into the cells. Insulin is needed for the entry of glucose into the muscle and fat cells, prevention of mobilization of fats from fat cells, and storage of glucose as glycogen in the cells of liver and muscle. Insulin is not needed for the entry of glucose into nerve cells or vascular tissue. The chemical composition and molecular structure of insulin are such that it fits into receptor sites on the cell membrane. Here it initiates a sequence of poorly defined chemical reactions that alter the cell membrane to facilitate the entry of glucose into the cell and stimulate enzymatic systems outside the cell that metabolize the glucose for energy production.

With a deficiency of insulin, glucose is unable to enter the cells, and its concentration in the bloodstream increases. The increased concentration of glucose (**hyperglycemia**) produces an osmotic gradient that causes the movement of body fluid from the intracellular space to the interstitial space and then to the extracellular space and into the glomerular filtrate to "dilute" the hyperosmolar filtrate. Normally, the renal tubular capacity to transport glucose is adequate to reabsorb all the glucose in the glomerular filtrate. When the glucose concentration in the glomerular filtrate exceeds the renal threshold (180 mg/dl), glucose spills into the urine (**glycosuria**) along with an osmotic diversion of water (**polyuria**), a cardinal sign of diabetes. The urinary fluid losses cause the excessive thirst (**polydipsia**) observed in diabetes. This water "washout" results in a depletion of other essential chemicals, especially potassium.

Protein is also wasted during insulin deficiency. Because glucose is unable to enter the cells, protein is broken down and converted to glucose by the liver (**glucogenesis**); this glucose then contributes to the hyperglycemia. These mechanisms are similar to those seen in starvation when substrate (glucose) is absent. The body is actually in a state of starvation during insulin deficiency. Without the use of carbohydrates for energy, fat and protein stores are depleted as the body attempts to meet its energy needs. The hunger mechanism is triggered, but increased food intake (polyphagia) enhances the problem by further elevating blood glucose.

Ketoacidosis

When insulin is absent or insulin sensitivity is altered, glucose is unavailable for cellular metabolism, and the body chooses alternate