Ivan Applebod returned to his doctor for a second visit. His initial efforts to lose weight had failed dismally. In fact, he now weighed 270 lb, an increase of 6 lb since his first visit 2 months ago (see Chapter 1). He reported that the recent death of his 45-year-old brother of a heart attack had made him realize that he must pay more attention to his health. Because

Hormones are compounds that are synthesized by the endocrine glands of the body. They are secreted into the bloodstream and carry messages to different tissues concerning changes in the overall physiologic state of the body or the needs of tissues.

Glucose

Oxidation
Energy

Storage
Glycogen
TAG

Synthesis
Many compounds

Amino acids

Protein synthesis

Synthesis of nitrogen-containing compounds

Oxidation
Energy

Fats

Storage
TAG

Oxidation
Energy

Synthesis
Membrane lipids

**THE WAITING ROOM**

Ivan Applebod returned to his doctor for a second visit. His initial efforts to lose weight had failed dismally. In fact, he now weighed 270 lb, an increase of 6 lb since his first visit 2 months ago (see Chapter 1). He reported that the recent death of his 45-year-old brother of a heart attack had made him realize that he must pay more attention to his health. Because

**2 The Fed or Absorptive State**

*The Fed State.* During a meal, we ingest carbohydrates, lipids, and proteins, which are subsequently digested and absorbed. Some of this food is oxidized to meet the immediate energy needs of the body. The amount consumed in excess of the body’s energy needs is transported to the fuel depots, where it is stored. During the period from the start of absorption until absorption is completed, we are in the fed, or absorptive, state. Whether a fuel is oxidized or stored in the fed state is determined principally by the concentration of two endocrine hormones in the blood, insulin and glucagon.

**Fate of Carbohydrates.** Dietary carbohydrates are digested to monosaccharides, which are absorbed into the blood. The major monosaccharide in the blood is glucose (Fig 2.1). After a meal, glucose is oxidized by various tissues for energy, enters biosynthetic pathways, and is stored as glycogen, mainly in liver and muscle. Glucose is the major biosynthetic precursor in the body, and the carbon skeletons of most of the compounds we synthesize can be synthesized from glucose. Glucose is also converted to triacylglycerols. The liver packages triacylglycerols, made from glucose or from fatty acids obtained from the blood, into very-low-density lipoproteins (VLDL) and releases them into the blood. The fatty acids of the VLDL are mainly stored as triacylglycerols in adipose tissue, but some may be used to meet the energy needs of cells.

**Fate of Proteins.** Dietary proteins are digested to amino acids, which are absorbed into the blood. In cells, the amino acids are converted to proteins or used to make various nitrogen-containing compounds such as neurotransmitters and heme. The carbon skeleton may also be oxidized for energy directly, or converted to glucose.

**Fate of Fats.** Triacylglycerols are the major lipids in the diet. They are digested to fatty acids and 2-monooacylglycerols, which are resynthesized into triacylglycerols in intestinal epithelial cells, packaged in chylomicrons, and secreted by way of the lymph into the blood. The fatty acids of the chylomicron triacylglycerols are stored mainly as triacylglycerols in adipose cells. They are subsequently oxidized for energy or used in biosynthetic pathways, such as synthesis of membrane lipids.

---

Fig. 2.1. Major fates of fuels in the fed state.
Mr. Applebod’s brother had a history of hypercholesterolemia and because Mr. Applebod’s serum total cholesterol had been significantly elevated (296 mg/dL) at his first visit, his blood lipid profile was determined, his blood glucose level was measured, and a number of other blood tests were ordered. (The blood lipid profile is a test that measures the content of the various triacylglycerol- and cholesterol-containing particles in the blood.) His blood pressure was 162 mm Hg systolic and 98 mm Hg diastolic or 162/98 mm Hg (normal = 140/90 mm Hg or less). His waist circumference was 48 inches (healthy values for men, less than 40; for women, less than 35).

I. DIGESTION AND ABSORPTION

After a meal is consumed, foods are digested (broken down into simpler components) by a series of enzymes in the mouth, stomach, and small intestine. The products of digestion eventually are absorbed into the blood. The period during which digestion and absorption occur constitutes the fed state (Fig. 2.2)

**Fig. 2.2.** The fed state. The circled numbers indicate the approximate order in which the processes occur. TG = triacylglycerols; FA = fatty acid; AA = amino acid; RBC = red blood cell; VLDL = very-low-density lipoprotein; I = insulin; ◦ = stimulated by.
Digestive enzymes convert complex sugars to single sugar units for absorption. Sugars are saccharides, and the prefixes “mono” (one), “di” (two), “tri” (three), “oligo” (some), and “poly” (many) refer to the number of sugar units linked together.

