muscle preceded by relaxation. This produces longitudinal movement of the bolus. (B) Segmentation occurs as alternating relaxations and contractions, primarily of circular muscle. The result is a kneading and mixing of the intestinal contents, moving the luminal contents back into the buccal cavity. Ruminants regularly use regurgitation to bring up the unchewed food for further chewing, and other vertebrates use it during emesis (vomiting).

Normal peristalsis in the vertebrate stomach occurs with the ring of contraction only partially closed. Consequently there is a mixing action in which the contents are squeezed backward (opposite to the direction of the wave) centrally through the partially open ring and forward peripherally in the direction of peristalsis as the partially closed ring of contraction moves from the cardiac to the pyloric end of the stomach.

**Control of Motility**

The coordinated contractions of circular and longitudinal smooth muscle layers that provide alimentary canal motility in vertebrates are regulated by a combination of distinct mechanisms.

**Intrinsic control**

The smooth muscle tissue in the wall of the alimentary tract is myogenic—that is, capable of producing an intrinsic cycle of electrical activity that leads to muscle contraction without external neural stimulation. This cycle occurs as rhythmic depolarizations and repolarizations called the basic electric rhythm (BER). This rhythm consists of spontaneous slow waves of depolarization that progress slowly along the muscle layers (Figure 15-25). Some of these slow waves give rise to action potentials (APs) produced by an inward current carried by calcium ions. These calcium “spikes” lead to contractions of the smooth muscle cells in which they occur. The amplitude of the slow-wave BER is modulated by local influences such as stretching of the muscle tissue. Such stretching would occur when a chamber of the alimentary canal is stretched by contents in its lumen. Another influence on contraction is chemical stimulation of the mucosa by substances in the chyme.

**Extrinsic (neural, hormonal) control**

Intrinsic patterns of the BER are modulated by locally released gastrointestinal peptide hormones (Table 15-1; also,
see Spotlight 9-1). Thus, a chemical stimulant in the chyme can cause the release of a local hormone, and this, in turn, can modulate the motility of the muscle tissue.

In addition to local stimuli, intestinal motility is influenced by diffuse innervation from the sympathetic, parasympathetic, and peptidergic (purinergic) divisions of the autonomic nervous system (see Chapter 9). Sympathetic and parasympathetic postganglionic neurons form networks dispersed throughout the smooth muscle layers (Figure 15-26). The parasympathetic network made up of cholinergic neurons is divided into the myenteric plexus and the submucosal plexus. These plexi, which receive their parasympathetic input primarily via branches of the vagus nerve, mediate excitatory actions (i.e., increased motility and gastrointestinal secretion) of the digestive tract. In contrast, the innervation from the sympathetic division is
primarily inhibitory. Postganglionic neurons of the sympathetic division directly innervate all the tissues of the gut wall as well as neurons of the myenteric and submucosal plexi. Activity of these sympathetic efferents inhibits the motility of the stomach and intestine.

The smooth muscle cells are inhibited (i.e., prevented from developing action potentials) by norepinephrine, released by the sympathetic nerve endings, and are excited by acetylcholine (ACh), released in response to the activity of the parasympathetic nerves (Figure 15-27A). Each impulse associated with excitation produces an increment of tension, which subsides with cessation of impulses (Figure 15-27B). Evidence of the importance of the smooth muscle innervation in maintaining tone is found in Hirschsprung's disease (also known as congenital megacolon), in which there is a congenital absence of ganglion cells in the wall of the rectum. Lacking smooth muscle tone, the colon becomes greatly extended, which can lead to recurrent fecal impactions.

The peristaltic movements described in the previous section are coordinated by the intrinsic BER, with the local participation of the myenteric plexus. This contrasts with the peristaltic movements of the swallowing reflex, in which the movements of the esophagus are under direct control of the central nervous system.

Smooth muscle in the alimentary canal of vertebrates is also regulated by non-adrenergic, non-cholinergic neurons that release a variety of peptides and purine nucleotides. In the nearly three decades since this was first discovered, aminergic neurons have been identified that release ATP, 5-HT, dopamine, GABA, while peptidergic neurons have been found that release enkephalins, vasoactive intestinal polypeptide (VIP), substance P, bombesin/gastrin-releasing peptide, neurotensin, cholecystokinin (CCK), and neu ropeptide Y/pancreatic polypeptide. This host of transmitter substances allows very fine control over the numerous interacting functions of the alimentary canal.
TABLE 15-1
Action of some enzymes secreted in the mouth, stomach, pancreas, and small intestine of mammals

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Site of action</th>
<th>Substrate</th>
<th>Products of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mouth</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary α-amylase</td>
<td>Mouth</td>
<td>Starch</td>
<td>Disaccharides (few)</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pepsinogen → pepsin</td>
<td>Stomach</td>
<td>Proteins</td>
<td>Large peptides</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic α-amylase</td>
<td>Small intestine</td>
<td>Starch</td>
<td>Disaccharides</td>
</tr>
<tr>
<td>Trypsinogen → trypsin</td>
<td>Small intestine</td>
<td>Proteins</td>
<td>Large peptides</td>
</tr>
<tr>
<td>Chymotrypsin</td>
<td>Small intestine</td>
<td>Proteins</td>
<td>Large peptides</td>
</tr>
<tr>
<td>Elastase</td>
<td>Small intestine</td>
<td></td>
<td>Elastin</td>
</tr>
<tr>
<td>Carboxypeptidases</td>
<td>Small intestine</td>
<td>Large peptide</td>
<td>Small peptides (oligopeptides)</td>
</tr>
<tr>
<td>Aminopeptidases</td>
<td>Small intestine</td>
<td>Large peptide</td>
<td>Oligopeptides</td>
</tr>
<tr>
<td>Lipase</td>
<td>Small intestine</td>
<td>Triglycerides</td>
<td>Monoglycerides, fatty acids, glycerol</td>
</tr>
<tr>
<td>Nucleases</td>
<td>Small intestine</td>
<td>Nucleic acids</td>
<td>Nucleotides</td>
</tr>
<tr>
<td><strong>Small intestine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterokinase</td>
<td>Small intestine</td>
<td>Trypsinogen</td>
<td>Trypsin</td>
</tr>
<tr>
<td>Disaccharidases</td>
<td>Small intestine*</td>
<td>Disaccharides</td>
<td>Monosaccharides</td>
</tr>
<tr>
<td>Peptidases</td>
<td>Small intestine*</td>
<td>Oligopeptides</td>
<td>Amino acids</td>
</tr>
<tr>
<td>Nucleotidases</td>
<td>Small intestine*</td>
<td>Nucleotides</td>
<td>Nucleosides</td>
</tr>
<tr>
<td>Nucleosidases</td>
<td>Small intestine*</td>
<td>Nucleosides</td>
<td>Sugars, purines, pyrimidines</td>
</tr>
</tbody>
</table>

*Intracellular

GASTROINTESTINAL SECRETIONS

The alimentary canal of most animals produces both endocrine and exocrine secretions. In fact, the alimentary canal in many animals has been described as the “largest endocrine and exocrine gland of the body.” As explained in Chapters 8 and 9, hormones are produced in the alimentary canal by cells of endocrine glands and are liberated directly into the bloodstream, acting as messengers to receptor molecules in target tissues, which usually include other tissues of the alimentary canal.

Exocrine gastrointestinal secretions usually consist of aqueous mixtures of substances rather than a single species of molecule. Exocrine tissues of the alimentary canal include the salivary glands, secretory cells in the stomach and intestinal epithelium, and secretory cells of the liver and pancreas. The primary secretions of the exocrine glands of the alimentary canal enter the acinar lumen of the gland, and then generally become secondarily modified in the gland’s secretory duct. This secondary modification can involve further transport of water and electrolytes into or out of the duct to produce the final secretory juice, as illustrated in the salivary gland (Figure 15-28) and described in detail in Chapter 8.

