ENDOCRINE GLANDS

Others: chemoreceptor organs, testis/ovary, placenta, kidney, thymus, pineal, G-I tract (DNES)
ENDOCRINE GLANDS

- scattered / no physical continuity / diverse embryological origins
- synthesize / store / release hormones directly into the bloodstream
- hormones interact with target cells \(\rightarrow\) biological response (maintain homeostasis)

- disorders are manifest by derangement of target organ functions
- Clin Dx - laboratory tests (eg CBC, serum chemistry, specific hormone assays, etc)
Polypeptide Hormones

- RER synthesis → secretory granule storage → fusion to plasma membrane

- target cell membrane receptors (eg GPCR’s) → signal transduction pathways
Steroid Hormones

- continuous biosynthesis on SER
- diffuse through plasma membrane of target cell → bind cytosolic receptors → nucleus → ↑ mRNA transcription → ↑ specific protein synthesis in target cells
Catecholamines & Iodothyronine Hormones

- hormones derived from tyrosine

- catecholamines act like polypeptides

- iodothyronines act like steroids
Mechanisms of Endocrine Disease

1) **Hyperactivity**

a) **Primary hyperfunction**
   - autonomous hypersecretion of hormone due to endocrine tumor

b) **Secondary hyperfunction**
   - excess trophic hormone → hypersecretion of hormones by the target organ

c) Hyperactivity secondary to diseases of other organs

d) Hypersecretion of hormones (hormone-like) by non-endocrine tumor

e) iatrogenic syndromes of hormone excess
Mechanisms of Endocrine Disease

2) **Hypoactivity**

a) **Primary Hypofunction**
   - subnormal hormone levels due to:
     - destruction of secretory cells
     - failure of development
     - genetic defect in biosynthesis

b) **Secondary hypofunction**
   - destruction of one organ (pituitary) interferes with the secretion of trophic hormone
     - hypofunction of target gland

c) **Endocrine dysfunction due to failure of target-cell response**
Pituitary Gland (Hypophysis)

- **embryologic development** → oropharyngeal ectoderm + diencephalic neuroectoderm

Figure 20–3. Formation of the pituitary gland. The pituitary gland forms from two separate embryonic structures. (a): During the third week of development, a hypophyseal pouch (or Rathke’s pouch, the future anterior pituitary) grows from the roof of the pharynx, while a neurohypophyseal bud (future posterior pituitary) forms from the diencephalon. (b): By late in the second month, the hypophyseal pouch detaches from the roof of the pharynx and merges with the neurohypophyseal bud. (c): During the fetal period, the anterior and posterior parts of the pituitary complete development.
Pituitary Gland (Hypophysis)

Sella turcica (= Turkish saddle) is a saddle-shaped depression in the sphenoid bone.
**Figure 12-02 (Zachary). Pituitary gland and brain stem, normal dog.** Longitudinal section of the pituitary region illustrating the close relationship to the optic chiasm (O), hypothalamus (H), and overlying brain. The pars distalis (D) forms a major part of the adenohypophysis and completely surrounds the pars nervosa (N). The residual lumen of Rathke’s pouch (arrow) separates the pars distalis and pars nervosa and is lined by the pars intermedia.
Histology of feline pituitary gland

- Third ventricle
- Hypothalamus
- Infundibulum
- Pars distalis (adenohypophysis)
- Pars intermedia (remnant, Rathke's pouch)
- Pars nervosa (neurohypophysis)
- Blood vessels in sinusoidal capillaries
- Capsule
Neurohypophysis

- Hormones from SO / PV nuclei → pars nervosa by axonal processes → terminate on fenestrated capillaries → released to general circulation
Adenohypophysis

Neurosecretory cells of the hypothalamus, producing, releasing, and inhibiting hormones

Stem and median eminence

Portal system

Pars distalis

Chromophobe

Basophil

Acidophil
Acidophils, basophils & chromophobes

Somatotroph of a cat

IHC for prolactin
Figure 12-21 (Zachary). Cystic Rathke’s pouch, brain, sagittal section, dog. A large, multiloculated cyst (C) is noted on the ventral aspect of this brain where the adenohypophysis would normally be located.
Pituitary cysts

1. Cysts from failure of differentiation of oropharyngeal ectoderm of Rathke’s pouch

- progressively enlarging cyst in the sella turcica → complete or partial absence of adenohypophysis & compression of neurohypophysis
Pituitary Dwarfism

- “juvenile panhypopituitarism” in German shepherd (AR)
- puppies stunted, retain juvenile hair, become alopecic & hyperpigmented
- secondary endocrine dysfunctions due to atrophy of thyroids, adrenals and gonads
- large cysts may cause diabetes insipidus
1) Pituitary Abscesses
- sporadically in ruminants and swine
- caused by bacteria or mycotic agents
- neurological signs due to local extension of the inflammation

2) Infiltration of mononuclear inflammatory cells
- in some viral and protozoan diseases as part of encephalitis or meningitis
Pituitary Abscesses

midsagittal section (above) and dorsal view through diaphragma sella (right) with abundant purulent exudate in both (asterisks)
Diabetes Insipidus

a) Hypophyseal form (= central DI)
- any lesion (neoplasm / cyst / trauma) that interferes with ADH synthesis / secretion

Cross-section of normal axons with secretory granules

Cross-section of axons of damaged neurons with reduced number of and empty (arrow) secretory granules
Diabetes Insipidus

b) Nephrogenic form

- hereditary defects in the ADH receptor or occasionally in the water channel (AQP-2)
- collecting duct cells fail to respond to normal or elevated circulating ADH

