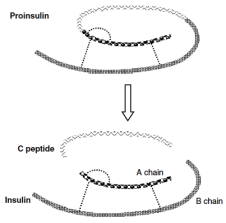
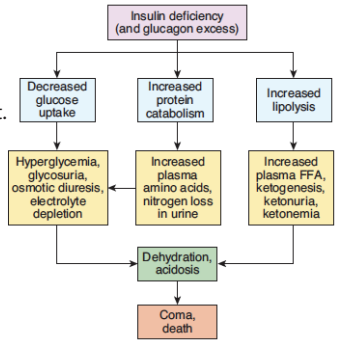
ENDOCRINE PHYSIOLOGY 1

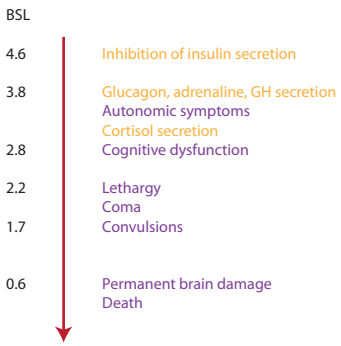
Hormones A hormone is a chemical substance produced by an organ or gland which enters the bloodstream and regulates tha actions of other cells or organs. There are three chemical classes of hormone: steroids, amines, and peptides/proteins. The amines are synthesized from tyrosine, the steroids from cholesterol, and the peptides/proteins through transcription and specific messenger RNA in the rough endoplasmic reticulum.There are four types of hormonal signaling: 1. endocrine, where the molecular signal is transmitted from an endocrine cell through the bloodstream to a distant target cell; 2. neurocrine, where a molecular signal is transmitted from a neuron, first down its axon and then into bloodstream to a distant target cell; 3. paracrine, where a molecular signal is transmitted from one cell type to a different cell type by diffusion through intercellular fluid channels; and 4. autocrine, where the molecular signal released is transmitted into the intercellular fluid back to the cell of origin or to neighboring identical cells.

Functions of the pancreas May separated into the exocrine functions and the endocrine functions. Exocrine functions relate to digestion. Secretion of the pancreas are from the acinar cells which produce the pancreatic digestive enzymes and the ductal cells which secrete water and HCO3. Approximately 1.5L of pancreatic juice is produced per day. At rest the secretions are similar to plasma but at higher flow rates it becomes more alkaline and has a higher concentration of HCO3. The islets of Langerhans are the anatomic units that determine the endocrine function of the pancreas. They are composed of four types of cell, each of which synthesizes and secretes a distinct polypeptide hormone: glucagon in the α (A) cell, insulin in the β (B) cell, somatostatin in the δ (D) cell, and pancreatic polypeptide in the PP or F cell. D1 and G cells secreting vasoactive intestinal peptide (VIP) and gastrin are rare. The amount of somatostatin and gastrin normally secreted by the islets is too small to be of any physiologic significance. Insulin is anabolic, increasing the storage of glucose, fatty acids, and amino acids. Although insulin acts on the whole of intermediary metabolism, its chief control is exerted on the glucose system. At concentrations below those required to affect glucose metabolism, insulin is anticatabolic. It inhibits the hormone-sensitive lipase in adipose tissue and thus decreases the hydrolysis of triglycerides stored in the adipocytes. Insulin stimulates amino acid uptake, enhances protein synthesis, and inhibits protein degradation in muscle and other tissues, thereby decreasing the plasma concentrations of most amino acids. The circulating concentration of glucose, unlike those of lipids or amino acids, is a strongly homeostatic variable, the excursions of which are confined to the very narrow range. Glucagon is catabolic, mobilizing glucose, fatty acids, and the amino acids from stores into the bloodstream. The two hormones are thus reciprocal in their overall action and are reciprocally secreted in most circumstances. Although glucagon is an important regulator of glucose homeostasis in humans, its absence has not been shown to cause clinical disease. Glucagon acts on G-Protien receptors, which in the liver increase adenylyl cyclase and cAMP increasing the breakdown of glycogen. It does not cause glycogenolysis in the muscles but does cause gluconeogenesis from available amino acids. Large does cause an increase in myocardial contractility, likely due to increase in cAMP. Somatostatin is the growth hormone inhibiting hormone originally isolated in the hypothalamus which is secreted as a paracrne hormone in the pancreas. Its actions are primarily inhibitory as the name suggests. It is secreted in response to acid in the lumen and inhibits the release of insulin, glucagon, pancreatic polypeptide, gastrin, VIP, GIP, secretin and motilin, reducing the absorption of glucose, amino acids and triglycerides.



