The hypothalamus and pituitary gland

Dr.mohammed talat

- A hormone can be defined as a substance secreted by an endocrine gland that is transported in the blood, thereby regulating the function of another tissue(s). Certain hormones, such as growth hormone (GH, secreted from the anterior pituitary gland), thyroxine (T4, from the thyroid gland) and insulin (from the pancreatic islet cells), influence tissue metabolism directly.

Conversely, trophic hormones from the pituitary gland stimulate target endocrine glands to synthesize and secrete further hormones, which in turn partly control trophic hormone release, usually by negative feedback inhibition. For example, hypercalcaemia inhibits the secretion of parathyroid hormone (PTH), and elevation of plasma T4 concentration inhibits the secretion of thyroid-stimulating hormone (TSH).

- Endocrine glands may secrete excessive or deficient amounts of hormone. Abnormalities of target glands may be primary or secondary to dysfunction of the controlling mechanism, usually located in the hypothalamus or anterior pituitary gland.

HYPOTHALAMUS AND PITUITARY GLAND

- The anterior and posterior lobes of the pituitary gland are developmentally and functionally distinct; both depend on hormones synthesized in the hypothalamus for normal function. The hypothalamus also has extensive neural connections with the rest of the brain, and stress and some psychological disorders affect the secretion of pituitary hormones and of the hormones from other endocrine glands;

Control of posterior pituitary hormones

- Two structurally similar peptide hormones, antidiuretic hormone (ADH) – also called vasopressin or arginine vasopressin (AVP) – and oxytocin, are synthesized in the hypothalamus and transported down the nerve fibres of the pituitary stalk attached to specific carrier proteins – neurophysins.

- The hormones are stored in the posterior pituitary gland and are released independently of each other into the bloodstream under hypothalamic control, together with neurophysin. Neurophysin has no apparent biological function and is rapidly cleared from plasma.

- *Oxytocin* is synthesized in the paraventricular nuclei of the hypothalamus. It controls the ejection of milk from the lactating breast and may have a role in initiating uterine contractions, although normal labour can proceed in its absence. It may be used therapeutically to induce labour.

- *Antidiuretic hormone* (arginine vasopressin) is mainly synthesized in the supraoptic nuclei of the hypothalamus and enhances water reabsorption from the collecting ducts in the kidneys .

Anterior pituitary hormones

- There is no direct neural connection between the hypothalamus and the anterior pituitary gland. The hypothalamus synthesizes small molecules (regulating hormones or factors) that are carried to the cells of the anterior pituitary lobe by the hypothalamic portal system.

- This network of capillary loops in the median eminence forms veins, which, after passing down the pituitary stalk, divide into a second capillary network in the anterior pituitary gland, from where hypothalamic hormones stimulate or inhibit pituitary hormone secretion into the systemic circulation.

- The cells of the anterior pituitary lobe can be classifi ed simply by their staining reactions as acidophils, basophils or chromophobes. Immunohistochemistry can identify specifi c hormone-secreting cells

- *Acidophils* are of two cell types: lactotrophs, which secrete prolactin, somatotrophs, which secrete GH (somatotrophin). These hormones, which are simple polypeptides with similar amino acid sequences, mainly affect peripheral tissues directly. Stimulation and inhibition of secretion via the hypothalamus is infl uenced by neural stimuli.

- *Basophils* secrete hormones that affect other endocrine glands. The hypothalamic control is mainly stimulatory. There are three cell types:

Corticotrophs synthesize a large polypeptide (pro-opiomelanocortin), which is a precursor of both adrenocorticotrophic hormone (ACTH; corticotrophin) and b-lipotrophin (Fig. 7.1). Secretion of these hormones occurs in parallel. Adrenocorticotrophic hormone stimulates the synthesis and secretion of steroids, other than aldosterone, from the adrenal cortex and maintains adrenal cortical growth. Part of the molecule has melanocyte-stimulating activity, and high circulating concentrations of ACTH are often associated with pigmentation.