Figure 15-28 Formation of saliva in the mammalian salivary gland depends on active transport and osmosis. The acinar cells transport electrolytes from their basal sides into the acinus and secrete mucin and amylase by exocytosis, with water flowing into the lumen by osmosis. As the salivary fluid moves down the duct, it undergoes modification by active transport across the epithelium of the duct. [Adapted from Davenport, 1985.]
Exocrine Secretions of the Alimentary Canal

There are large variations in the composition of the secretions from different regions of the alimentary canal. However, these mixtures usually consist of some combination of water, ions, mucus, and enzymes.

Water and electrolytes

The exocrine glands of the alimentary canal typically secrete large quantities of water-based fluids bearing digestive enzymes and other chemicals into the alimentary canal lumen (Figure 15-29). Most of this water is reabsorbed in the distal portions of the gut.

In aqueous solution, the mucus produced in the goblet cells of the stomach and intestine (see Figures 15-18 and 15-21) provides a slippery, thick lubricant that helps prevent mechanical and enzymatic injury to the lining of the gut. The salivary glands and pancreas secrete a thinner mucoid solution.

Secretion of inorganic constituents of digestive fluids generally occurs in two steps. First, water and ions are secreted into the lumen of the gland either by passive ultrafiltration due to a hydrostatic pressure gradient across the luminal epithelium, or by active (energy-requiring) processes from the interstitial fluid bathing the basal portions of the acinar cells. The latter is believed usually to entail active transport of ions by these cells, which is then followed by the osmotic flow of water into the acinus. There is subsequent secondary modification of this ultrafiltrate by active or passive transport across the epithelium lining the ducts as the fluid passes along the exocrine ducts toward the alimentary canal.

Bile and bile salts

The vertebrate liver does not produce digestive enzymes. However, it does secrete bile, a fluid essential for digestion of fats. Bile consists of water and a weakly basic mixture of cholesterol, lecithin, inorganic salts, bile salts, and bile pigments. The bile salts are organic salts composed of bile acids manufactured by the liver from cholesterol and conjugated with amino acids complexed with sodium (Figure 15-30). The bile pigments derive from biliverdin and bilirubin, which are products of the breakdown of hemoglobin spilled into plasma from old, ruptured red blood cells. Bile produced in the liver is transported via the hepatic duct to the gallbladder, where it is concentrated and stored. Water is removed osmotically, following active transport of Na⁺ and Cl⁻ from the bile across the gallbladder epithelium.

Bile serves numerous functions important to digestion. First, its high alkalinity is important in the terminal stages of digestion because it buffers the high acidity provided by the gastric juice secreted earlier in the digestive process.

<table>
<thead>
<tr>
<th>Region</th>
<th>Secretion</th>
<th>Daily amount (L)</th>
<th>pH</th>
<th>Composition*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal cavity</td>
<td>Saliva</td>
<td>1+</td>
<td>6.5</td>
<td>Amylase, bicarbonate</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Gastric juice</td>
<td>1–3</td>
<td>1.5</td>
<td>Pepsinogen, HCl, rennin in infants, &quot;intrinsic factor&quot;</td>
</tr>
<tr>
<td>Stomach</td>
<td>Pancreatic juice</td>
<td>1</td>
<td>7–8</td>
<td>Trypsinogen, chymotrypsinogen, carboxy- and aminopeptidase, lipase, amylase, maltase, nucleases, bicarbonate</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Bile</td>
<td>1</td>
<td>7–8</td>
<td>Fats and fatty acids, bile salts and pigments, cholesterol</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>&quot;Succus entericus&quot;</td>
<td>1</td>
<td>7–8</td>
<td>Enterokinase, carboxy- and aminopeptidases, maltase, lactase, sucrase, lipase, nucleases</td>
</tr>
<tr>
<td>Duodenum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jejunum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cecum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Excluding mucus and water, which together make up some 95% of the actual secretion.

Figure 15-29 Important digestive secretions occur at all points along the human alimentary canal. The approximate volume and pH of each secretion is shown on the right.
Second, bile salts facilitate enzymatic fat digestion by breaking down fat into microscopic droplets that collectively have a much higher surface area. The ability of the bile salts to disperse fatty, water-insoluble substances derives from their amphipathic nature. That is, the bile salt molecule contains a lipid-soluble bile acid together with a water-soluble amino acid. Thus, it acts as a detergent for the emulsification of fat droplets, dispersing them in aqueous solution for more effective attack by digestive enzymes. Ultimately, the bile salts are removed from the large intestine by highly efficient active transport and returned to the bloodstream. The bile salts then become bound to a plasma carrier protein and are returned to the liver to be recycled. Bile salts also disperse lipid-soluble vitamins for transport in the blood.

Third, bile fluid contains waste substances removed from the blood by the liver, such as hemoglobin pigments, cholesterol, steroids, and drugs. These substances are either digested or excreted in the feces.

Digestive enzymes
An animal must first digest food before it can be used for tissue maintenance and growth and as a source of chemical energy. Digestion is primarily a complex chemical process in which special digestive enzymes catalyze the hydrolysis of large foodstuff molecules into simpler compounds that are small enough to cross cell membranes of the intestinal barrier. For example, starch, a long-chain polysaccharide, is degraded to much smaller disaccharides and monosaccharides; proteins are hydrolyzed into polypeptides and then into tripeptides, dipeptides, and amino acids.

All digestive enzymes carry out hydrolysis, adding $\text{H}^+$ to one residue and $\text{OH}^-$ to the other (Figure 15-31). Hydrolysis of the anhydrous bonds frees the constituent residues (e.g., monosaccharides, amino acids, monoglycerides) from which the polymer is formed, making them small enough for absorption from the alimentary canal into the circulating body fluids and for subsequent entry into cells to be metabolized.

Digestive enzymes, like all enzymes, exhibit substrate specificity and are sensitive to temperature, pH, and certain ions (see Chapter 3). Corresponding to the three major types of foodstuffs are three major groups of digestive enzymes: proteases, carbohydrases, and lipases.

Proteases Proteases are proteolytic enzymes, categorized as either endopeptidases or exopeptidases. Both types of enzymes attack peptide bonds of proteins and polypeptides (Figure 15-31A, Table 15-2). They differ in that endopeptidases confine their attacks to bonds well within (endo, "within") the protein molecule, breaking large peptide chains into shorter polypeptide segments. These shorter
segments provide a much greater number of sites of action for the exopeptidases. The exopeptidases attack only peptide bonds near the end (exo, "outside") of a peptide chain, providing free amino acids, plus dipeptides and tripeptides. Some proteases exhibit marked specificity for particular amino acid residues located on either side of the bonds they attack. Thus, the endopeptidase trypsin attacks only those peptide bonds in which the carboxyl group is provided by arginine or lysine, regardless of where they occur within the peptide chain. The endopeptidase chymotrypsin attacks peptide bonds containing the carbonyl groups of tyrosine, phenylalanine, tryptophan, leucine, and methionine.

In mammals, protein digestion usually begins in the stomach by the action of the gastric protease pepsin. There are different forms of this enzyme, but the most powerful form functions best at a low pH value of around 2. The action of pepsin is aided by secretion of gastric HCl and results in the hydrolysis of proteins into polypeptides and some free amino acids. In the mammalian intestine, several proteases produced by the pancreas continue the proteolytic process, yielding a mixture of free amino acids and small peptide chains. Finally, proteolytic enzymes intimately associated with the epithelium of the intestinal wall hydrolyze the polypeptides into oligopeptides, which consist of residues of two or three amino acids, and then further break these down into individual amino acids.

