Protein metabolism

The transformation and fate of food proteins from their ingestion and assimilation to the elimination of their excretion products. Proteins are polymers of α-amino acids that are connected by peptide bonds. An average polypeptide chain in a protein contains about 500 amino acid residues. Insulin is a small protein with 51 amino acid residues. Titin, which is the largest known human protein, contains 34,350 residues. A dipeptide contains two amino acid residues, an oligopeptide contains several, and a polypeptide contains many amino acid residues.

Proteins are the chief structural and functional components of all living organisms. Their importance was recognized by scientists in the mid nineteenth century who coined the name from the Greek protein, meaning first or primary. Proteins are the main building blocks of the cells, tissues, organs, and systems of the body. Proteins of one species differ from those of another species and, within a single animal, proteins of muscle differ from those of the brain, kidney, liver, and other organs. See AMINO ACIDS; METABOLISM; PEPTIDE; PROTEIN.

Functions of protein. A 70-kg (154-lb) person contains 10–12 kg (22–26 lb) of protein. After water, proteins are the most abundant component of human beings, other animals, and bacteria. Muscle accounts for about half of the mass of human protein. Collagen is the most abundant protein in animals and is responsible for the strength of the connective tissue found in muscle and tendons. Actin is a protein that occurs in nearly all animal cells and is responsible for cell motility. Myosin is the chief contractile protein of muscle. Hemoglobin is the main protein of red blood cells and is responsible for oxygen transport from the lungs to the tissues. Many hormones, including insulin, are protein in nature. Enzymes that catalyze the myriad reactions in the breakdown of glucose and fatty acids in intermediary metabolism are proteins. Moreover, the adenosine triphosphate synthase that mediates the conversion of adenosine diphosphate and phosphate into ATP, the common currency of energy exchange in all living organisms, is a protein. See ADENOSINE TRIPHOSPHATE (ATP); COLLAGEN; ENERGY METABOLISM; ENZYME; HEMOGLOBIN; MUSCLE; MUSCLE PROTEINS.

Protein turnover. Body proteins are continually broken down and resynthesized, a process called turnover. There are two main pathways that participate in intracellular protein degradation: the ubiquitin-proteasome pathway and the lysosomal pathway. The first step in the former pathway involves the joining of ubiquitin molecules with lysine residues in the target protein in a process that requires ATP as an energy source. Ubiquitin is a small protein containing 76 amino acid residues. Following the attachment of several ubiquitin molecules to the target protein, the complex interacts with the proteasome, a large multicomponent complex that degrades the target protein into peptides while liberating ubiquitin, which is then recycled. Proteasomes are located in the soluble portion of the cell, or the cytosol. The proteasomal pathway is responsible for degrading proteins that are damaged because of oxidative stress or are no longer needed owing to changing metabolic needs. The lysosome is a membrane-enclosed vesicle inside the cell that contains a variety of proteolytic enzymes and operates under acidic conditions. It degrades proteins that combine with receptors found on the plasma membrane of the cell and that are subsequently taken up by the cell where they fuse with lysosomes. See CELL (BIOLOGY); LYSOSOME.

Normal adults are in nitrogen balance; nitrogen intake equals the amount of excreted nitrogen. Proteins, which are made up of amino acid residues, are the main nitrogen-containing compounds in animals. Growing animals are in positive nitrogen balance; nitrogen intake exceeds nitrogen excretion. During starvation, animals are in negative nitrogen balance; nitrogen excretion exceeds nitrogen intake. People with infections, traumatic injuries (such as from automobile accidents), and major burns also exhibit negative nitrogen balance. Under these conditions, tissue and protein breakdown occurs more rapidly than protein synthesis. Even in the absence of trauma, surgery itself results in accelerated protein breakdown, possibly as a result of increased adrenal steroid (glucocorticoid) production and action. When these conditions are accompanied by reduced food intake, which typically occurs in people with these maladies, this imbalance results in wasting and an impaired immune response. During the healing phase of these illnesses, people exhibit positive nitrogen balance.

Besides the breakdown of endogenous proteins, ingested proteins contribute to the amino acid pool. Protein is digested to amino acids in the stomach and small intestine. These amino acids are absorbed and undergo a degree of metabolic interconversion prior to release into the portal vein, which takes them to the liver. Many of the amino acids are taken up by the liver, and the remainder circulates to the other tissues and organs in the body. The newly absorbed amino acids equilibrate with amino acids in cells that result from protein breakdown.