b-Lipotrophin is inactive until rapidly converted to endorphins. These are neurotransmitters which, because they have opiate-like effects, help control pain. Gonadotrophs secrete the gonadotrophins, folliclestimulating hormone (FSH) and luteinizing hormone (LH), which act on the gonads. Thyrotrophs secrete TSH (thyrotrophin), which acts on the thyroid gland. These hormones are structurally similar glycoproteins consisting of two subunits, a and b. The a-subunit is common to all three hormones; the b-subunit is important for receptor recognition and therefore in specific biological activity

DISORDERS OF ANTERIOR PITUITARY HORMONE SECRETION

- The main clinical syndromes associated with excessive or deficient anterior pituitary hormone secretion are shown in Table 7.1. Excessive secretion usually involves a single hormone, but deficiencies are often multiple. However, many pituitary tumours are non-secretory and may present clinically with eye signs or headaches.

- Growth hormone

Growth hormone secretion from the anterior pituitary gland is mainly controlled by hypothalamic Ghreleasing hormone (GHRH). After synthesis by the hypothalamus, this is transported via the hypothalamic portal system to the somatotrophs of the anterior pituitary. Secretion of GHRH, and therefore of GH, is pulsatile, occurring about seven or eight times a day, usually associated with: exercise, onset of deep sleep, in response to the falling plasma glucose concentration about an hour after meals.

- At other times, plasma concentrations are usually very low or undetectable, especially in children. Growth hormone release is inhibited in a negative feedback pathway by another hypothalamic hormone, somatostatin (GH-release inhibiting hormone).

- Somatostatin is found not only in the hypothalamus and elsewhere in the brain, but also in the gastrointestinal tract and pancreatic islet cells, where it inhibits the secretion of many gastrointestinal hormones. Insulinlike growth factor 1 (IGF-1) acts by feedback to inhibit GHRH action.

- Growth hormone secretion may be stimulated by:
- stress, one cause of which is hypoglycaemia, glucagon, some amino acids, for example arginine, drugs such as levodopa and clonidine. All these stimuli have been used to assess GH secretory capacity, which may also be impaired in obese patients, in hypothyroidism and hypogonadism, some cases of Cushing's syndrome and in patients receiving large doses of steroids.

- Actions of growth hormone
- The main function of GH is to promote growth. Its action is primarily mediated by IGFs, polypeptides that are synthesized in many tissues, where they act locally. Plasma concentrations of one of these, IGF-1 (also known as somatomedin C), correlate with GH secretion.

- Carbohydrate metabolism is affected by GH: GH
- antagonizes the insulin-mediated cell uptake of glucose,and excess secretion may produce glucose intolerance. Fat metabolism is stimulated by GH: lipolysis is stimulated, with a consequent increase in the concentration of circulating free fatty acids. Free fatty acid antagonizes insulin release and action. Growth hormone enhances protein synthesis, in conjunction with insulin, to stimulate amino acid uptake by cells.

- The production of IGF-1 is also infl uenced by other factors, the most important of which is nutritional status. In undernutrition, plasma concentrations are low, whereas GH concentrations are elevated, suggesting that plasma IGF-1 may infl uence GH secretion by negative feedback. Other factors, such as adequate nutrition and T4, are also needed for normal growth.

- Growth hormone excess: gigantism and acromegaly Growth hormone excess causes gigantism during childhood and acromegaly in adults. Most patients with GH excess have acidophil adenomas of the anterior pituitary gland, which may be secondary to excessive hypothalamic stimulation. Rarely, malignant tumours may release GH or GHRH.

- Acromegaly is sometimes one of the manifestations of multiple endocrine neoplasia (MEN). The clinical manifestations of GH excess depend on whether the condition develops before or after fusion of the bony epiphyses. Gigantism is caused by excess GH secretion in childhood before fusion of the epiphyseal plates, which may be delayed by accompanying hypogonadism.