**Carbohydrases** Carbohydrases can be divided functionally into polysaccharidases and glycosidases. Polysaccharidases hydrolyze the glycosidic bonds of long-chain carbohydrates such as cellulose, glycogen, and starch. The most common polysaccharidases are the amylases, which hydrolyze all but the terminal glycosidic bonds within starch and glycogen, producing disaccharides and oligosaccharides. The glycosidases, which occur in the glycosocalyx attached to the surface of the absorptive cells (see Figure 15-21C), act on disaccharides such as sucrose, fructose, maltose, and lactose by hydrolyzing the remaining alpha-1,6 and alpha-1,4 glycosidic bonds. This breaks these sugars down into their constituent monosaccharides for absorption (see Figure 15-31B). Amylases are secreted in vertebrates by the salivary glands and pancreas and in small amounts by the stomach, and in most invertebrates by salivary glands and intestinal epithelium. Many herbivores consume large amounts of plant cell walls, containing cellulose, hemicellulose, and lignin. Cellulose, which is in greatest abundance, consists of glucose molecules polymerized via beta-1,4 bonds. Cellulase, an enzyme that digests cellulose and

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**TABLE 15-2**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Tissues of origin</th>
<th>Target tissue</th>
<th>Primary action</th>
<th>Stimulus to secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrin</td>
<td>Stomach and duodenum</td>
<td>Secretory cells and muscles of stomach</td>
<td>HCl production and secretion; stimulation of gastric motility</td>
<td>Vagus nerve activity; peptides and proteins in stomach</td>
</tr>
<tr>
<td>Cholecystokinin (COX)*</td>
<td>Upper small intestine</td>
<td>Gallbladder</td>
<td>Contraction of gallbladder</td>
<td>Fatty acids and amino acids in duodenum</td>
</tr>
<tr>
<td>Secretin*</td>
<td>Duodenum</td>
<td>Pancreas, secretory cells, and muscles of stomach</td>
<td>Water and NaHCO₃ secretion; inhibition of gastric motility</td>
<td>Food and strong acid in stomach and small intestine</td>
</tr>
<tr>
<td>Gastric inhibitory peptide (GIP)</td>
<td>Upper small intestine</td>
<td>Gastric mucosa and musculature</td>
<td>Inhibition of gastric secretion and motility</td>
<td>Monosaccharides and fats in duodenum</td>
</tr>
<tr>
<td>Bulbogastrone</td>
<td>Upper small intestine</td>
<td>Stomach</td>
<td>Increase of blood flow; secretion of thin pancreatic fluid; inhibition of gastric secretion</td>
<td>Acid in duodenum</td>
</tr>
<tr>
<td>Vasoactive intestinal peptide (VIP)*</td>
<td>Duodenum</td>
<td>Stomach, intestine</td>
<td>Inhibition of gastric secretion and motility</td>
<td>Fats in duodenum</td>
</tr>
<tr>
<td>Enteroglucagon</td>
<td>Duodenum</td>
<td>Jejunum, pancreas</td>
<td>Inhibition of motility and secretion</td>
<td>Carbohydrates in duodenum</td>
</tr>
<tr>
<td>Enkephalin*</td>
<td>Small intestine</td>
<td>Stomach, pancreas, intestine</td>
<td>Stimulation of HCl secretion; inhibition of pancreatic enzyme secretion and intestinal motility</td>
<td>Basic conditions in stomach and intestine</td>
</tr>
<tr>
<td>Somastostatin*</td>
<td>Small intestine</td>
<td>Stomach, pancreas, intestines, splanchnic arterioles</td>
<td>Inhibition of HCl secretion, pancreatic secretion, intestinal motility, and splanchnic blood flow</td>
<td>Acid in lumen of stomach</td>
</tr>
</tbody>
</table>

*Peptides marked with an asterisk are also found in central nervous tissue as neuropeptides. Neuropeptides not listed here, but identified in both brain and gut tissue, include substance P, neuropeptide, bombesin, insulin, pancreatic polypeptide, and ACTH.
which themselves are incapable of producing cellulase. In the gut of host animals as diverse as termites and cattle, wood. In cattle, the symbiotic microbes take up cellulase is liberated into the intestinal lumen by the symbiont and functions extracellularly to digest the ingested hemicellulose, is produced by symbiotic microorganisms in major nutritional constituent of grass, hay, and leaves) would be unavailable as food for grazing and browsing animals. Only a few animals, such as the shipworm Toredo (a wood-boring clam), Limnoria (an isopod), and the silverfish (an insect), can secrete cellulase without the help of symbionts.

Lipases Fats are water-insoluble, which presents a special problem for their digestion. Fats must undergo a special, two-stage treatment before they can be processed in the aqueous contents of the digestive tract. First, fats are emulsified—that is, they are rendered water-soluble by dispersing them into small droplets through the mechanical churning of the intestinal contents produced by segmentation (see Figure 15-24). The process of emulsification is aided by the chemical action of detergents such as bile salts and the phospholipid lecithin under conditions of neutral or alkaline pH. Bile salts have a hydrophobic, fat-soluble end and a hydrophilic, water-soluble end. Lipid attaches to the hydrophobic end, while water attaches to the hydrophilic end, dispersing the fat in the water-based fluid of the digestive tract. The overall effect is comparable to making mayonnaise, in which salad oil is dispersed in vinegar and egg yolk.

The second step, in vertebrates, is the formation of micelles (see Figure 2-16), aided by bile salts. Micelles are exceedingly small spherical structures formed from molecules which have polar hydrophilic groups at one end and nonpolar hydrophobic groups at the other end and which are assembled so that their polar ends face outward into the aqueous solution. The lipid core of each micelle is about 10^6 times the size of the original emulsified fat droplets, greatly increasing the surface area available for pancreatic lipase digestion. Enzymatic degradation then results from the action of intestinal lipases (in invertebrates) or pancreatic lipases (in vertebrates), producing fatty acids plus monoglycerides and diglycerides. In the absence of sufficient bile salts, fat digestion by the lipase is incomplete, and undigested fat is allowed to enter the colon.

Proenzymes Certain digestive enzymes, in particular proteolytic enzymes, are synthesized, stored, and released in an inactive molecular form known as a proenzyme, or zymogen. Proenzymes require activation, usually by hydrochloric acid in the lumen of the gastric gland, before they can carry out their degradative functions. Initial packaging of the enzyme in an inactive form prevents self-digestion of the enzyme and its tissue container while it is stored in zymogen granules. The proenzyme is activated by the removal of a portion of the molecule, either by the action of another enzyme specific for this purpose or through a rise in ambient acidity. Trypsin and chymotrypsin are good examples of enzymes originally constituted as proenzymes. The proenzyme trypsinogen, a 249-residue polypeptide, is inert until a 6-residue segment is cleaved from the NH_2-terminal end. This cleavage is achieved either by the action of another trypsin molecule or by enteropeptidase, an intestinal proteolytic enzyme. Trypsin also activates chymotrypsinogen through hydrolytic active form, chymotrypsin.

Other digestive enzymes In addition to the major classes of digestive enzymes just described, there are others playing a less important role in digestion. Nuclease, nucleotidases, and nucleosidases, as their names imply, hydrolyze nucleic acids and their residues. Esterase hydrolyze esters, which include those fruity-smelling compounds characteristic of ripe fruit. These and other minor digestive enzymes are not essential for nutrition, but they enhance the efficient use of ingested food.

Control of Digestive Secretions Among vertebrates, the primary stimulus for secretion of digestive juices in a given part of the digestive tract is the presence of food there or, in some instances, elsewhere in the tract. The presence of food molecules stimulates chemosensory endings, which leads to the reflex activation of autonomic efferents that activate or inhibit motility and exocrine secretion. Appropriate food molecules also directly stimulate epithelial endocrine cells by contact with their receptors, causing reflex secretion of gastrointestinal hormones into the local circulation. These reflexes permit secretory organs outside the alimentary tract proper (the liver and pancreas, for example) to be properly coordinated with the need for digestion of food passing along the digestive tract. Gastrointestinal secretion is largely under the control of gastrointestinal peptide hormones secreted by endocrine cells of the gastric and intestinal mucosa. Several of these hormones turn out to be identical with neuropeptides that act as transmitters in the central nervous system. This suggests that the genetic machinery for producing these biologically active peptides has been put to use by cells of both the central nervous system and the gastrointestinal tract. Some gastrointestinal hormones are listed in Table 15-2.