Enzymes are proteins that catalyze biochemical reactions; in other words, they increase the speed at which reactions occur. Their names usually end in “ase.”

Proteins are amino acids linked through peptide bonds. Dipeptides have two amino acids, tripeptides have three amino acids, and so on. Digestive proteases are enzymes that cleave the peptide bonds between the amino acids (see Chap.1, Fig. 1.5).

Fats must be transported in the blood bound to protein or in lipoprotein complexes because they are insoluble in water. Thus, both triacylglycerols and cholesterol are found in lipoprotein complexes.

The laboratory studies ordered at the time of his second office visit show that Ivan Applebod has hyperglycemia, an elevation of blood glucose above normal values. At the time of this visit, his 2-hour postprandial blood glucose level was 205 mg/dL. (Two-hour postprandial refers to the glucose level measured 2 hours after a meal, when glucose should have been taken up by tissues and blood glucose returned to the fasting level, approximately 80–100 mg/dL.) His blood glucose determined after an overnight fast was 162 mg/dL. Because both of these blood glucose measurements were significantly above normal, a diagnosis of type 2 diabetes mellitus, formerly known as non–insulin-dependent diabetes mellitus (NIDDM), was made. In this disease, liver, muscle, and adipose tissue are relatively resistant to the action of insulin in promoting glucose uptake into cells and storage as glycogen and triacylglycerols. Therefore, more glucose remains in his blood.

A. Carbohydrates

Dietary carbohydrates are converted to monosaccharides. Starch, a polymer of glucose, is the major carbohydrate of the diet. It is digested by salivary α-amylase, and then by pancreatic α-amylase, which acts in the small intestine. Di-, tri-, and oligosaccharides produced by these α-amylases are cleaved to glucose by digestive enzymes located on the surface of the brush border of the intestinal epithelial cells. Dietary disaccharides also are cleaved by enzymes in this brush border. Sucrase converts the disaccharide sucrose (table sugar) to glucose and fructose, and lactase converts the disaccharide lactose (milk sugar) to glucose and galactose. Monosaccharides produced by digestion and dietary monosaccharides are absorbed by the intestinal epithelial cells and released into the hepatic portal vein, which carries them to the liver.

B. Proteins

Dietary proteins are cleaved to amino acids by proteases (see Fig. 2.2, circle 3). Pepsin acts in the stomach, and the proteolytic enzymes produced by the pancreas (trypsin, chymotrypsin, elastase, and the carboxypeptidases) act in the lumen of the small intestine. Aminopeptidases and di- and tripeptidases associated with the intestinal epithelial cells complete the conversion of dietary proteins to amino acids, which are absorbed into the intestinal epithelial cells and released into the hepatic portal vein.

C. Fats

The digestion of fats is more complex than that of carbohydrates or proteins because they are not very soluble in water. The triacylglycerols of the diet are emulsified in the intestine by bile salts, which are synthesized in the liver and stored in the gallbladder. Pancreatic lipase converts the triacylglycerols in the lumen of the intestine to fatty acids and 2-monoacylglycerols (glycerol with a fatty acid esterified at carbon 2), which interact with bile salts to form tiny microdroplets called micelles. The fatty acids and 2-monoacylglycerols are absorbed from these micelles into the intestinal epithelial cells, where they are resynthesized into triacylglycerols. The triacylglycerols are packaged with proteins, phospholipids, cholesterol, and other compounds into the lipoprotein complexes known as chylomicrons, which are secreted into the lymph and ultimately enter the bloodstream (see Fig. 2.2, circle 2).

II. CHANGES IN HORMONE LEVELS AFTER A MEAL

After a typical high carbohydrate meal, the pancreas is stimulated to release the hormone insulin, and release of the hormone glucagon is inhibited (see Fig. 2.2, circle 4). Endocrine hormones are released from endocrine glands, such as the pancreas, in response to a specific stimulus. They travel in the blood, carrying messages between tissues concerning the overall physiologic state of the body. At their target tissues, they adjust the rate of various metabolic pathways to meet the changing conditions. The endocrine hormone insulin, which is secreted from the pancreas in response to a high-carbohydrate meal, carries the message that dietary glucose is available and can be used and stored. The release of another hormone, glucagon, is suppressed by glucose and insulin. Glucagon carries the message that glucose must be generated from endogenous fuel stores. The subsequent changes in circulating hormone levels cause changes in the body’s metabolic patterns, involving a number of different tissues and metabolic pathways.
CHAPTER 2 / THE FED OR ABSORPTIVE STATE

III. FATE OF GLUCOSE AFTER A MEAL

A. Conversion to Glycogen, Triacylglycerols, and CO₂ in the Liver

Because glucose leaves the intestine via the hepatic portal vein, the liver is the first tissue it passes through. The liver extracts a portion of this glucose from the blood. Some of the glucose that enters hepatocytes (liver cells) is oxidized in adenosine triphosphate (ATP)-generating pathways to meet the immediate energy needs of these cells and the remainder is converted to glycogen and triacylglycerols or used for biosynthetic reactions. In the liver, insulin promotes the uptake of glucose by increasing its use as a fuel and its storage as glycogen and triacylglycerols (see Fig. 2.2, circles 5, 6, and 7).

