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Pharmacology

Endocrine and system pharmacology

1) Pharmacology of the pituitary gland

The pituitary gland is responsible for maintaining vertebrate homeostasis, regulating processes as varied as somatic growth, response to stress, reproduction, flux through metabolic pathways and lactation. It is composed of two parts, the adenohypophysis and the neurohypophysis.

The adenohypophysis forms the bulk of the gland and is composed

of three parts: the pars distalis, pars intermedia and pars tuberalis. The neurohypophysis is composed of nerve fibres projecting from hypothalamic nuclei to the median eminence. The pituitary gland is located in the

sella turcica, a bony cavity in the sphenoid bone that is roofed by the diaphragma sellae; defective development of which results in the ‘empty sella syndrome’.

The anterior pituitary has no direct nerve supply other than autonomic nerves. The posterior lobe, in contrast, is composed almost exclusively of hypothalamic nerve fibres.

Hypothalamic projections release hormones and trophic factors by neurosecretion into the median eminence and portal system.

Two principal tracts; the hypothalamo-hypophyseal tract arises in the magnocellular neurones of the supraoptic and paraventricular nuclei and releases vasopressin and oxytocin into the posterior pituitary, the parvocellular neurones of the tubero-infundibular tract originate in multiple hypothalamic nuclei and project to the median eminence.

The adenohypophysis and hypothalamus share a complex portal blood supply carrying trophic and inhibitory hormones from the hypothalamus, thus regulating systemic release of anterior pituitary hormones. The anterior pituitary has no direct arterial supply.

Branches of the superior, middle and inferior hypophyseal arteries supply the median eminence and posterior pituitary. The superior hypophyseal arteries branch into an internal and external plexus. The internal plexus forms glomeruloid structures known as gomitoli. Gomitoli regulate the flow of regulatory hormones in the pituitary paracrine ‘biological network’ and are the presumed origin of sellar glomangiomas. The inferior arteries supply the pituitary capsule, the neural lobe and the pituitary stalk.

The venous drainage of the pituitary gland is to the inferior petrosal sinuses via the cavernous sinus. The capacity of the venous drainage

is exceeded by the volume of blood entering the gland, thus forming a reservoir. Reversal of blood flow here results in secretory products from the adenohypophysis entering the neurohypophysis and median eminence. This vascular anatomy is important in the pathophysiology of apoplexy.

The anterior pituitary structures derive from Rathke’s pouch, an endodermal invagination of the primitive oral cavity. At the third week of gestation, endoderm from the roof of the stomodeum invaginates and, by 6 weeks, the connection with the oropharynx is obliterated. Rathke’s pouch then establishes contact with the infundibulum of the hypothalamus.

Early organogenesis is regulated by specific temporal and spatial expression of transcription factors and homeobox genes including the Rathke pouch homeobox (Rpx) protein, Pax-6, and the bicoid-related pituitary homeobox factors (Ptx-1 and Ptx-2). Two members of the LIM- homeodomain transcription factor family, encoded by LHX3 and LHX4, and the P-LIM protein are expressed during Rathke pouch development and mutations are associated with combined pituitary hormone deficiency. An early determinant of pituitary differentiation is the prophet protein (PROP-1).

By mid-gestation, Rathke’s pouch is virtually obliterated and is replaced by the pars intermedia. The pituitary portal system forms between 7 and 12 weeks and is fully established by 18–20 weeks. Remnants of adenohypophysis may be deposited along the migration route of Rathke’s pouch, the most common site being the roof of the nasopharynx.