- Heights of up to about 2 metres may be reached. Acromegalic features may develop after bony fusion, but these patients may die in early adult life from infection or cardiac failure or as a consequence of progressive pituitary tumour growth

The features of acromegaly may include the following (Fig. 7.3):

- An increase in the bulk of bone and soft tissues with enlargement of, for example, the hands, tongue, jaw and heart. Changes in facial appearance are often marked, due to the increasing size of the jaw and sinuses; the gradual coarsening of the features may pass unnoticed for many years. Thyroid gland enlargement may be clinically detectable, but the patient is usually euthyroid.

- Excessive hair growth, hyperhidrosis and sebaceous gland secretion are common. Menstrual disturbances are common in females. Impaired glucose tolerance is present in about 25 per cent of patients, about half of whom develop symptomatic diabetes mellitus. In most cases the pancreas can secrete enough insulin to overcome theantagonistic effect of GH.

- There is a predisposition to multiple pre-malignant colon polyposis and hypertension. Hyperphosphataemia, hypercalcaemia and hypertriglyceridaemia may also be present.

Compression of the optic chiasma may cause visual field defects such as bitemporal hemianopsia.

If destruction of the gland progresses, other anterior pituitary hormones such as ACTH, LH, FSH and TSH may become deficient (see above). Plasma prolactin concentrations may, however, be raised as prolactin differs from all other pituitary hormones in its method of control.

- Growth hormone deficiency
- In adults, GH deficiency may cause clinical symptoms, such as tiredness, dyslipidaemia and increased cardiovascular disease. Growth hormone defi ciency can cause short stature in children. It is present in a small percentage of normally proportioned small children: the birthweight may be normal but the rate of growth is subnormal.

HYPOPITUITARISM

Hypopituitarism is a syndrome of deficiency of pituitary hormone production that may result from disorders of the hypothalamus, pituitary or surrounding structures. The anterior pituitary gland has considerable functional reserve. Clinical features of deficiency are usually absent until about 70 per cent of the gland has been destroyed, unless there is associated hyperprolactinaemia,

When amenorrhoea and infertility may be early symptoms. Panhypopituitarism alludes to the involvement of all pituitary hormones; alternatively, only one or more may be involved, as in partial hypopituitarism.

DISORDERS OF POSTERIOR PITUITARY HORMONE SECRETION

- Disorders of the posterior pituitary are rare compared with those of the anterior pituitary. Deficiency of ADH in diabetes insipidus may present as polyuria. In the syndrome of inappropriate ADH, hyponatraemia due to water excess occurs.

- Pituitary tumours
- The clinical presentation of pituitary tumours depends on the type of cells involved and on the size of the tumour (microadenomas less than 10 mm and macroadenomas more than 10 mm). Tumours of secretory cells may produce the clinical effects of excess hormone secretion: excess prolactin causes infertility, amenorrhoea and varying degrees of galactorrhoea , excess GH causes acromegaly or gigantism, excess ACTH causes Cushing's syndrome

SUMMARY

- The anterior pituitary gland releases a number of peptide hormones, which are themselves regulated by hypothalamus hormones that reach the pituitary via the portal blood system. The anterior pituitary hormones include ACTH, TSH, LH and FSH; their respective target organs are the adrenal and thyroid glands and the ovaries/testes

- . Growth hormone (GH) is also an anterior pituitary hormone but does not have a specifi c target organ – instead it infl uences most tissues. Hypopituitarism can be due to many conditions, such as pituitary infi ltration or destruction, and results in a defi ciency of all (panhypopituitarism) or some of the pituitary hormones.

- Conversely, excess release of certain anterior pituitary hormones can occur because of pituitary tumours. For example, acromegaly is due to excess GH, and Cushing's disease to excess ACTH release. The posterior pituitary releases oxytocin and ADH.

- The former is involved in uterine contraction during labour. Antidiuretic hormone controls water elimination by changing the renal collecting ducts’ permeability. Defi ciency of ADH results in diabetes insipidus

- THANK YOU