Beans, peas, soybeans, and other leguminous plants contain oligosaccharides with (1,6)-linked galactose residues that cannot be hydrolyzed for absorption, including sucrose with one, two, or three galactose residues attached (see Fig. 27.10). What is the fate of these polysaccharides in the intestine?

The dietician explained to **Ann Sulin** the rationale for a person with diabetes to follow an American Diabetes Association diet plan. It is important for Ann to add a variety of fibers to her diet. The gel-forming, water-retaining pectins and gums delay gastric emptying and retard the rate of absorption of disaccharides and monosaccharides, thus reducing the rate at which blood glucose levels rise. The glycemic index of foods also needs to be considered for appropriate maintenance of blood glucose levels in persons with diabetes. Consumption of a low-glycemic-index diet results in a lower rise in blood glucose levels after eating, which can be more easily controlled by exogenous insulin. For example, Ms. Sulin is advised to eat pasta and rice (glycemic indices of 67 and 65, respectively) instead of potatoes (glycemic index of 80 to 120, depending on the method of preparation) and to incorporate breakfast cereals composed of wheat bran, barley, and oats into her morning routine.

are recommended to consume 21 g of fiber per day. These numbers are increased during pregnancy and lactation. One beneficial effect of fiber is seen in diverticular disease in which sacs or pouches may develop in the colon because of a weakening of the muscle and submucosal structures. Fiber is thought to "soften" the stool, thereby reducing pressure on the colonic wall and enhancing expulsion of feces.

Certain types of soluble fiber have been associated with disease prevention. For example, pectins may lower blood cholesterol levels by binding bile acids. β-Glucan (obtained from oats) has also been shown, in some studies, to reduce cholesterol levels through a reduction in bile acid resorption in the intestine (see Chapter 34). Pectins also may have a beneficial effect in the diet of individuals with diabetes mellitus by slowing the rate of absorption of simple sugars and preventing high blood glucose levels after meals. However, each of the beneficial effects that have been related to "fiber" is relatively specific for the type of fiber and the physical form of the food that contains the fiber. This factor, along with many others, has made it difficult to obtain conclusive results from studies of the effects of fiber on human health.

IV. ABSORPTION OF SUGARS

Once the carbohydrates have been split into monosaccharides, the sugars are transported across the intestinal epithelial cells and into the blood for distribution to all tissues. Not all complex carbohydrates are digested at the same rate within the intestine, and some carbohydrate sources lead to a near-immediate rise in blood glucose levels after ingestion, whereas others slowly raise blood glucose levels over an extended period after ingestion. The *glycemic index of a food* is an indication of how rapidly blood glucose levels rise after consumption. Glucose and maltose have the highest glycemic indices (142, with white bread defined as an index of 100). Table 27.4 indicates the glycemic index for a variety of food types. Although there is no need to memorize this table, note that cornflakes and potatoes have high glycemic indices, whereas yogurt and skim milk have particularly low glycemic indices.

The glycemic response to ingested foods depends not only on the glycemic index of the foods but also on the fiber and fat content of the food as well as its method of preparation. Highly glycemic carbohydrates can be consumed before and after exercise because their metabolism results in a rapid entry of glucose into the blood, where it is then immediately available for use by muscle cells. Low-glycemic carbohydrates enter the circulation slowly and can be used to best advantage if

Table 27.4 Glycemic Indices of Selected Foods, with Values Adjusted to White Bread of 100

Breads		*Legumes*	
Whole wheat	100	Baked beans (canned)	70
Pumpernickel (whole-grain rye)	88	Butter beans	46
Pasta		Garden peas (frozen)	85
Spaghetti, white, boiled	67	Kidney beans (dried)	43
Cereal grains		Kidney beans (canned)	74
Barley (pearled)	36	Peanuts	15
Rice (instant, boiled 1 min)	65	Fruit	
Rice, polished (boiled 10–25 min)	81	Apple	52
Sweet corn	80	Apple juice	45
Breakfast cereals		Orange	59
All bran	74	Raisins	93
Cornflakes	121	Sugars	
Muesli	96	Fructose	27
Cookies		Glucose	142
Oatmeal	78	Lactose	57
Plain water crackers	100	Sucrose	83
Root vegetables		Dairy products	
Potatoes (instant)	120	Ice cream	69
Potato (new, white, boiled)	80	Whole milk	44
Potato chips	77	Skim milk	46
Yam	74	Yogurt	52

consumed before exercise, such that as exercise progresses, glucose is slowly being absorbed from the intestine into the circulation in which it can be used to maintain blood glucose levels during the exercise period.