As glucose is being oxidized to CO₂, it is first oxidized to pyruvate in the pathway of glycolysis. Pyruvate is then oxidized to acetyl CoA. The acetyl group enters the tricarboxylic acid (TCA) cycle, where it is completely oxidized to CO₂. Energy from the oxidative reactions is used to generate ATP.

Liver glycogen stores reach a maximum of approximately 200 to 300 g after a high-carbohydrate meal, whereas the body’s fat stores are relatively limitless. As the glycogen stores begin to fill, the liver also begins converting some of the excess glucose it receives to triacylglycerols. Both the glycerol and the fatty acid moieties of the triacylglycerols can be synthesized from glucose. The fatty acids are also obtained preformed from the blood. The liver does not store triacylglycerols, however, but packages them along with proteins, phospholipids, and cholesterol into the lipoprotein complexes known as very-low-density lipoproteins (VLDL), which are secreted into the bloodstream. Some of the fatty acids from the VLDL are taken up by tissues for their immediate energy needs, but most are stored in adipose tissue as triacylglycerols.

B. Glucose Metabolism In Other Tissues

The glucose from the intestine that is not metabolized by the liver travels in the blood to peripheral tissues (most other tissues), where it can be oxidized for energy. Glucose is the one fuel that can be used by all tissues. Many tissues store small amounts of glucose as glycogen. Muscle has relatively large glycogen stores.

Insulin greatly stimulates the transport of glucose into the two tissues that have the largest mass in the body, muscle and adipose tissue. It has much smaller effects on the transport of glucose into other tissues.

1. BRAIN AND OTHER NEURAL TISSUES

The brain and other neural tissues are very dependent on glucose for their energy needs. They generally oxidize glucose via glycolysis and the TCA cycle completely to CO₂ and H₂O, generating ATP (see Fig. 2.2, circle 8)). Except under conditions of starvation, glucose is their only major fuel. Glucose is also a major precursor of neurotransmitters, the chemicals that convey electrical impulses (as ion gradients) between neurons. If our blood glucose drops much below normal levels, we become dizzy and light-headed. If blood glucose continues to drop, we become comatose and ultimately die. Under normal, nonstarving conditions, the brain and the rest of the nervous system require roughly 150 g glucose each day.

2. RED BLOOD CELLS

Glucose is the only fuel used by red blood cells, because they lack mitochondria. Fatty acid oxidation, amino acid oxidation, the TCA cycle, the electron transport chain, and oxidative phosphorylation (ATP generation that is dependent on oxygen...
and the electron transport chain) occur principally in mitochondria. Glucose, in contrast, generates ATP from anaerobic glycolysis in the cytosol and, thus, red blood cells obtain all their energy by this process. In anaerobic glycolysis, the pyruvate formed from glucose is converted to lactate and then released into the blood (see Fig. 2.2, circle 9).

Without glucose, red blood cells could not survive. Red blood cells carry O₂ from the lungs to the tissues. Without red blood cells, most of the tissues of the body would suffer from a lack of energy because they require O₂ to completely convert their fuels to CO₂ and H₂O.

3. MUSCLE

Exercising skeletal muscles can use glucose from the blood or from their own glycogen stores, converting glucose to lactate through glycolysis or oxidizing it completely to CO₂ and H₂O. Muscle also uses other fuels from the blood, such as fatty acids (Fig. 2.3). After a meal, glucose is used by muscle to replenish the glycogen stores that were depleted during exercise. Glucose is transported into muscle cells and converted to glycogen by processes that are stimulated by insulin.

4. ADIPOSE TISSUE

Insulin stimulates the transport of glucose into adipose cells as well as into muscle cells. Adipocytes oxidize glucose for energy, and they also use glucose as the source of the glycerol moiety of the triacylglycerols they store (see Fig. 2.2, circle 10).