Often ignored in the control of digestive secretion in animals is the role of cognition or thought processes. Cephalic influences such as mental images of food as well as learned behaviors also stimulate digestive secretion, at least in mammals (Spotlight 15-1). However, none of these neural and hormonal mechanisms regulating secretion is under simple voluntary control.

The characteristics of digestive secretion (rate of secretion, quantity of secretion) depends on several interacting features, including: (1) whether secretion is neurally or hormonally controlled, (2) where in the alimentary canal
secretion occurs, and (3) how long food is normally present in the region being stimulated. For example, salivary secretion is very rapid and entirely under involuntary neural control, gastric secretions are under hormonal as well as neural control, and intestinal secretions are slower and are primarily under hormonal control. As in other systems, neural control predominates in rapid reflexes, whereas endocrine mechanisms are involved in reflexes that develop over minutes or hours.

Compared with vertebrates, very little is known about the control of digestive secretions in the invertebrates. Filter feeders evidently maintain a steady secretion of digestive fluids while they continuously feed. Other invertebrates secrete enzymes in response to the presence of food in the alimentary canal, but the precise control mechanisms have yet to be intensively studied. The formidable variety of invertebrate types further precludes generalization about their digestive systems.

**Salivary and gastric secretions**

Mammalian saliva contains water, electrolytes, mucin, amylase, and antimicrobial agents such as lysozyme and thiocyanate (see Figure 15-28). In the absence of food, the salivary glands produce a slow flow of watery saliva. Secretion of saliva is stimulated by the presence of food in the mouth, or, indeed, by any mechanical stimulation of tissues within the mouth, via cholinergic parasympathetic nerves to the salivary glands. Cognitive awareness of food has an identical effect (see Spotlight 15-1). The amylase in saliva mixes with the food during chewing and digests starches. The mucin and watery fluid conditions the food bolus to help it slide smoothly toward the stomach by the peristaltic movements of the esophagus.

A major secretion of the stomach lining is hydrochloric acid (HCl), which is produced by the parietal, or oxyntic, cells located in the gastric mucosa. The secretion of HCl is stimulated by:

- Vagal motor discharges.
- The action of the gastric hormone gastrin, in conjunction with histamine, a local hormone with paracrine actions synthesized in the mast cells of the gastric mucosa. (Both hormones are required for HCl secretion because they bind to different receptors on the parietal cell membrane, both of which must be filled for HCl secretion to occur.)
- Secretagogues in food, such as caffeine, alcohol, and the active ingredients of spices.

The secreted HCl helps break the peptide bonds of proteins, activates some gastric enzymes, and kills microorganisms that enter with the food. In some animals, the amount of H⁺ used to produce secreted HCl is so great that blood and other extracellular fluids may actually become alkaliotic for hours or days after ingestion of a large meal. This so-called alkaline tide can result in a rise in blood pH of 0.5 or even 1.0 pH unit in crocodiles, snakes, and other predators that have large, infrequent meals.

The parietal cells produce a concentration of hydrogen ions in the gastric juice 10⁴ times greater than in plasma (Figure 15-32). They do this with the aid of the enzyme carbonic anhydrase, which catalyzes the reaction of water with carbon dioxide:

$$\text{CO}_2 + \text{H}_2\text{O} \xrightarrow{\text{carbonic anhydrase}} \text{H}_2\text{CO}_3$$
Pepsin is the major enzyme secreted by the stomach. This proteolytic enzyme is secreted in the form of the proenzyme pepsinogen by the exocrine cells called chief cells, or zymogenic cells (Figure 15-33). Chief cell secretion is under vagal control and is also stimulated by the hormone gastrin, which arises from the gastric wall (Figure 15-34). The inactive pepsinogen, of which there are several variants, is converted to the active pepsin by a low-pH-dependent cleavage of a part of the peptide chain. Pepsin, an endopeptidase, selectively cleaves inner peptide bonds that occur adjacent to carboxylic side groups of large protein molecules.

Figure 15-33 The powerful proteolytic enzyme pepsin is secreted in an inactive form (pepsinogen), which is then activated by HCl. The chief (zygomatic) cell secretes the pepsinogen, while the parietal cell secretes the HCl, as well as intrinsic factor.

Figure 15-34 Vertebrate gastrointestinal hormones influence secretion and mechanical activity of the digestive tract. Gastrin from the lower stomach stimulates the flow of both HCl and pepsin from stomach secretory cells as well as the churning action of the muscular walls. Gastrin is secreted in response to intragastric protein, stomach distension, and input from the vagus nerve. Gastric inhibitory peptide (GIP), liberated from the small intestine in response to high levels of fatty acids, inhibits these activities. Neutralization and digestion of the chyme is accomplished by pancreatic secretions stimulated by cholecystokinin (CCK), which also induces contraction of the gallbladder, liberating the fat-emulsifying bile into the small intestine. CCK is secreted in response to the presence of amino and fatty acids in the duodenum. Secretin stimulates pancreatic secretion, but inhibits gastric activity. The plus and minus signs indicate stimulation and inhibition, respectively.
Goblet cells in the lining of the stomach secrete a gastric mucus containing various mucopolysaccharides. The mucus coats the gastric epithelium, protecting it from digestion by pepsin and HCl. HCl can penetrate the layer of mucus but is neutralized by alkaline electrolytes trapped within the mucus.

In some young mammals, including bovine calves (but not human infants), the stomach secretes rennin, an endopeptidase that clots milk by promoting the formation of calcium caseinate from the milk protein casein. The curdled milk is then digested by proteolytic enzymes, including rennin.

Gastric secretion in mammals occurs in three distinct phases: the cephalic, the gastric, and the intestinal phase. In the cephalic phase, gastric secretion occurs in response to the sight, smell, and taste of food, or in response to conditioned reflexes (see Spotlight 15-1). This phase is mediated by the brain (hence the term cephalic) and is abolished by section of the vagus nerve. In the gastric phase, mediated by the hormone gastrin and the compound histamine, the secretion of HCl and pepsin is stimulated directly by the presence of food in the stomach, which stimulates both chemoreceptors and mechanoreceptors. The intestinal phase is controlled by gastrin, as well as the hormones secretin, vasoactive intestinal peptide (VIP), and gastric inhibitory peptide (GIP) (see Table 15-2). GIP, for instance, is liberated by endocrine cells in the mucosa of the upper small intestine in response to the entry of fats and sugar into the duodenum (see Table 15-2 and Figure 15-34).

Understanding how the gastric phase of secretion is regulated was determined by use of the “Heidenhain pouch,” which is a denervated pouch surgically constructed within an animal from part of the stomach. Secretions from the pouch are directed outside the body wall, where they can be collected and their volume measured. The pouch’s only contact with the rest of the stomach is indirect, through the circulation. Since it is not innervated, the pouch can exhibit no cephalic phase secretion. However, it does secrete gastric juice in response to food placed into the stomach proper. The researchers correctly interpreted this finding as evidence that a hormonal messenger is released into the bloodstream when food is in the stomach. The hormone was named gastrin (see Table 15-2) and was later found to be a polypeptide. Gastrin is secreted from endocrine cells of the pyloric mucosa of the stomach in response to gastric chyme containing protein and to distension of the stomach. It stimulates stomach motility by binding to smooth muscle, and it induces a strong secretion of HCl and moderate secretion of pepsin by binding to secretory cells in the stomach lining. When the pH of the gastric chyme drops to 3.5 or below, gastrin secretion slows, and at pH 1.5 it stops. As already noted, secretion of histamine by the gastric mucosa also stimulates secretion of HCl, as does mechanical distension of the stomach.

The intestinal phase of gastric secretion is more complex (see Figure 15-34). As food enters the duodenum of the small intestine, partially digested proteins in acidic chyme directly stimulate the duodenum’s mucosa to secrete enteric gastrin (also called intestinal gastrin). Enteric gastrin has the same action as stomach gastrin, stimulating the gastric glands to increase their rate of secretion. In humans, at least, the intestinal phase is thought to play a relatively small role in overall regulation of gastric secretion.