The amino acid pool serves as the source of precursors for new protein synthesis and for the conversion to other metabolites. Protein synthesis occurs on the ribosome in a messenger ribonucleic acid–dependent process. About 50 grams of muscle protein, 12 g of albumin, 2 g of fibrinogen, 3 g of γ-globulin (antibodies), 8 g of hemoglobin, 30 g of gastrointestinal epithelial protein, and 25 g of enzymes and mucins in the salivary glands, stomach, intestine, and pancreas are synthesized and degraded in the body daily. For normal human adults, about 250 g of protein is degraded and synthesized each...
Foods of plant origin can be more difficult to digest because the amino acid tryptophan, is not a high-quality protein. Gelatin, an animal protein that lacks the essential amino acids of high-quality protein, their essential amino acid content meets the human need for protein synthesis. Their essential amino acids complement each other. For example, legumes such as beans are high in lysine percentage of methionine. Thus, if beans and rice are eaten together, their joint amino acid composition is more complete and as a source of various other body constituents derived from amino acids. Twenty amino acids are required for protein synthesis. The amino acids of proteins fall into two nutritional categories: essential or indispensable and nonessential or dispensable.

The essential amino acids cannot be synthesized by the body or cannot be synthesized in adequate quantities and therefore must be taken in the diet, while the nonessential amino acids can be synthesized by the body in sufficient quantities to sustain health. The 20 genetically encoded amino acids required for protein synthesis are as follows:

<table>
<thead>
<tr>
<th>Essential</th>
<th>Nonessential</th>
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<tbody>
<tr>
<td>1. Histidine</td>
<td>1. Alanine</td>
</tr>
<tr>
<td>2. Isoleucine</td>
<td>2. Arginine</td>
</tr>
<tr>
<td>3. Leucine</td>
<td>3. Asparagine</td>
</tr>
<tr>
<td>4. Lysine</td>
<td>4. Aspartate</td>
</tr>
<tr>
<td>5. Methionine</td>
<td>5. Cysteine</td>
</tr>
<tr>
<td>6. Phenylalanine</td>
<td>6. Glutamate</td>
</tr>
<tr>
<td>7. Threonine</td>
<td>7. Glutamine</td>
</tr>
<tr>
<td>8. Tryptophan</td>
<td>8. Glycine</td>
</tr>
<tr>
<td>10. Serine</td>
<td>10. Phenylalanine</td>
</tr>
<tr>
<td>11. Tyrosine</td>
<td>11. Methionine</td>
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</tbody>
</table>

The relative proportions of the 20 amino acids vary in different foods. Foods of animal origin, including meat, fish, eggs, milk, and dairy products, are sources of high-quality protein. Their essential amino acid content meets the human need for protein synthesis. Gelatin, an animal protein that lacks the essential amino acid tryptophan, is not a high-quality protein.

Foods of plant origin can be more difficult to digest and are of lower quality. Plant proteins contain less lysine, methionine, and tryptophan than animal proteins, and these amino acids thus limit the synthesis of body proteins. However, a varied vegetarian diet can readily fulfill human protein requirements if the protein-containing foods are balanced such that their essential amino acids complement each other. For example, legumes such as beans are high in lysine and low in methionine, while rice has a higher percentage of methionine. Thus, if beans and rice are eaten together, their joint amino acid composition will complement each other and provide a higher-quality diet than would either food alone. Traditional food patterns in various cultures have made good use of protein complementarity.

The recommended daily protein intake is 0.8 g/kg body weight for adults, for example, 56 g for a 70-kg (154-lb) person. This amount of protein is easily obtained in a judicious diet: for example, one cup of dry cereal with a cup of low-fat milk for breakfast, a peanut butter sandwich and an 8 oz glass of milk for lunch, and 4 oz of fish, a cup of rice, and cup of split peas amount to 70 g of protein, enough for the average adult. A daily 2000 calorie diet consisting of 6 oz of grains, 2 1/2 cups of vegetables, 2 cups of fruit, 3 cups of milk, and 5 1/2 oz of meat and beans contains about 90 g of protein. The recommended daily protein intake is greater for infants, for growing children, and for women during pregnancy and during nursing. See NUTRITION.

Inadequate protein intake affects health. Kwashiorkor, also called protein malnutrition, is a condition in young children with adequate caloric but inadequate protein intake. Kwashiorkor is most often encountered in developing countries in which the diet is high in starch and low in protein. Signs and symptoms include reddish skin, abdominal swelling, weakness, and nervous irritability. Marasmus results from both insufficient protein and caloric intake in infants under conditions of famine. Marasmus is characterized by growth retardation (in weight more than in height), emaciation, and generalized wasting of muscle and subcutaneous fat. Ribs, joints, and facial bones are prominent owing to the loss of muscle and fat. See MALNUTRITION.