IV. FATE OF LIPROTEINS IN THE FED STATE

Two types of lipoproteins, chylomicrons and VLDL, are produced in the fed state. The major function of these lipoproteins is to provide a blood transport system for triacylglycerols, which are very insoluble in water. However, these lipoproteins also contain the lipid cholesterol, which is also somewhat insoluble in water. The triacylglycerols of chylomicrons are formed in intestinal epithelial cells from the products of digestion of dietary triacylglycerols. The triacylglycerols of VLDL are synthesized in the liver.

When these lipoproteins pass through blood vessels in adipose tissue, their triacylglycerols are degraded to fatty acids and glycerol (see Fig. 2.2, circle 12). The fatty acids enter the adipose cells and combine with a glycerol moiety that is produced from blood glucose. The resulting triacylglycerols are stored as large fat droplets in the adipose cells. The remnants of the chylomicrons are cleared from the blood by the liver. The remnants of the VLDL can be cleared by the liver, or they can form low-density lipoprotein (LDL), which is cleared by the liver or by peripheral cells.

Most of us have not even begun to reach the limits of our capacity to store triacylglycerols in adipose tissue. The ability of humans to store fat appears to be limited only by the amount of tissue we can carry without overloading the heart.

V. FATE OF AMINO ACIDS IN THE FED STATE

The amino acids derived from dietary proteins travel from the intestine to the liver in the hepatic portal vein (see Fig. 2.2, circle 3). The liver uses amino acids for the synthesis of serum proteins as well as its own proteins, and for the biosynthesis of nitrogen-containing compounds that need amino acid precursors, such as the

Ivan Applebod’s total cholesterol level is now 315 mg/dL, slightly higher than his previous level of 296. (The currently recommended level for total serum cholesterol is 200 mg/dL or less.) His triacylglycerol level is 250 mg/dL (normal is between 60 and 160 mg/dL). These lipid levels clearly indicate that Mr. Applebod has a hyperlipidemia (high level of lipoproteins in the blood) and therefore is at risk for the future development of atherosclerosis and its consequences, such as heart attacks and strokes.
CHAPTER 2 / THE FED OR ABSORPTIVE STATE

Nonessential amino acids, heme, hormones, neurotransmitters, and purine and pyrimidine bases (e.g., adenine and cytosine in DNA). The liver also may oxidize the amino acids or convert them to glucose or ketone bodies and dispose of the nitrogen as the nontoxic compound urea.

Many of the amino acids will go into the peripheral circulation, where they can be used by other tissues for protein synthesis and various biosynthetic pathways, or oxidized for energy (see Fig. 2.2, circle 14). Proteins undergo turnover; they are constantly being synthesized and degraded. The amino acids released by protein breakdown enter the same pool of free amino acids in the blood as the amino acids from the diet. This free amino acid pool in the blood can be used by all cells to provide the right ratio of amino acids for protein synthesis or for biosynthesis of other compounds. In general, each individual biosynthetic pathway using an amino acid precursor is found in only a few tissues in the body.

VI. SUMMARY OF THE FED (ABSORPTIVE) STATE

After a meal, the fuels that we eat are oxidized to meet our immediate energy needs. Glucose is the major fuel for most tissues. Excess glucose and other fuels are stored, as glycogen mainly in muscle and liver, and as triacylglycerols in adipose tissue. Amino acids from dietary proteins are converted to body proteins or oxidized as fuels.

**CLINICAL COMMENTS**

**Ivan Applebod.** Mr. Applebod was advised that his obesity represents a risk factor for future heart attacks and strokes. He was told that his body has to maintain a larger volume of circulating blood to service his extra fat tissue. This expanded blood volume not only contributes to his elevated blood pressure (itself a risk factor for vascular disease) but also puts an increased workload on his heart. This increased load will cause his heart muscle to thicken and eventually to fail.

Mr. Applebod’s increasing adipose mass has also contributed to his development of type 2 diabetes mellitus, characterized by hyperglycemia (high blood glucose levels). The mechanism behind this breakdown in his ability to maintain normal levels of blood glucose is, at least in part, a resistance by his triacylglycerol-rich adipose cells to the action of insulin.

In addition to diabetes mellitus, Mr. Applebod has a hyperlipidemia (high blood lipid level—elevated cholesterol and triacylglycerols), another risk factor for cardiovascular disease. A genetic basis for Mr. Applebod’s disorder is inferred from a positive family history of hypercholesterolemia and premature coronary artery disease in a brother.

At this point, the first therapeutic steps should be nonpharmacologic. Mr. Applebod’s obesity should be treated with caloric restriction and a carefully monitored program of exercise. A reduction of dietary fat and sodium would be advised in an effort to correct his hyperlipidemia and his hypertension, respectively.