The secretion of gastric juices can be reduced both by the absence of stimulating factors and by reflex inhibition. The enterogastric reflex, which inhibits gastric secretion, is triggered when the duodenum is stretched by chyme pumped from the stomach, and when this chyme contains partially digested proteins or has particularly low pH. Gastric secretion can also be inhibited by strong activation of the sympathetic nervous system. Action potentials in the sympathetic nerves terminating in the stomach release noradrenaline, which inhibits both gastric secretion and gastric emptying.

**Intestinal and pancreatic secretions**

The epithelium of the mammalian small intestine secretes intestinal juice, or succus entericus, which is a mixture of two fluids. Brunner’s glands in the first part of the duodenum between the pyloric sphincter and the pancreatic duct secrete a viscous, enzyme-free, alkaline mucoid fluid that enables the duodenum to withstand the acidic chyme coming from the stomach until it can be neutralized by the alkaline pancreatic and biliary secretions coming from the pancreatic duct. A thinner, enzyme-rich alkaline fluid arises in the crypts of Lieberkühn (see Figure 15-20) and mixes with duodenal secretions. The secretion of intestinal juice is regulated by several hormones, including secretin, gastrin inhibitory peptide (GIP), and gastrin, and additionally is under neural control. Distension of the wall of the small intestine elicits a local secretory reflex. Vagal innervation also stimulates secretion.

The large intestine secretes no enzymes. However, it does secrete a thin alkaline fluid containing bicarbonate and potassium ions plus some mucus that binds the fecal matter together.

In addition to its endocrine secretion of insulin from the islets of Langerhans (see Chapter 9), the pancreas contains exocrine tissue that produces several digestive secretions that enter the small intestine through the pancreatic duct. The pancreatic enzymes, including alpha-amylase, trypsin, chymotrypsin, elastase, carboxypeptidases, aminopeptidases, lipases, and nucleases, are delivered in an alkaline, bicarbonate-rich fluid that helps neutralize the acid chyme formed in the stomach. This buffering is essential, since the pancreatic enzymes require a neutral or slightly alkaline pH for optimum activity.

Exocrine secretion by the pancreas is controlled by the peptide hormones produced in the upper small intestine. Acid chyme reaching the small intestine from the stomach stimulates the release of secretin and VIP, both produced by endocrine cells in the upper small intestine (see Table 15-2). These peptides are transported in the blood, reaching the duct cells of the pancreas and stimulating them to produce
its thin bicarbonate fluid. Peptide hormones only weakly stimulate secretion of pancreatic enzymes, however. Gastrin secreted from the stomach lining also elicits a small flow of pancreatic juice in anticipation of the food that will enter the duodenum.

Secretion of pancreatic enzymes is elicited by another upper intestinal hormone—the peptide cholecystokinin (see Table 15-2)—secreted from epithelial endocrine cells in response to fatty acids and amino acids in the intestinal chyme. Cholecystokinin is now known to be identical with pancreozymin, and so both are currently referred to as cholecystokinin (CCK). It stimulates pancreatic secretion of enzymes as well as contraction of the smooth muscle wall of the gallbladder, forcing bile into the duodenum (see Figure 15-34).

The neuropeptides somatostatin and enkephalin have also been identified in endocrine cells of the upper intestinal mucosa in vertebrate guts. Both hormones have a variety of actions on gastrointestinal function. Somatostatin, which normally acts through paracrine effects, inhibits gastric acid secretion, pancreatic secretion, and intestinal motility, as well as blood flow. The enkephalins inhibit gastric acid secretion, stimulate pancreatic enzyme secretion, and inhibit intestinal motility.

The composition of pancreatic secretions can be modified in some species by the content of the diet. Thus, a diet high in carbohydrates over several weeks will result in an increase in the amylase content of pancreatic enzymes. Similar correlations have been noted between protein and proteases, and fat and lipases.

**Nutrient Uptake in the Intestine**

The carbohydrate-rich filaments composing the glycocalyx covering the microvilli arise from, and are continuous with, the surface membrane of the microvillus itself. The filaments of the glycocalyx appear to be the carbohydrate side chains of glycoproteins embedded in the membrane. Further, the brush border (microvilli plus glycocalyx) has been found to contain digestive enzymes for the final digestive stages of various small foodstuff molecules. These enzymes are membrane-associated glycoproteins having carbohydrate side chains protruding into the lumen. The enzymes found associated with the brush border include disaccharidases, aminopeptidases, and phosphatases. Thus, some of the terminal stages of digestion are carried out at the absorptive cell membrane, close to the sites of uptake from the lumen into the absorptive cells.

Several transfer processes are involved in absorption. These include passive diffusion, facilitated diffusion, cotransport, countertransport, and active transport (see Chapter 4), and endocytosis. The type of transfer mechanism used depends on the type of molecule being transported during the absorption process.

**Simple diffusion**

Simple diffusion can take place across the lipid bilayer (providing the diffusing substance has a high lipid solubility) or through water-filled pores. Substances that diffuse across the brush border membrane of the intestine include fatty acids, monoglycerides, cholesterol, and other fat-soluble substances. Substances that pass through water-filled pores include water, certain sugars, alcohols, and other small, water-soluble molecules. For nonelectrolytes, net diffusion rate is proportional to their chemical concentration gradient. For electrolytes, it is proportional to the electrochemical gradient. In passive diffusion, net transfer is always "downhill," using the energy of the concentration gradient.

**Carrier-mediated transport**

The absorption of monosaccharides and amino acids presents two problems. First, these molecules are hydrophilic because of their —OH groups, because of charges they may bear, or because of both. Second, they are too large to be carried through water-filled pores by solvent drag or simple diffusion. These problems are overcome by carrier-mediated transport across the absorptive cell membrane (Figure 15-35). For example, sugars such as fructose are carried down their concentration gradient by facilitated diffusion, a process in which a hydrophilic, lipid-insoluble substance diffuses down its chemical gradient with the help

**ABSORPTION**

The breakdown products of digestion (amino acids from proteins, sugars from carbohydrates, etc.) are transported from the gut to the animal's tissues and cells. In a unicellular organism, the products of digestion leave the food vacuole to enter the surrounding cytoplasm. In a multicellular animal, these products must be transported across the absorptive epithelium into the circulation, and then move from the blood into the tissues.

Digestion products are absorbed mainly via the microvilli of the apical membrane of the absorptive cell (see Figure 15-21). The digestive and absorptive mechanisms of the microvilli include the glycocalyx, digestive enzymes intimately associated with the membrane, and specific intramembrane transporter proteins. In the basolateral membranes other mechanisms transfer these substances out of the absorptive cell into the interstitial fluid and eventually into the general circulation.

**What effect would a diminished flow of secretions from the pancreatic duct have on digestion? Why does blockage of the pancreatic duct of mammals potentially lead to rapid death?**

**Can you design an experiment that would indicate the metabolic cost of taking up a nutrient by active transport compared with one taken up by passive diffusion?**

**Carrier-mediated transport**

The absorption of monosaccharides and amino acids presents two problems. First, these molecules are hydrophilic because of their —OH groups, because of charges they may bear, or because of both. Second, they are too large to be carried through water-filled pores by solvent drag or simple diffusion. These problems are overcome by carrier-mediated transport across the absorptive cell membrane (Figure 15-35). For example, sugars such as fructose are carried down their concentration gradient by facilitated diffusion, a process in which a hydrophilic, lipid-insoluble substance diffuses down its chemical gradient with the help...
of specific protein channels located in the membranes. This process is powered by coupling sugar transport to the sodium gradients and electrical gradients across the plasma membrane. SGLT1 is the integral membrane protein that couples the transport of Na⁺ to that of glucose or galactose. Fructose passes through the brush border by way of the GLUT5 transport protein. Sugar uptake is powered by sodium and electrical gradients across the membrane. Then, sugars are transported down their concentration gradients via the GLUT2 transport proteins on the basolateral membrane. A basolateral Na⁺/K⁺ pump pumps out Na⁺, creating the gradient that powers the whole process.