A. Absorption by the Intestinal Epithelium

Glucose is transported through the absorptive cells of the intestine by facilitated diffusion and by Na^+-dependent facilitated transport. (See Chapter 10 for a description of transport mechanisms.) The glucose molecule is extremely polar and cannot diffuse through the hydrophobic phospholipid bilayer of the cell membrane. Each hydroxyl group of the glucose molecule forms at least two hydrogen bonds with water molecules, and random movement would require energy to dislodge the polar hydroxyl groups from their hydrogen bonds and to disrupt the van der Waals forces between the hydrocarbon tails of the fatty acids in the membrane phospholipid. Glucose, therefore, enters the absorptive cells by binding to transport proteins, membrane-spanning proteins that bind the glucose molecule on one side of the membrane and release it on the opposite side (Fig. 27.11). Two types of glucose transport proteins are present in the intestinal absorptive cells: the Na^+-dependent glucose transporters and the facilitative glucose transporters (Fig. 27.12).

1. NA^+-DEPENDENT TRANSPORTERS

Na^+-dependent glucose transporters, which are located on the luminal side of the absorptive cells, enable these cells to concentrate glucose from the intestinal lumen.

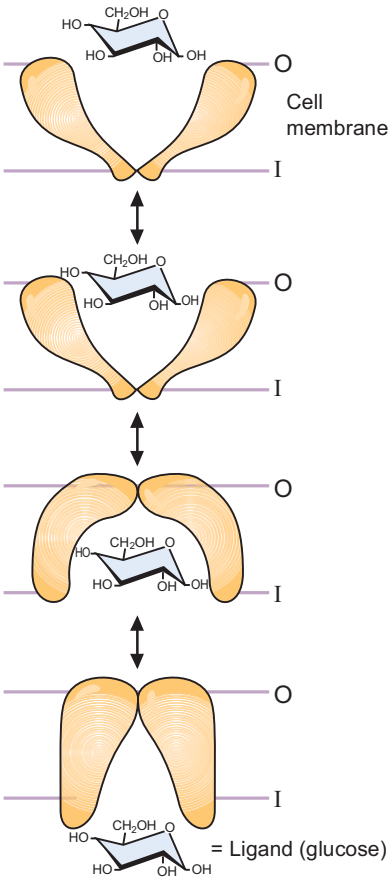

FIG. 27.11. Facilitative transport. Transport of glucose occurs without rotation of the glucose molecule. Multiple groups on the protein bind the hydroxyl groups of glucose and close behind it as it is released into the cell (i.e., the transporter acts like a "gated pore"). *O*, outside; *I*, inside.

A: These sugars are not digested well by the human intestine but form good sources of energy for the bacteria of the gut. These bacteria convert the sugars to H_2, lactic acid, and short-chain fatty acids. The amount of gas released after a meal containing beans is especially notorious.

