

Introduction

Part 1

Chapter

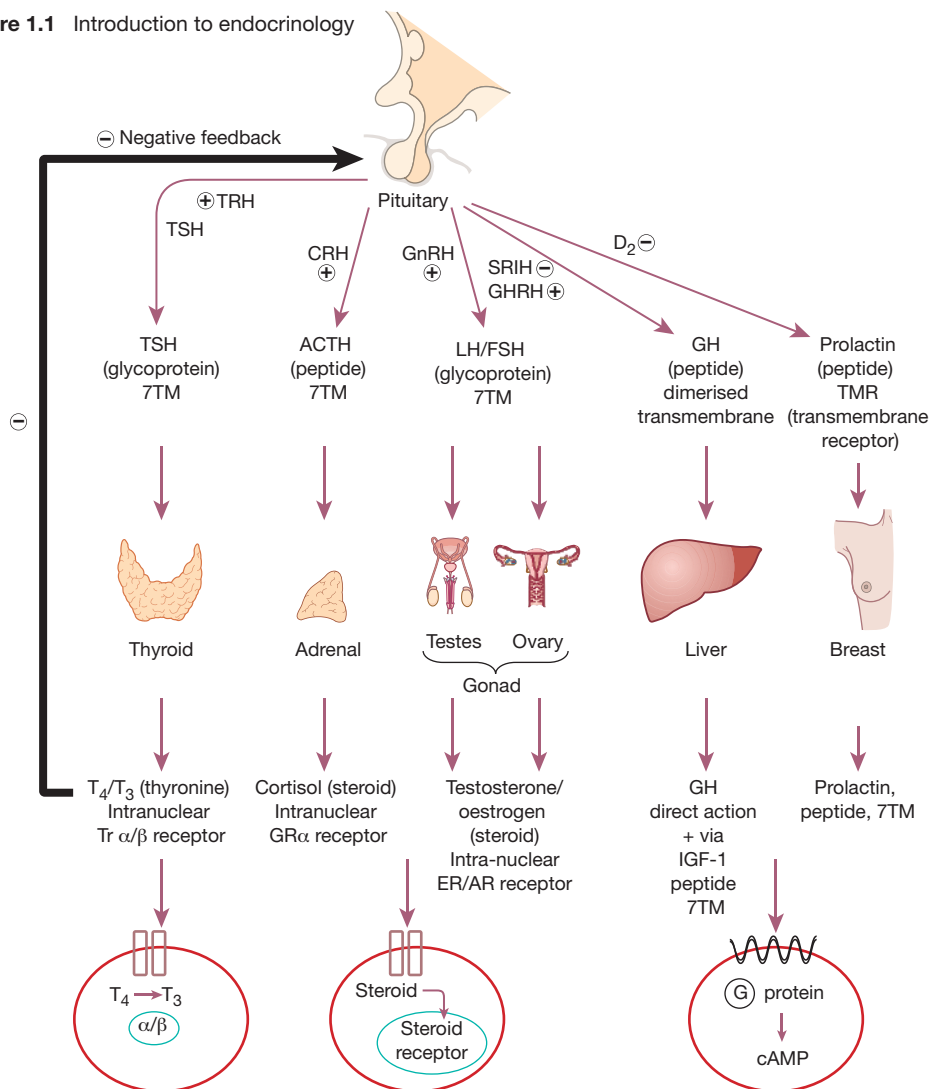
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Introduction to endocrinology

Figure 1.1 Introduction to endocrinology



Abbreviations: 7TM, 7-trans-membrane; ACTH, adrenocorticotrophic hormone; CRH, corticotrophin releasing hormone; cAMP, cyclic adenosine monophosphate; GH, growth hormone; GHRH, growth hormone releasing hormone; GnRH, gonadotropin-releasing hormone; SRIH, somatostatin; TRH, thyrotrophin releasing hormone; TSH, thyroid stimulating hormone; TSH, trophic hormone.