**Digestion of protein.** Protein digestion is initiated in the stomach and completed in the duodenum of the small intestine. The main proteolytic enzyme of the stomach is pepsin, which is secreted by the chief cells in an inactive form called pepsinogen. The hydrogen ion concentration in the stomach is thousands of times greater than that of the blood or in cells; stomach acid is secreted by parietal cells. The conversion of precursor pepsinogen to active pepsin is accelerated by stomach acid and by active pepsin. The activation process involves the hydrolytic removal of an inhibitory 44-amino-acid peptide from pepsinogen. Pepsin preferentially hydrolyzes peptide bonds adjacent to an aromatic amino acid (phenylalanine, tyrosine, tryptophan), and pepsin requires an acid medium in which to function. Stomach acid also unfolds, or denatures, digested proteins and increases their susceptibility to digestion. See DIGESTIVE SYSTEM; PEPsin.

The acidic stomach contents, which contain partially degraded proteins, are discharged as chyme (semifluid, partially digested food mass) into the slightly alkaline fluid in the duodenum of the small intestine. The pancreatic juice released into the duodenum contains several digestive enzymes that are secreted as zymogens (inactive enzyme precursors) including trypsinogen, chymotrypsinogen, procarboxypeptidase, and proelastase. The activation of trypsinogen involves its proteolytic cleavage by yet another enzyme secreted by the pancreas, namely enteropeptidase, to produce active trypsin. Trypsin, in turn, catalyzes the formation of chymotrypsin, carboxypeptidase, and elastase from their inactive zymogen precursors. In each of these processes, certain peptide bonds are broken to yield the active enzymes. The cells lining the small intestine contain
Protein metabolism

Tissue protein synthesis. Turnover of tissue proteins occurs in the adult animal in nitrogen balance, with no net gain of body nitrogen. Body proteins are continually undergoing synthesis and degradation, but the total body protein remains relatively constant in quantity. The rate of replacement varies greatly for different tissues. In humans, it is estimated that the average half-life of total body protein is 80 days; that of lung, brain, bone, and muscle together is about 160 days, while that of liver and serum proteins is only 10 days.

Plasma protein synthesis. The liver is the major organ for plasma protein synthesis. It synthesizes albumin, the predominant blood plasma protein. The liver also synthesizes fibrinogen, one of the main components of blood clots. The plasma proteins offer the most readily available test material in determining the protein nutritional status of an individual. A blood sample is easily drawn, and estimation of the different plasma proteins is now a standard procedure. Plasma proteins exhibit fluctuations in conditions associated with inadequate intake or abnormal protein metabolism. The serum albumin level is the traditional standard for nutritional assessment. Protein deprivation diminishes the albumin content to levels below 30 g/liter, whereas the normal levels are 35–70 g/liter. See ALBUMIN; FIBRINOGEN; LIVER.

Blood proteins have numerous physiological functions. Albumin is a major factor in the regulation of blood volume by counteracting fluid expulsion into tissues as a result of hydrostatic blood pressure. Fibrinogen is the chief protein that results in blood clot formation. The globulins include proteins that transport iron, copper, cholesterol, cholesteryl esters, and other lipids. Antibodies, which are synthesized by cells of the immune system, form part of the globulin fraction of plasma proteins. Antibodies defend the body against various pathogenic bacteria and viruses. Protein hormones such as insulin and glucagon, which form a tiny but important fraction of plasma protein, are synthesized in endocrine glands. See BLOOD; HORMONE.

Amino acid derivatives. Selected components of the general amino acid pool serve as precursors for numerous nonprotein organic compounds. For example, glycine is converted into heme, an organic component found in hemoglobin. Glycine and aspartate serve as building blocks for the nucleotide bases that occur in deoxyribonucleic acid and ribonucleic acid. Both histidine, which is derived from histidine, and serotonin, which is derived from tryptophan, function as signaling molecules. Tyrosine is converted to norepinephrine, a neurotransmitter, in selected nerve cells and to the melanin pigment in skin cells. See DEOXYRIBONUCLEIC ACID (DNA); RIBONUCLEIC ACID (RNA).

Nitrogen excretion. Excess amino acids in cells, tissues, and organs undergo metabolic degradation. The amino group is lost by transamination or deamination (hydrolysis of amino compounds, removing the amino group). About 85% of excess nitrogen is excreted as urea in the urine. Urea [C(=O)(NH₂)₂] is produced in the liver by the Krebs-Henseleit cycle.

Utilization of absorbed amino acids. Protein homeostasis differs from that of carbohydrate and lipid because protein lacks a storage form. Carbohydrate is stored as glycogen, and lipids are stored as triacylglycerol or triglyceride. The absorbed amino acids become part of the amino acid pool of the body. From these amino acids, new tissue proteins are synthesized to meet body needs. To serve the needs for protein synthesis, all of the 20 genetically encoded amino acids must be present. The absence of any amino acid retards the rate of protein synthesis. See CARBOHYDRATE; CARBOHYDRATE METABOLISM; LIPID; LIPID METABOLISM.
The overall process is