Some monosaccharides are taken up into the absorptive cells by a related mechanism, hydrolase transport, in which a glycosidase attached to the membrane hydrolyzes the parent disaccharide (e.g., sucrose, maltose) and also acts as, or is coupled to, the transfer mechanism of the monosaccharide into the absorptive cell.

Once through the epithelium, sugar and amino acid molecules enter the blood by diffusion into the capillaries within the villi. Upon reaching other tissues of the body, sugars and amino acids are transferred by the same types of active transport and facilitated diffusion mechanisms into other body cells.

Active transport
In the mammalian intestine, the sodium-driven transport of amino acids into the absorptive cells takes place via four separate and non-competing cotransport systems. Each system transports just one of four categories of amino acids:

1. The 3 dibasic amino acids (lysine, arginine, and histidine) having two basic amino groups each
2. The diacidic amino acids (glutamate and aspartate), having two carboxyl groups each
3. A special class consisting of glycine, proline, and hydroxyproline
4. The remaining neutral amino acids

Yet another separate transport system exists for dipeptides and tripeptides. Once inside the cell, dipeptides and tripeptides are cleaved into their constituent amino acids by intracellular peptidases. This has the advantage of preventing a concentration buildup of the oligopeptides within the cell, so there is always a large inwardly directed gradient promoting their inward transport.

Special handling of lipids
The digestion products of fats, monoglycerides, fatty acids, and glycerol diffuse through the brush border membrane and are reconstructed within the absorptive cell into triglycerides. They are collected together with phospholipids and cholesterol into tiny droplets termed chylomicrons, about 150 μm in diameter (Figure 15-36). Chylomicrons are coated with a layer of protein, and are loosely contained in vesicles formed by the Golgi apparatus. They are subsequently expelled by exocytosis through fusion of these vesicles with the basolateral membrane of the absorptive cell.

Endocytosis
Transport of sugars and amino acids across the basolateral membranes occurs by facilitated transport, as noted earlier. Some oligopeptides are taken up by absorptive cells through endocytosis. In newborn mammals this process is responsible for the uptake in the intestine of immunoglobulin molecules derived from the mother's milk that escape digestion. Once inside the absorptive cell, nutrients pass through the basolateral membranes of the absorptive cell (see Figure 15-36) into the interior of the villus and then move from the interstitial fluid into the circulatory system.

Blood Transport of Nutrients
From the interstitial fluid of the villus, digestion products enter the blood or the lymphatic circulation (see Figure 15-36). Fishes have relatively simple lymphatic vessels, but these are well developed in all other vertebrates. In humans, about 80% of the chylomicrons, for example, enter the bloodstream via lymph carried in the lymphatic system, a modified ultrafiltrate of blood plasma, while the rest enter the blood directly. The pathway into the lymphatic system begins with the blind central lacteal of the villus (see Figure 15-21A). In humans lymph is returned to the circulation via the thoracic lymph duct. Sugars and amino acids primarily enter the capillaries of the villus, which are drained by venules that lead into the hepatic portal vein. This vein takes the blood from the intestine directly to the
liver. There, under the influence of insulin, much of the glucose is taken up into hepatocytes, and in these cells it is converted to glycogen granules for storage and subsequent release into the circulation after being converted back into glucose. The hormonal regulation of glycogen breakdown, sugar metabolism, fat metabolism, and amino acid metabolism is discussed in Chapter 9.

Water and Electrolyte Balance in the Gut

In the process of producing and secreting their various digestive juices, the exocrine tissues of the alimentary canal and its accessory organs pass a great deal of water and electrolytes into the lumen of the alimentary canal. In humans, this can normally amount to over 8 liters per day (Figure 15-37), or about 1.5 times the total blood volume. Clearly, this quantity of water, not to mention the electrolytes contained within it, cannot be lost from the body with the feces. In fact, nearly all secreted water and electrolytes, along with ingested water, is recovered by uptake in the intestine. Although water is reabsorbed throughout the intestine, most of the reabsorption takes place in the lower part of the small intestine.

The cells in the alimentary canal responsible for water uptake are bound together by tight junctions near their apical borders (see Figure 15-21B), nearly obliterating free paracellular pathways. Tracer studies using deuterium oxide, D₂O, indicate that water leaves the intestinal lumen through channels in the absorptive cell membrane that occupy only 0.1% of the epithelial surface. Flux studies employing isotopically labeled solutes indicate that these
Fluid fluxes occur all along the length of the human alimentary canal. Volumes vary with the condition and body mass of the subject. Values in black, in milliliters, are the amounts of fluid entering the alimentary tract, and those in red are the amounts reabsorbed from the lumen. [Adapted from Madge, 1975.]

Channels exclude water-soluble molecules with molecular weights exceeding 200 g·mol⁻¹. Smaller solute molecules are carried passively along with the water by solvent drag as it flows down its osmotic gradient through hydrated channels.

Because osmotic pressure is the motive force leading to net water movement from the intestinal lumen to the interior of the villus, this movement is entirely passive. In fact, there is no evidence of active transport of water in any living organism—animal, plant, or microbe. The osmotic gradient driving water from the lumen into the villus is set up primarily by the active transport of substances from the lumen into the villus, in particular the transport of salt, sugar, and amino acids. The elevated osmotic pressure within the villus that results from this active transport, especially in the lateral clefts of the epithelium (see Figures 4-48 and 4-49), draws water osmotically from the absorptive cell. This water is then replenished by water entering osmotically across the apical membrane from the lumen.

Most of the absorption of water and electrolytes across the absorptive cell epithelium occurs at or near the tips of the villi. The greater proportion of water absorption at the villus tip results from an elevated concentration of Na⁺ near the upper end of the villus lumen, which decreases with increasing distance from the villus tip. There are two reasons for this concentration gradient. First, most of the active absorption of Na⁺ takes place across absorptive cells located at the tip of each villus. Chloride follows, and NaCl accumulation is therefore greatest at the blind upper end of the villus lumen. Second, the organization of circulation within the villus leads to a further concentration of NaCl at the upper end of the villus lumen because of a countercurrent mechanism (see Spotlight 12-2). Arterial blood flowing toward the tip of the villus picks up Na⁺ and Cl⁻ from NaCl-enriched blood leaving the villus in a descending venule. The "short-circuiting" of NaCl in this manner recirculates and concentrates it in the villus tip, promoting osmotic flow of water from the intestinal lumen into the villus.

The absorption of Na⁺ and Cl⁻ into the villus is enhanced by high concentrations of glucose and certain other hexose sugars in the intestinal lumen, which stimulate sodium-sugar cotransport.

Excessive uptake of water from the lumen across the intestinal wall results in abnormally dry lumen contents (and hence constipation). This situation is normally prevented by an inhibitory action on electrolyte and water uptake by some of the gastrointestinal hormones. Gastrin acts indirectly to inhibit water absorption from the small intestine, while secretin and CCK reduce the uptake of Na⁺, K⁺, and Cl⁻ in the upper jejunum. Bile acids and fatty acids also inhibit the absorption of water and electrolytes.

Unlike water, Ca²⁺ requires a special active transport mechanism for absorption from the gut. The calcium ion is first bound to a calcium-binding protein found in the microvillus membrane and is then transported as a complex into the absorptive cell by an energy-consuming process. From the absorptive cell the Ca²⁺ then passes into the blood. The presence of calcium-binding protein is regulated by the hormone calcitriol, formerly known as 1,25-dihydroxy-vitamin D₃. The release of Ca²⁺ from the absorptive cell into the blood is accelerated by parathyroid hormone.
Vitamin $\text{B}_{12}$, which has a molecular weight of $1357 \text{ g/mol}$, is the largest water-soluble essential nutrient taken up intact across the intestinal lumen in the region of the distal ileum. This highly charged cobalt-containing compound is associated with food protein, to which it is bound as a coenzyme. In the process of absorption, $\text{B}_{12}$ transfers from the dietary protein to a mucoprotein known as intrinsic factor (or hemopoietic factor) that is produced by the $\text{H}^+$-secreting parietal cells of the stomach. Since $\text{B}_{12}$ is essential for the synthesis and maturation of red blood corpuscles, pernicious anemia occurs when $\text{B}_{12}$ absorption is prevented by interference with its binding to intrinsic factor. Some tapeworms "steal" $\text{B}_{12}$ in the intestine of the host by producing a compound that removes it from intrinsic factor, making it unavailable to the host but available to the tapeworm.