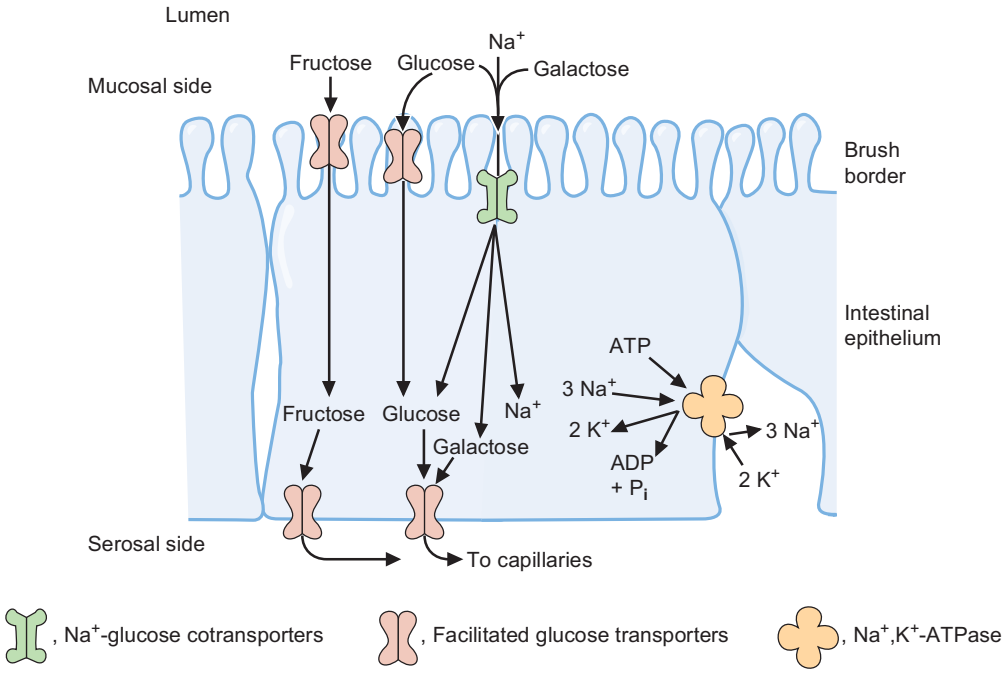

FIG. 27.12. Na^+-dependent and facilitative transporters in the intestinal epithelial cells. Both glucose and fructose are transported by the facilitated glucose transporters on the luminal and serosal sides of the absorptive cells. Glucose and galactose are transported by the Na^+-glucose cotransporters on the luminal (mucosal) side of the absorptive cells.

A low intracellular Na^+ concentration is maintained by a Na^+,K^+-ATPase on the serosal (blood) side of the cell that uses the energy from adenosine triphosphate (ATP) cleavage to pump Na^+ out of the cell into the blood. Thus, the transport of glucose from a low concentration in the lumen to a high concentration in the cell is promoted by the cotransport of Na^+ from a high concentration in the lumen to a low concentration in the cell (secondary active transport).

2. FACILITATIVE GLUCOSE TRANSPORTERS

Facilitative glucose transporters, which do not bind Na^+, are located on the serosal side of the cells. Glucose moves via the facilitative transporters from the high concentration inside the cell to the lower concentration in the blood without the expenditure of energy. In addition to the Na^+-dependent glucose transporters, facilitative transporters for glucose also exist on the luminal side of the absorptive cells. The best characterized facilitative glucose transporters found in the plasma membranes of cells (referred to as *GLUT 1* to *GLUT 5*) are described in Table 27.5. One common structural theme to these proteins is that they all contain 12 membrane-spanning domains. Note that the sodium-linked transporter on the luminal side of the intestinal epithelial cell is not a member of the GLUT family.

The epithelial cells of the kidney, which reabsorb glucose from the lumen of the renal tubule back into the blood, have Na^+-dependent glucose transporters similar to those of intestinal epithelial cells. They are thus also able to transport glucose against its concentration gradient. Other types of cells use mainly facilitative glucose transporters that carry glucose down its concentration gradient.

3. GALACTOSE AND FRUCTOSE ABSORPTION THROUGH GLUCOSE TRANSPORTERS

Galactose is absorbed through the same mechanisms as glucose. It enters the absorptive cells on the luminal side via the Na^+-dependent glucose transporters and

Table 27.5 Properties of the GLUT 1 to GLUT 5 Isoforms of the Glucose Transport Proteins

Transporter	*Tissue Distribution*	*Comments*
GLUT 1	Human erythrocyte Blood–brain barrier Blood–retinal barrier Blood–placental barrier Blood–testis barrier	Expressed in cell types with barrier functions; a high-affinity glucose transport system
GLUT 2	Liver Kidney Pancreatic β-cell Serosal surface of intestinal mucosa cells	A high-capacity, low-affinity transporter May be used as the glucose sensor in the pancreas
GLUT 3	Brain (neurons)	Major transporter in the central nervous system; a high-affinity system
GLUT 4	Adipose tissue Skeletal muscle Heart muscle	Insulin-sensitive transporter. In the presence of insulin, the number of GLUT 4 transporters increases on the cell surface; a high-affinity system
GLUT 5	Intestinal epithelium Spermatozoa	This is actually a fructose transporter

Genetic techniques have identified additional GLUT transporters (GLUT 6 to GLUT 12), but the roles of these transporters have not yet been fully described.

facilitative glucose transporters and is transported through the serosal side on the facilitative glucose transporters.