Note: There can be genetic defects in ADH (=V2) receptor or less frequently defects in the aquaporin 2 water channel.

i) both forms → PU/PD & urine of low osmolality (even after $H_2O$ deprivation)

ii) exogenous ADH → increase in urine osmolality in hypophyseal DI (not nephrogenic)
• neoplasms may be **functional** (stimulate target organ) or **nonfunctional** (destructive to adjacent structures)

• nodular hyperplasia vs adenomas (larger, capsule, compression)
Adenomas of Pars Distalis

a) ACTH-Secreting (Corticotroph) Adenoma

- esp dogs, tumors often small

Figure 12-17 (Zachary) Secondary hyperfunction of an endocrine organ, brain, pituitary gland and adrenal glands, dog. Corticotroph (adrenocorticotropic hormone [ACTH]-secreting) chromophobe adenoma (A) in the pituitary gland and bilateral enlargement of the adrenal glands. The chronic secretion of ACTH has resulted in hypertrophy and hyper-plasia of secretory cells of the zona fasciculata and zona reticularis in the adrenal cortex (arrows) and excessive secretion of cortisol.

Normal adrenal
Adenomas of Pars Distalis

a) ACTH-Secreting (Corticotroph) Adenoma

- esp dogs, tumors often small

Histology of a pituitary ACTH-secreting adenoma:
cords and nests of proliferating neoplastic corticotrophs

Immunohistochemistry:
positive staining for ACTH.
Adenomas of Pars Distalis

b) Nonfunctional Adenoma

- usually become large before causing clinical signs

Figure 12-20 (Zachary). Adenoma, pituitary gland, dog. A large pituitary adenoma (A) has extended dorsally and compresses the overlying brain. The optic chiasm (arrow) is also severely compressed. The adenohypophysis, neurohypophysis, and hypothalamus have been destroyed by the neoplasm.
Figure 12-16 (Zachary) Secondary hypofunction of an endocrine gland, brain, pituitary gland and adrenal glands, dog. A large nonfunctional chromophobe adenoma (A) has invaded and completely destroyed the adenohypophysis and hypothalamus, and infiltrated into the thalamus. Destruction of the adenohypophysis has resulted in a lack of secretion of thyrotropin, adrenocorticotropin, and other pituitary trophic hormones. This resulted in severe trophic atrophy of the adrenal cortex (arrowheads), especially the adrenocorticotropic hormone–dependent zona fasciculata and zona reticularis, and consequently, in a relatively more prominent medulla (M).
Adenomas of Pars Distalis

c) Somatotroph Adenoma
- these tumors cause gigantism in the young and acromegaly in adults

gigantism: six-foot-five-inch, 12 yr-old boy with his mother

d) Adenomas of Lactotrophs, Gonadotrophs and Thyrotrophs
- excess prolactin secretion, reported in non-pregnant, lactating goats
Adenomas of Pars Intermedia

**in dogs:**
- can be inactive or active

**in horses:**
- often large and compress neurohypophysis and hypothalamus
- hirsutism, altered CHO metabolism, polyphagia, muscle atrophy / weakness, laminitis, intermittent hyperpyrexia, hyperhidrosis and PU/PD

Hirsuitism due to failure of hair shedding associated with adenoma of the pars intermedia
Figure 12-23 (Zachary). Adenoma, brain, pituitary gland, horse. The pituitary gland is notably enlarged because of an adenoma (A) of the pars intermedia.
Physiology of the equine pituitary pars intermedia. The melanotropes of the pars intermedia produce the hormone precursor protein proopiomelanocortin (POMC), which in the pars intermedia is cleaved into the hormones α-melanocytes-stimulating hormone (α-MSH), β-endorphin (β-END) and corticotropin-like intermediate lobe peptide (CLIP). Production of POMC in the pars intermedia is under inhibitory control by dopamine released from the nerve terminals of the periventricular neurons (cell bodies in hypothalamus).

Pathophysicsiology of equine pituitary pars intermedia dysfunction. Loss of functional dopaminergic periventricular neurons leads to a decrease in dopamine at the pars intermedia. This in turn results in disinhibition of the melanotropes of the pars intermedia. The outcome is hypertrophy and hyperplasia (and often adenomas) of the pars intermedia and increased systemic release of the pars intermedia POMC-derived peptides α-MSH, β-END and CLIP.
Adenomas of Pars Intermedia

- tumor cells produce excess proopiomelanocortin (POMC) → aberrant posttranslational processing → varying amounts of ACTH/CLIP, MSH, β-endorphin.

**Figure 41-2 (from Large Animal Internal Medicine 4th edition).** Proopiomelanocortin (POMC) processing. POMC is cleaved by prohormone convertase I into ACTH in the pars distalis and into α-melanocytes-stimulating hormone (α-MSH), β-endorphin (β-END) and corticotropin-like intermediate lobe peptide (CLIP) by prohormone convertase I & II in the pars intermedia. Only a small amount of ACTH is produced by the normal pars intermedia.
Pituitary Carcinoma

- most inactive
- can lead to: panhypopituitarism, diabetes insipidus, CNS dysfunction, +/- metastasis

Pituitary carcinoma showing destruction of normal pituitary and extension into overlying brainstem

Histology of pituitary carcinoma showing local invasion (arrow) of adjacent neuroparenchyma (brain tissue).
Metastatic Tumors

• Tumors metastasizing to the pituitary would be uncommon, but could also lead to panhypopituitarism, CNS signs, etc.