**NUTRITIONAL REQUIREMENTS**

Whatever the form of food capture, ingestion, and digestion, all animals must acquire an appropriate variety and amount of nutritive substances, as we will now consider. **Nutrients** are substances that serve as sources of metabolic energy and as raw material for growth, repair of tissues, and production of gametes. Nutrients also include essential trace elements such as iodine, zinc, and other metals that may be required in extremely small quantities. There is wide variation between the nutritional needs of different species. Within a species, nutritional needs vary according to phenotypic differences in body size and composition and activity, and also with age, sex, and reproductive state. A gravid (egg-bearing) or pregnant female may require more nutrients than a male, while a male producing sperm may have greater nutritive needs than one that is not producing sperm. Regardless of reproductive state, a small animal requires more food for energy per gram of body weight than does a larger animal, because its metabolic rate per unit body weight is higher. Similarly, an animal with a high body temperature requires more food, to satisfy greater energy needs, than does an animal with lower body temperature. (The energetics of temperature, size, and other factors are discussed in Chapter 16).

**Energy Balance**

A balanced nutritional state exists when an animal has sufficient food intake of all nutrients necessary for long-term growth and maintenance. The nutritional requirements include (1) sufficient sources of energy to power all body processes, (2) enough protein and amino acids to maintain a positive nitrogen balance (i.e., to avoid net loss of body proteins), (3) enough water and minerals to compensate for their loss or incorporation into body tissues, and (4) those essential amino acids and vitamins not synthesized within the body.

Energy balance requires that caloric intake over a given period of time equal the number of calories consumed for tissue maintenance and repair and for work (metabolic and otherwise), plus the production of body heat in birds and mammals. Thus,

\[
\text{caloric intake} = \text{caloric output} = \text{calories consumed by tissues} + \text{heat produced}
\]

Insufficient intake of calories can be temporarily offset by using stores of fat and carbohydrates or proteins within tissues, but this produces a resultant loss of body weight. Conversely, caloric intake in excess of what is required for energy balance will result in increased storage of body fat, as in the large fat stores accumulated before long migrations in migratory birds or laid down by mammals before onset of hibernation.

Animals differ in their abilities to synthesize the substances fundamental to maintenance and growth. Thus, for a given animal species, certain cofactors (Zn, I etc.) or building blocks (amino acids, etc.) essential for important biochemical reactions or for the production of tissue molecules may be required from food sources simply because those substances cannot be produced by the animal itself. Such items are known as essential nutrients.

**Nutrient Molecules**

A wide variety of molecules serve as nutrient molecules, including water, proteins and amino acids, carbohydrates, fats and lipids, nucleic acids, inorganic salts, and vitamins.

**Water**

Of all the constituents of animal tissue, none is more pervasively important to living tissue than water. This unique and marvelous substance can constitute 95% or more of the weight of some animal tissues. It is replenished in most animals by drinking (see Chapter 12) and by ingestion with food. Some marine and desert animals depend almost entirely on "metabolic water"—water produced during the oxidation of fats and carbohydrates—to replace water lost by evaporation, defecation, and urination (see Chapter 16).

**Proteins and amino acids**

Proteins are used as structural components of tissues and as enzymes. They can also be utilized as energy sources if first broken down to amino acids (see Chapter 3). The proteins of animal tissues are composed of about 20 different amino acids. The ability to synthesize amino acids differs among species. Those amino acids that cannot be synthesized by an animal, but are required for synthesis of essential proteins, are the so-called essential amino acids for that animal. Recognition of this requirement has been of enormous economic significance in the poultry industry. The rate of growth of chickens at one time was limited by too small a proportion of a few essential amino acids in the grain diet they were provided. Supplementing the diet with these amino acids allowed full utilization of the other amino acids present in the feed, greatly increasing the rate of
protein synthesis and hence the rate of poultry growth and egg laying. Microbiologists artificially induce this limiting condition by genetically engineering microbes that require a specific amino acid (e.g., lysine) not normally found in their environment. Thus, the microbes will grow only in an environment enriched with the amino acid, serving as a safeguard preventing their spread through normal populations.

**Carbohydrates**

Carbohydrates are used primarily as immediate (glucose 6-phosphate) or stored (glycogen) sources of chemical energy. However, they may also be converted to metabolic intermediates or to fats (see Chapter 3). Conversely, proteins and fats can be converted by most animals into carbohydrates. The major sources of carbohydrate are the sugars, starches, and cellulose found in plants and the glycogen stored in animal tissues.

**Lipids**

Lipid (fat) molecules are especially suitable as concentrated energy reserves. Each gram of fat provides over 2 times as much caloric energy as a gram of protein or carbohydrate. Consequently, lipids can store significantly more chemical energy per unit volume of tissue. Fat is commonly stored by animals for periods of caloric deficit, as during hibernation, when energy expenditure exceeds energy intake. Lipids are

<table>
<thead>
<tr>
<th>TABLE 15-3</th>
<th>Some mammalian vitamins</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vitamin</strong></td>
<td><strong>Major dietary sources; solubility</strong></td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Carotene (A)</td>
<td>Egg yolk, green or yellow vegetables, fruits; FS</td>
</tr>
<tr>
<td>Calciferol (D&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>Fish oils liver; FS</td>
</tr>
<tr>
<td>Tocopherol (E)</td>
<td>Green leafy vegetables, meat, milk, eggs, butter; FS</td>
</tr>
<tr>
<td>Napthoquinone (K)</td>
<td>Synthesis by intestinal flora, liver, green leafy vegetables; FS</td>
</tr>
<tr>
<td>Thiamine (B&lt;sub&gt;1&lt;/sub&gt;)</td>
<td>Brain, liver, kidney, heart, whole grains, nuts, beans, potatoes</td>
</tr>
<tr>
<td>Riboflavin (B&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>Milk, eggs, lean meat, liver, whole grains; WS</td>
</tr>
<tr>
<td>Niacin</td>
<td>Lean meat, liver, whole grains; WS</td>
</tr>
<tr>
<td>Cyanocobalamin (B&lt;sub&gt;12&lt;/sub&gt;)</td>
<td>Liver, kidney, brain, fish, eggs, bacterial synthesis in gut; WS</td>
</tr>
<tr>
<td>Folic acid (folacin, pteroylglutamic acid)</td>
<td>Meats; WS</td>
</tr>
<tr>
<td>Pyridoxine (B&lt;sub&gt;6&lt;/sub&gt;)</td>
<td>Whole grains, traces in many foods; WS</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>Many foods; WS</td>
</tr>
<tr>
<td>Biotin</td>
<td>Egg yolk, tomatoes, liver, synthesis by flora of GI tract; WS</td>
</tr>
<tr>
<td>Ascorbic acid (C)</td>
<td>Citrus; WS</td>
</tr>
</tbody>
</table>

*FS = fat-soluble; WS = water-soluble

*Most vitamins have numerous functions. Listed are a mere sampling.
also important in certain tissue components such as plasma membranes and other membrane-based organelles of the cell and the myelin sheaths of axons. The fatty molecules or lipids include fatty acids, monoglycerides, triglycerides, sterols, and phospholipids.

**Nucleic acids**

Although nucleic acids are essential for the genetic machinery of the cell, all animal cells appear to be capable of synthesizing them from simple precursors. Thus, the intake of intact nucleic acids is not necessary from a nutritional perspective.