Fructose both enters and leaves absorptive epithelial cells by facilitated diffusion, apparently via transport proteins that are part of the GLUT family. The transporter on the luminal side has been identified as GLUT 5. Although this transporter can transport glucose, it has a much higher activity with fructose (see Fig. 27.12). Other fructose transport proteins also may be present. For reasons yet unknown, fructose is absorbed at a much more rapid rate when it is ingested as sucrose than when it is ingested as a monosaccharide.

B. Transport of Monosaccharides into Tissues

The properties of the GLUT transport proteins differ among tissues, reflecting the function of glucose metabolism in each tissue. In most cell types, the rate of glucose transport across the cell membrane is not rate limiting for glucose metabolism. This is because the isoform of transporter present in these cell types has a relatively low K_m for glucose (i.e., a low concentration of glucose will result in half the maximal rate of glucose transport) or is present in relatively high concentration in the cell membrane so that the intracellular glucose concentration reflects that in the blood. Because the hexokinase isozyme present in these cells has an even lower K_m for glucose (0.05 to 0.10 mM), variations in blood glucose levels do not affect the intracellular rate of glucose phosphorylation. However, in several tissues, the rate of transport becomes rate limiting when the serum level of glucose is low or when low levels of insulin signal the absence of dietary glucose.

The *erythrocyte* (red blood cell) is an example of a tissue in which glucose transport is not rate limiting. Although the glucose transporter (GLUT 1) has a K_m of 1 to 7 mM, it is present in extremely high concentrations, constituting approximately 5% of all membrane proteins. Consequently, as the blood glucose levels fall from a postprandial level of 140 mg/dL (7.5 mM) to the normal fasting level of 80 mg/dL (4.5 mM), or even the hypoglycemic level of 40 mg/dL (2.2 mM), the supply of glucose is still adequate for the rates at which glycolysis and the pentose phosphate pathway operate.

In the liver, the K_m for the glucose transporter (GLUT 2) is relatively high compared with that of other tissues, probably 15 mM or higher. This is in keeping with

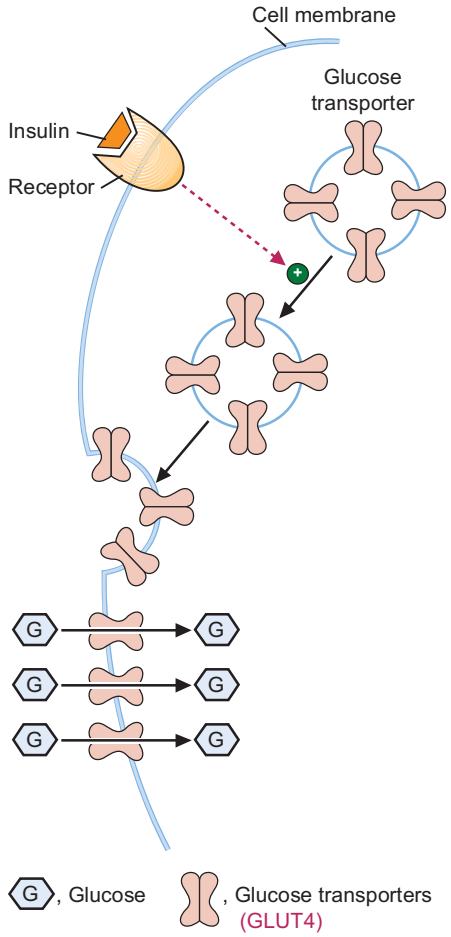

FIG. 27.13. Stimulation by insulin of glucose transport into muscle and adipose cells. Binding of insulin to its cell membrane receptor causes vesicles containing glucose transport proteins to move from inside the cell to the cell membrane.