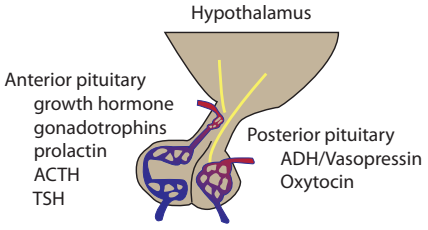
Insulin deficiency One of the key features of insulin deficiency is decreased entry of glucose into many tissues (decreased peripheral utilization). Also, the net release of glucose from the liver is increased (increased production), due in part to glucagon excess. The resultant hyperglycemia leads to glycosuria and a dehydrating osmotic diuresis. Dehydration leads to polydipsia. In the face of intracellular glucose deficiency, appetite is stimulated, glucose is formed from protein (gluconeogenesis), and energy supplies are maintained by metabolism of proteins and fats. Weight loss, debilitating protein deficiency, and inanition are the result. Fat catabolism is increased and the system is flooded with triglycerides and FFA. Fat synthesis is inhibited and the overloaded catabolic pathways cannot handle the excess acetyl- CoA that is formed. In the liver, the acetyl-CoA is converted to ketone bodies. Two of these are organic acids, and metabolic acidosis develops as ketones accumulate. Na+ and K+ depletion is added to the acidosis because these plasma cations are excreted with the organic anions not covered by the H+ and NH4 + secreted by the kidneys. Finally, the acidotic, hypovolemic, hypotensive, depleted animal or patient becomes comatose because of the toxic effects of acidosis, dehydration, and hyperosmolarity on the nervous system and dies if treatment is not instituted. All of these abnormalities are corrected by administration of insulin. Although emergency treatment of acidosis also includes administration of alkali to combat the acidosis and parenteral water, Na+, and K+ to replenish body stores, only insulin repairs the fundamental defects in a way that permits a return to normal.





Insulin excess / Hypoglycaemia All the known consequences of insulin excess are manifestations, directly or indirectly, of the effects of hypoglycemia on the nervous system. Except in individuals who have been fasting for some time, glucose is the only fuel used in appreciable quantities by the brain. The carbohydrate reserves in neural tissue are very limited and normal function depends on a continuous glucose supply. As the plasma glucose level falls, the first symptoms are palpitations, sweating, and nervousness due to autonomic discharge. At lower plasma glucose levels, so-called neuroglycopenic symptoms begin to appear. These include hunger as well as confusion and the other cognitive abnormalities. At even lower plasma glucose levels, lethargy, coma, convulsions, and eventually death occur. One important compensation for hypoglycemia is cessation of the secretion of endogenous insulin. Inhibition of insulin secretion is complete at a plasma glucose level of about 4.6mmol/L. . In addition, hypoglycemia triggers increased secretion of at least four counter-regulatory hormones: glucagon, epinephrine, growth hormone, and cortisol. The epinephrine response is reduced during sleep. Glucagon and epinephrine increase the hepatic output of glucose by increasing glycogenolysis. Growth hormone decreases the utilization of glucose in various peripheral tissues, and cortisol has a similar action. The keys to counter-regulation appear to be epinephrine and glucagon: if the plasma concentration of either increases, the decline in the plasma glucose level is reversed; but if both fail to increase, there is little if any compensatory rise in the plasma glucose level. The actions of the other hormones are supplementary.

Hypothalamus and pituitary The hypothalamus is part of the diencephalon and is located in the area of the third ventricle. It is anatomically and functionally related to the pituitary gland. The entire pituitary gland is situated in a socket of the sphenoid bone called the sella turcica. It consists of two parts, the anterior or adenohypophysis (which is controlled by the hypothalamus via the hypopophyseal vein), and the posterior or neurohypophysis (so called because it is actually a continuation of the hypothalamus). Two peptides are synthesized in the cell bodies of hypothalamic neurons and secreted from the posterior pituitary gland: oxytocin, and antidiuretic hormone (ADH) or arginine vasopressin (VAP). Oxytocin's role is to facilitate the ejection of milk from the lactating mammary gland. ADH or VAP has a role to conserve body water and regulate the tonicity of body fluids. The anterior pituitary gland or adenohypophysis is a collection of endocrine cells that are regulated by bloodborne stimuli originating in the neural tissue. The hypothalamic–pituitary unit regulates growth, lactation, and the function of the thyroid gland, adrenal glands, and gonads.



Christopher Andersen 2012