**Inorganic salts**

Some chloride, sulfate, phosphate, and carbonate salts of the metals calcium, potassium, sodium, and magnesium are important constituents of intra- and extracellular fluids. Calcium phosphate occurs as hydroxyapatite [Ca$_{10}$(PO$_4$)$_6$(OH)$_$_$_2$], a crystalline material that lends hardness and rigidity to the bones of vertebrates and the shells of mollusks. Iron, copper, and other metals are required for redox reactions (as cofactors) and for oxygen transport and binding (hemoglobin, myoglobin). Many enzymes require specific metal atoms to complete their catalytic functions. Animal tissues need moderate quantities of some ions (Ca, P, K, Na, Mg, S, and Cl) and trace amounts of others (Mn, Fe, I, Co, Cu, Zn, and Se).

**Vitamins**

Vitamins are a diverse and chemically unrelated group of organic substances that generally are required in small quantities primarily to act as cofactors for enzymes. Some vitamins important in human nutrition are listed in Table 15-3, along with their diverse functions. Detailed nutritional vitamin requirements are known primarily for domesticated animals grown for their meat, eggs, or other products. Very little is known about the vitamins involved in the metabolism of lower vertebrates and especially invertebrates.

The ability to synthesize different vitamins differs between species, and those essential vitamins that an animal cannot produce itself must be obtained from other sources, primarily from plants but also from dietary animal flesh or from intestinal microbes. Ascorbic acid (vitamin C) is synthesized by many animals, but not by humans, who acquire it mainly from citrus fruits. Scurvy, a condition of ascorbic acid deficiency in humans, was common on board ships before the British admiralty instituted the use of citrus fruit—especially limes—to supplement the diet of the crews. Their use of limes led to the general term limey to describe the English. Humans also are unable to produce vitamins K and B$_{12}$, which are produced by intestinal bacteria and then absorbed for distribution to the tissues. Fat-soluble vitamins such as A, D$_3$, E, and K are stored in body fat deposits. Water-soluble vitamins such as ascorbic acid are not stored in the body, however, and so must be ingested or produced continually to maintain adequate levels.

**SUMMARY**

All heterotrophic organisms acquire carbon compounds of moderate to high energy content from the tissues of other plants and animals. The chemical energy contained in these compounds originally was converted from radiant energy into chemical energy trapped in sugar molecules by photosynthesizing autotrophs. Subsequent synthetic activity by autotrophs and heterotrophs converts these simple carbon compounds into more complex carbohydrates, fats, and proteins.

Animals obtain food in many different ways, including absorption through the body surface in some aquatic or marine species, endocytosis in microorganisms, filter feeding, mucus trapping, sucking, biting, and chewing. Once ingested, the food may be temporarily stored, as in a crop or rumen, or immediately subjected to digestion. Digestion consists of the enzymatic hydrolysis of large molecules into their monomeric building blocks. In multicellular animals, this takes place extracellularly in an alimentary canal. Digestive hydrolysis occurs only at low-energy bonds, most of the chemical energy of foodstuffs being conserved for intracellular energy metabolism once the products of digestion have been assimilated into the animal's tissues. Stepwise intracellular oxidations by coupled reactions then lead to a controlled release of chemical bond energy and material for cell growth and functioning.

Digestion in vertebrates begins in a region of low pH, the stomach, and proceeds to a region of higher pH, the small intestine. Proteolytic enzymes are released as proenzymes, orzymogens, which are inactive until a portion of the peptide chain is removed by digestion. This procedure avoids the problem of proteolytic destruction of the enzyme-producing cells that store and secrete thezymogen granules containing the proenzyme. Other exocrine cells secrete digestive enzymes (e.g., carbohydrases and lipases), mucin, or electrolytes such as HCl or NaHCO$_3$.

The motility of the vertebrate digestive tract depends on the coordinated activity of longitudinal and circular layers of smooth muscle. Peristalsis occurs when a ring of circular contraction proceeds along the gut preceded by a region in which the circular muscles are relaxed. The parasympathetic innervation stimulates motility, whereas the sympathetic innervation inhibits motility.

The motility of smooth muscle as well as the secretion of digestive juices is under fine neural and endocrine control. All gastrointestinal hormones are peptides, and many of them also function as neuropeptides in the central nervous system, where they act as transmitters or short-range neurohormones. Both direct activation by food in the gut and neural activation stimulate the endocrine cells of the gastrointestinal mucosa that secrete peptide hormones. These hormones are active in either stimulating or inhibiting the activity of the various kinds of exocrine cells in the gut that produce digestive enzymes and juices.

Digestion products are taken up by the absorptive cells of the intestinal mucosa and transferred to the lymphatic and circulatory systems. The absorptive surface, in effect
consisting of a continuous membrane sheet formed by the apical membranes of the myriad absorptive cells joined by tight junctions, is greatly increased in area by virtue of microvilli, the microscopic evaginations of the apical membrane. The absorptive cells cover larger finger-like villi that reside on convoluted folds and ridges in the wall of the intestine, further increasing the surface area.

The process of terminal digestion takes place in the brush border, formed by the microvilli and the glycocalyx, that covers the apical membrane. Here short-chain sugars and peptides are hydrolyzed into monomeric residues before membrane transport takes place. Transport of some sugars can occur by facilitated diffusion, which requires a membrane transport protein but no metabolic energy. Most sugars and amino acids require energy expenditure for adequate rates of absorption. An important transport mechanism for these substances is cotransport with \( \text{Na}^+ \), utilizing a common membrane protein and the potential energy of the electrochemical gradient driving \( \text{Na}^+ \) from the lumen into the cytoplasm of the absorptive cell. Endocytosis plays a role in the uptake of small polypeptides and, rarely, of larger proteins, such as immunoglobulin in newborn animals. Fatty substances enter the absorptive cell by simple diffusion across the cell membrane.

Water and electrolytes enter the alimentary canal as constituents of digestive juices, but these quantities are nearly all recovered by active uptake of solutes by the intestinal mucosa. Active transport of solutes from the intestinal lumen results in the passive osmotic movement of water from the lumen into the cells and eventually back into the bloodstream. Without such recycling of electrolytes and water, the digestive system would impose a lethal osmotic load on the animal.

**REVIEW QUESTIONS**

1. Define the terms *digestion*, *absorption*, *assimilation*, and *nutrition*.
2. In what way is Bernoulli's effect significant to the feeding of a sponge?
3. Cite two unrelated examples of proteins produced specifically for the purpose of obtaining and utilizing food.
4. What is an essential amino acid?
5. Explain why it would be inadvisable for the digestive system to fragment amino acids, hexose sugars, and fatty acids into still smaller molecular fragments, even though doing so might facilitate absorption.
6. Explain why proteolytic enzymes fail to digest the exocrine cells in which they are produced and stored before release.
7. Give several examples of symbiotic microorganisms in alimentary canals, and explain how they benefit the host.
8. State two adaptive advantages of the digastric stomach. Since it has three or four chambers, why is it referred to as digastric?
9. Explain how bile aids the digestive process even though it contains little or no enzyme.
10. Outline the autonomic innervation of the intestinal wall, explaining the organization and functions of sympathetic and parasympathetic innervation.
11. How is \( \text{HCl} \) produced and secreted into the stomach by parietal cells?
12. Compare and contrast endocrine and exocrine systems. What do they have in common?
13. What is meant by secondary modification of an exocrine secretion?
14. Describe the roles of gastrin, secretin, and cholecystokinin in mammalian digestion.
15. Why are some gastrointestinal hormones also classified as neuropeptides? Give examples.
16. Explain what is meant by the cephalic, the gastric, and the intestinal phases of gastric secretion. How are they regulated?
17. How are amino acids and some sugars transported against a concentration gradient from intestinal lumen into epithelial cells?
18. Why is the countercurrent principle important in the removal of the water from the intestinal lumen?
19. How is pernicious anemia related to intestinal function?

**SUGGESTED READINGS**


