Important Endocrine Organs and Hormones

Figure 6.1 The location of endocrine glands involved in energy metabolism.
Figure 6.2 Islets of Langerhans in the pancreas. The pancreatic tissue has been immunostained to show the presence of insulin (and hence the islets). Courtesy of Dr Anne Clark.

Figure 6.3 Synthesis of insulin. Insulin is first synthesized as one long polypeptide, preproinsulin. The N-terminal portion is a "signal sequence" that directs preproinsulin into the secretory vesicles. It is then removed (arrows show sites of proteolytic action). Three disulfide bonds are formed between cysteine residues. (These will hold the mature protein in a particular folded structure.) Further proteolytic cleavage releases the connecting peptide, or C-peptide, to produce mature insulin. Insulin and C-peptide are secreted in equimolar amounts from the β-cell. Some proinsulin is also secreted into the plasma.
Figure 6.4 Glucose stimulation of insulin secretion in the pancreatic β-cell. Glucose enters the cell via the transporter GLUT2 (but see below) and is phosphorylated by glucokinase (GK) (hexokinase IV). These steps are similar to glucose utilization in the liver and allow the β-cell to “sense” the plasma glucose concentration. Generation of ATP from glucose utilization closes ATP-sensitive K+ channels in the cell membrane, stopping the outward flow of K+ ions that normally maintains the resting membrane potential (see Box 8.1, p. 215, for full description of this). This leads to membrane depolarization and opening of voltage-sensitive Ca2+ channels. Insulin is present in multiple secretory vesicles in the cell, as a crystalline complex in the center of the vesicle. An inward flux of Ca2+ ions causes exocytosis of the insulin-containing secretory vesicles, and hence insulin secretion. Glucose also stimulates synthesis of new insulin (Section 4.3.1). Although this scenario is true in rodent islets, there is some question over the presence of GLUT2 in human β-cells and it may be that GLUT1 and GLUT3 give the human β-cell sufficient glucose transport capacity (for discussion, see Schuit (1997)). The ATP-sensitive K+ channel has been much studied. It has two subunits. One is the K+ channel itself. This belongs to the family of inwardly-rectifying K+ channels (Kir, family 6 no. 2, hence Kir6.2). The other sub-unit modulates the activity of the channel and is the “receptor” for ATP (strictly, the complex Mg2+-ATP). But it is also the target for the drugs used to treat type 2 diabetes, the sulfonylureas (see later, Section 11.4.2). They bind, and cause channel closure, just as ATP does. Hence, this has become known as the sulfonylurea receptor, SUR. Again, there is a family of related proteins, and the one expressed in the β-cell is known as SUR1.
Figure 6.6  Pituitary hormones and their target organs.
**Figure 6.7** The anatomy of the thyroid gland.

**Figure 6.8** Biosynthesis of the thyroid hormones. Thyroxine (T₄) and triiodothyronine (T₃) are synthesized in the thyroid gland from tyrosine residues in the protein thyroglobulin. The conversion of T₄ to T₃, the active hormone, occurs mainly in peripheral tissues.
Figure 6.9 The anatomy of the adrenal glands.
Figure 6.10  **Biosynthesis of the catecholamines.**  Noradrenaline is released from sympathetic nerve terminals, whereas adrenaline is a true hormone, released into the bloodstream from the adrenal medulla.
Figure 6.11 The leptin system and regulation of fat stores. Leptin is produced in, and secreted from, adipose tissue according to the extent of the fat stores. Leptin signals to the brain (hypothalamus) to (1) reduce energy intake and (2) increase energy expenditure (the latter has only been shown convincingly in small animals). When fat stores are depleted, low leptin levels signal to the brain to (1) increase energy intake and (2) reduce energy expenditure. The system was discovered in the spontaneously obese ob/ob mouse, which has a defective leptin gene. Therefore, the brain of the ob/ob mouse “thinks” that it is connected to a small fat mass and increases energy intake, while in fact the fat mass expands and expands.
Figure 6.12 The idea of ‘incretins’ (gut-derived hormones that augment insulin secretion). Volunteers received either an infusion of glucose directly into their duodenum or an equal infusion into a vein. The plasma glucose concentration (top panel) rose considerably more with the intravenous infusion. But the response of plasma insulin (lower panel) was greater with the duodenal glucose infusion, despite the lower plasma glucose concentration. Therefore, some factor associated with glucose in the small intestine must augment glucose-stimulated insulin secretion. As discussed in the text, the major incretins are glucagon-like peptide-1 and gastric inhibitory polypeptide (GIP) (which was studied in this paper). Adapted from McCullough et al. (1983) with permission, Effect of graded intraduodenal glucose infusions on the release and physiological action of gastric inhibitory polypeptide, *The Journal of Clinical Endocrinology & Metabolism*, 56, 234–241. Copyright 1983, The Endocrine Society.