**BIOCHEMICAL COMMENTS**

**Anthropometric Measurements.** Anthropometry uses measurements of body parameters to monitor normal growth and nutritional health in well-nourished individuals and to detect nutritional inadequacies or excesses. In adults, the measurements most commonly used are: height, weight,
To obtain reliable measures of skinfold thickness, procedures are carefully defined. For example, in the triceps measurement, a fold of skin in the posterior aspect of the nondominant arm midway between shoulder and elbow is grasped gently and pulled away from the underlying muscle. The skinfold thickness reading is taken at a precise time, 2 to 3 seconds after applying the caliper, because the caliper compresses the skin. Even when these procedures are performed by trained dieticians, reliable measurements are difficult to obtain.

Weight and height. Weight should be measured by using a calibrated beam or lever balance-type scale, and the patient should be in a gown or in underwear. Height for adults should be measured while the patient stands against a straight surface, without shoes, with the heels together, and with the head erect and level. The weight and height are used in calculation of the body mass index (BMI).

Skinfold thickness. Over half of the fat in the body is deposited in subcutaneous tissue under the skin, and the percentage increases with increasing weight. To provide an estimate of the amount of body fat, a standardized calipers is used to pinch a fold of the skin, usually at more than one site (e.g., the biceps, triceps, subscapular, and suprailliac areas). Obesity by this physical anthropometric technique is defined as a fatfold thickness greater than the 85th percentile for young adults; that is, 18.6 mm for males and 25.1 mm for females.

Mid-Arm Anthropometry. The arm muscle circumference (AMC), also called the mid upper arm muscle circumference (MUAMC), reflects both caloric adequacy and muscle mass and can serve as a general index of marasmic-type malnutrition. The arm circumference is measured at the midpoint of the left upper arm by a fiberglass flexible-type tape. The arm muscle circumference can be calculated from a formula that subtracts a factor related to the skinfold thickness (SFT) from the arm circumference:

\[
\text{MUAMC (cm)} = \frac{\text{arm circumference (cm)}}{3.14} - \frac{(3.14 \times \text{SFT mm})}{10}
\]

Where MUAMC is the mid upper arm muscle circumference in cm and SFT is the skinfold thickness, expressed in millimeters.

MUAMC values can be compared with reference graphs available for both sexes and all ages. Protein–calorie malnutrition and negative nitrogen balance induce muscle wasting and decrease muscle circumference.

Waist Circumference. The waist circumference is another anthropometric measurement that serves as an indicator of body composition but is used as a measure of obesity and body fat distribution (the “apple shape”), not malnutrition. It is the distance around the natural waist of a standing individual (at the umbilicus). A high-risk waistline is more than 35 inches (88 cm) for women and more than 40 inches (102 cm) for men.

Suggested References


1. During digestion of a mixed meal,
   (A) starch and other polysaccharides are transported to the liver.
   (B) proteins are converted to dipeptides, which enter the blood.
   (C) dietary triacylglycerols are transported in the portal vein to the liver.
   (D) monosaccharides are transported to adipose tissue via the lymphatic system.
   (E) glucose levels increase in the blood.

2. After digestion of a high carbohydrate meal,
   (A) glucagon is released from the pancreas.
   (B) insulin stimulates the transport of glucose into the brain.
   (C) liver and skeletal muscle use glucose as their major fuel.
   (D) skeletal muscles convert glucose to fatty acids.
   (E) red blood cells oxidize glucose to CO₂.

3. Amino acids derived from digestion of dietary protein
   (A) provide nitrogen for synthesis of nonessential amino acids in the liver.
   (B) can be converted to glucose in most tissues.
   (C) cannot be converted to adipose tissue fat.
   (D) release nitrogen that is converted to urea in skeletal muscle.
   (E) are generally converted to body proteins or excreted in the urine.

4. Elevated levels of chylomicrons were measured in the blood of a patient. What dietary therapy would be most helpful in lowering chylomicron levels?
   (A) Decreased intake of calories
   (B) Decreased intake of fat
   (C) Decreased intake of cholesterol
   (D) Decreased intake of starch
   (E) Decreased intake of sugar

5. A male patient exhibited a BMI of 33 kg/m² and a waist circumference of 47 inches. What dietary therapy would you consider most helpful?
   (A) Decreased intake of total calories, because all fuels can be converted to adipose tissue triacylglycerols
   (B) The same amount of total calories, but substitution of carbohydrate calories for fat calories
   (C) The same amount of total calories, but substitution of protein calories for fat calories
   (D) A pure-fat diet, because only fatty acids synthesized by the liver can be deposited as adipose triacylglycerols
   (E) A limited food diet, such as the ice cream and sherry diet