The endocrine system consists of glands, which secrete hormones that circulate and act at distant sites in the body. The key endocrine glands are the pituitary, thyroid, parathyroids, adrenals, pancreas and gonads. Endocrine disease can lead to hypo- or hypersecretion of hormones. Endocrine diseases include tumours, which are commonly benign, autoimmune diseases, enzyme defects and hormone receptor abnormalities.

Synthesis, release and transport

The chemical structure of hormones includes steroids, polypeptides, glycoproteins and amines (Figure 1.1). Hormones are secreted by the hypothalamus at low concentration, acting locally on the anterior pituitary, which in turn secretes trophic hormones to the relevant target gland. Hormones are secreted directly into the circulation either in their final form or as a larger precursor molecule, such as proopiomelanocortin (POMC), which is cleaved to adrenocorticotrophic hormone (ACTH), melanocyte stimulating hormone (MSH) and other smaller peptides. Many hormones are transported in the circulation by binding proteins, but only the free hormone acts on the receptor. Examples of binding proteins are sex hormone binding globulin (SHBG), which binds testosterone, and cortisol binding globulin (CBG), which binds cortisol.

Mechanisms of hormone action

Cell-surface receptors

Peptide hormones act on cell-surface receptors and exert their effect by activating cyclic adenosine monophosphate (cAMP). Most peptide hormones act via G-protein coupled receptors, most commonly a 7-trans-membrane (7TM) receptor (Figure 1.1). Examples of peptide hormones are growth hormone (GH), thyroid stimulating hormone (TSH), prolactin and ACTH.

Intranuclear receptors

Lipid-soluble hormones such as steroids and thyroid hormones pass through the cell membrane and act on intranuclear receptors, causing altered gene transcription (Figure 1.1).

Control and feedback

Hormones are usually controlled by a negative feedback mechanism (Figure 1.1). Using the thyroid axis as an example, the hypothalamus secretes its thyrotrophin releasing hormone (TRH), which travels down the portal tract to act on the anterior pituitary. The pituitary releases its trophic hormone (TSH) into

the circulation, which acts on the target gland, stimulating the production of the relevant hormone (thyroxine). If the target gland hormone is too low, there is loss of negative feedback and a compensatory increase in the pituitary hormone (low T4, high TSH). If the target gland hormone is too high, there is increased negative feedback and suppression of the pituitary hormone (high T4, low TSH). All pituitary hormones are under predominantly stimulatory control by the hypothalamus apart from prolactin, which is under tonic inhibition by dopamine.

Patterns of hormone secretion

Some hormones are produced in a stable pattern with little circadian rhythmicity, for example thyroxine and prolactin. Other hormones have a significant diurnal variation. For example, cortisol is highest in the morning and lowest at midnight. Minor circadian rhythms can be seen with certain hormones such as testosterone, which is slightly higher in the morning than the afternoon. It is important to measure hormones at the appropriate time of day when assessing for deficiency or excess. Female hormones have a monthly cyclical variation and must be interpreted according to the time of the menstrual cycle.

Measurement of hormones

Hormones are usually measured by immunoassay, which uses specific labelled antibodies that give a signal according to the concentration of hormone. Interfering antibodies can affect blood results, so some results are not reflective of the true concentration of hormone. Assay interference should be suspected in any blood result that does not match the clinical picture. Mass spectrometry is a newer technique that provides a more specific measure, and is increasingly being adopted in endocrine laboratories.

Dynamic endocrine tests

When basal investigations are difficult to interpret because of diurnal variation or equivocal results, 24-hour urine collection or dynamic blood tests can be helpful. If hormone deficiency is suspected, a stimulation test is used. This involves administration of a hormone that stimulates the target gland to increase its hormone secretion. Examples are the Synacthen test (to stimulate cortisol in suspected primary adrenal failure) and the insulin tolerance test (to stimulate GH and ACTH in suspected hypopituitarism). If hormone excess is suspected, a suppression test is used. Examples are the dexamethasone suppression test (to suppress cortisol in suspected Cushing's syndrome) and the oral glucose tolerance test (to suppress GH in suspected acromegaly).