the liver's role as the organ that maintains blood glucose levels. Thus, the liver will convert glucose into other energy storage molecules only when blood glucose levels are high, such as the time immediately after ingesting a meal. In muscle and adipose tissue, the transport of glucose is greatly stimulated by insulin. The mechanism involves the recruitment of glucose transporters (specifically, GLUT 4) from intracellular vesicles into the plasma membrane (Fig. 27.13). In adipose tissue, the stimulation of glucose transport across the plasma membrane by insulin increases its availability for the synthesis of fatty acids and glycerol from the glycolytic pathway. In skeletal muscle, the stimulation of glucose transport by insulin increases its availability for glycolysis and glycogen synthesis.

V. GLUCOSE TRANSPORT THROUGH THE BLOOD–BRAIN BARRIER AND INTO NEURONS

A hypoglycemic response is elicited by a decrease of blood glucose concentration to some point between 18 and 54 mg/dL (1 and 3 mM). The hypoglycemic response is a result of a decreased supply of glucose to the brain and starts with lightheadedness and dizziness and may progress to coma. The slow rate of transport of glucose through the blood–brain barrier (from the blood into the cerebrospinal fluid) at low levels of glucose is thought to be responsible for this neuroglycopenic response. Glucose transport from the cerebrospinal fluid across the plasma membranes of neurons is rapid and is not rate limiting for ATP generation from glycolysis.

In the brain, the endothelial cells of the capillaries have extremely tight junctions, and glucose must pass from the blood into the extracellular cerebrospinal fluid by GLUT 1 transporters in the endothelial cell membranes (Fig. 27.14) and then through the basement membrane. Measurements of the overall process of glucose transport from the blood into the brain (mediated by GLUT 3 on neural cells) show a $K_{m,app}$ of 7 to 11 mM and a maximal velocity not much greater than the rate of glucose utilization by the brain. Thus, decreases of blood glucose below

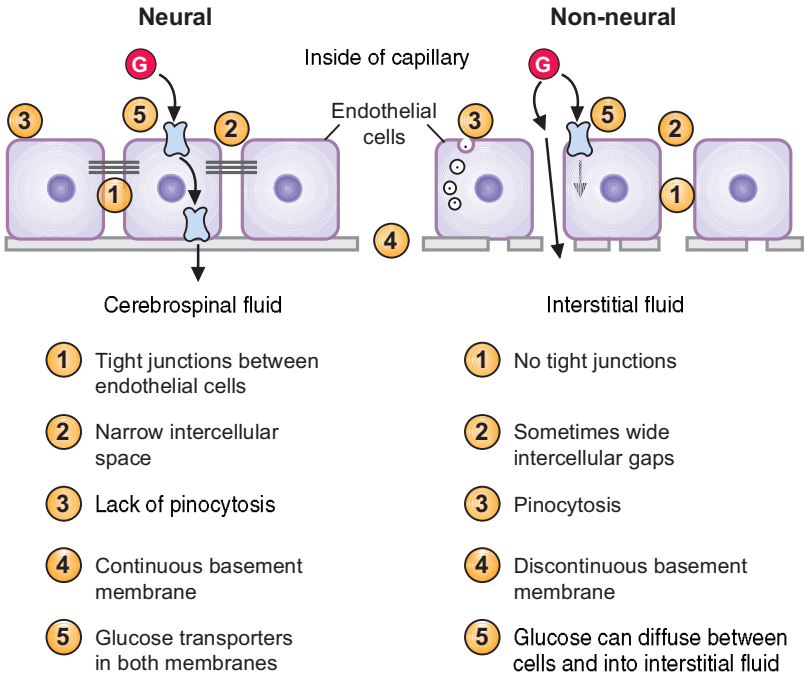

FIG. 27.14. Glucose transport through the capillary endothelium in neural and nonneural tissues. Characteristics of transport in each type of tissue are listed by numbers that refer to the numbers in the drawing. *G*, glucose.