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\text{Ammonia} + \text{carbon dioxide} + \text{aspartate} + 3\text{ATP} + 2\text{H}_2\text{O} \rightarrow \\
\text{urea} + \text{fumarate} + 2\text{ADP} + 2\text{phosphate} \\
+ \text{adenosine monophosphate} + \text{pyrophosphate}
\]

The carbon and oxygen are derived from carbon dioxide, one nitrogen is derived from ammonia, and the second nitrogen is derived from the amino acid aspartate. The process requires the expenditure of three ATP molecules. Ornithine, a nonprotein amino acid, is required for urea biosynthesis; it is continuously regenerated and recycled for additional urea synthesis: About 2% of nitrogen in the

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\text{Arginine} + \text{H}_2\text{O} \rightarrow \text{urea} + \text{ornithine}
\]

urine is excreted as uric acid, which is derived from DNA, RNA, and nucleotides. A small amount of nitrogen is eliminated in the feces. The remainder is secreted in approximately equal amounts as ammonia, amino acids, and creatinine. Creatinine is a breakdown product of muscle creatine phosphate, an energy-rich storage compound. The residual carbon portions of the amino acids are further metabolized by pathways common to the other major foodstuffs—carbohydrates and fats. Proteins account for about 15% of the calories consumed in an average diet. See NITROGEN EXCRETION; UREA.

Robert Roskoski, Jr.; David M. Greenberg


**Proterozoic**

A major division of geologic time spanning from 2500 to 545 million years before present (Ma). The beginning of Proterozoic time is an arbitrary boundary that roughly coincides with the transition from a tectonic style dominated by extensive recycling of the Earth’s continental crust to a style characterized by preservation of the crust as stable continental platforms. The end of the Proterozoic coincides with the Precambrian-Cambrian boundary, which is formally defined on the basis of the first appearance of diverse eocoeomate invertebrate animals. Proterozoic Earth history testifies to several remarkable biogeochemical events, including the formation and dispersal of the first supercontinent, the maturation of life and evolution of animals, the rise of atmospheric oxygen, and the decline of oceanic carbonate saturation (see table). Tremendous iron and lead-zinc mineral deposits occur in Proterozoic rocks, as do the first preserved accumulations of oil and gas. See CAMBRIAN; PRECAMBRIAN.

**Tectonics.** Many of the Earth’s Archean cratons are blanketed by little-deformed sequences of Proterozoic sedimentary rocks, which indicate that vigorous recycling of the Earth’s crust, characteristic of Archean time, had slowed markedly by the beginning of Proterozoic time. This decrease in crustal recycling is attributed to the development of thick continental roots, which stabilized the cratons, and the decrease in heat that was escaping from the Earth’s interior, believed to drive thermal convection in the Earth’s mantle and recycling of the crust. The sedimentary record that is present atop the major cratons is sufficiently continuous and well enough preserved that a rather detailed accounting of major events in Proterozoic Earth history is possible.

Most of the Earth’s Archean cratons appear to have participated in the formation of a supercontinent in Mesoproterozoic time, about 1200 Ma. This supercontinent, called Rodinia, was the first for which there is now substantial evidence. Rodinia seems to have assembled with the North American craton (Laurentia) at its center. Rodinia persisted until the latest part of the Neoproterozoic, about 600 Ma, when it fragmented and ejected Laurentia in the process. Almost immediately, the other cratons reassembled to form the supercontinent of Gondwanaland, whose assembly was complete by about 450 Ma. See ARCHEAN; CONTINENTS, EVOLUTION OF; EARTH, CONVECTION IN; EARTH, HEAT FLOW IN; EARTH CRUST; EARTH INTERIOR; PLATE TECTONICS.

**Environment.** Giant iron oxide deposits were formed by precipitation from seawater about 2000 Ma. These iron formations coincide with the first appearance of red, oxidized sedimentary rocks formed in terrestrial river environments and with the retention of ferric iron in soil horizons. During most of Paleoproterozoic time the oceans and atmosphere were reducing and ferrous iron was abundant in seawater. When photosynthetic microbes produced oxygen in shallow waters, the ferrous iron became oxidized to ferric iron, which is highly insoluble; and the ferric iron precipitated and settled to the sea floor, making the giant iron formations. The iron formations were produced until the iron sink was depleted about 2000 Ma, whereupon oxygen was free to accumulate in the atmosphere and shallow ocean. See ATMOSPHERE, EVOLUTION OF.

The partial pressure of carbon dioxide on the early Earth was very high. During Proterozoic time, much of the mass of carbon shifted from the ocean and atmosphere to the solid Earth. Enormous volumes of limestone [CaCO₃] and dolostone [CaMg(CO₃)₂] were deposited and testify to this shift. These carbonate deposits show significant textural variations, indicating that in the Paleoproterozoic supersaturation with respect to calcium carbonate was very high but declined markedly during the Mesoproterozoic. Neoproterozoic levels of calcium carbonate saturation were similar to those documented for