

ENDOCRINE PATHOLOGY (1)

PATHOGENETIC MECHANISMS OF ENDOCRINE DISEASE

1. Primary gland hypofunction

- Destruction of secretory cells by a disease process, e.g. immune-mediated or other inflammatory injury in thyroid glands, parathyroid glands or adrenal cortex.
- Failure of gland development (hypoplasia or agenesis).
- Biochemical defect in synthetic pathway of the hormone; usually genetic; not commonly identified in veterinary species.

2. Secondary gland hypofunction

Destruction of glandular tissue – failure of secretion of a trophic hormone – hypofunction of target organ, e.g. endocrinologically inactive pituitary neoplasms interfere with secretion and release of adrenocorticotrophic hormone (ACTH), thyroid stimulating hormone (TSH) and follicle stimulating hormone (FSH) – hypofunction of adrenal cortex, thyroid follicular cells and gonads – atrophy.

3. Primary gland hyperfunction

Often a hyperplasia/neoplasia of endocrine cells is involved – primary source synthesises and secretes hormone autonomously at a rate in excess of the ability of the body to utilise and degrade the hormone.

Lesion	Hormone	Effect
Adrenal cortical adenoma/carcinoma	Cortisol	Hyperadrenocorticism
Pancreatic islet β -cell tumour	Insulin	Hypoglycaemia
Adrenal medulla (phaeochromocytoma)	Adrenaline	Hypertension
Thyroid follicular cell adenoma	T4, T3	Hyperthyroidism

4. Secondary gland hyperfunction

Lesion in one gland causes excessive trophic hormone secretion, which results in long-term hypersecretion in a target organ – canine ACTH-secreting pituitary tumour which results in adrenal cortical hyperplasia/hypertrophy and hypercortisolism (canine Cushing's syndrome).

5. Hypersecretion of hormones or hormone-like factors by non-endocrine tumours

- Adenocarcinoma of the apocrine glands of the anal sac in dogs – produces parathyroid hormone-related peptide (PTHrP) and induces a pseudo-hyperparathyroidism → hypercalcaemia.
- Some canine lymphomas (lymphosarcomas) may also exhibit a similar effect, i.e. the tumour secretes or is associated with a factor which induces hypercalcaemia.

6. Failure of target cell response

- Failure of the cell surface receptor mechanism or lack of a second intracellular messenger, e.g. insulin resistance in obesity – receptor loss in connective tissue cells which then fail to react to insulin, i.e. diabetes mellitus.

7. Endocrine hyperactivity secondary to disease in other organs

- Secondary hyperparathyroidism associated with chronic renal failure – retention of phosphorous and alterations in vitamin D metabolism lead to hypocalcaemia, hyperparathyroidism and skeletal demineralisation.

8. Abnormal hormone degradation

- Decreased degradation.
- Increased degradation, e.g. chronic drug administration.

9. Iatrogenic

- Corticosteroid excess → cortisol → muscle weakness, calcinosis cutis, hair loss and adrenal cortical atrophy.

PITUITARY GLAND

Pituitary Cysts

Pituitary dwarfism – juvenile panhypopituitarism – German shepherd dog – most cases are associated with development of a pituitary cyst.

Neoplasia of the pituitary gland

- **ACTH secreting adenomas** – Most common in the dog. Leads to syndrome of cortisol excess → hyperadrenocorticism (Cushing's syndrome).
- **Pituitary pars intermedia dysfunction in horses** – Hyperplasia/neoplasia of the pars intermedia in the horse.
- **Non-functional pituitary adenomas** – Atrophy of surrounding pituitary gland and compression/local extension into the brain.
- **Pituitary carcinoma** – Relatively uncommon.

ADRENAL GLAND

Hypofunction

- **Hypoadrenocorticism – Addison's disease** – bilateral idiopathic atrophy – immune mediated, also inflammation or bilateral haemorrhage (sepsis related).
 - Mineralocorticoid insufficiency – alterations in sodium, potassium and chloride levels – bradycardia (hyperkalaemia).
 - Glucocorticoid insufficiency – hypoglycaemia.

Hyperfunction

Hyperadrenocorticism (Canine Cushing's disease) – Syndrome of cortical excess – Most common cause is a functional corticotroph pituitary gland adenoma → bilateral adrenal gland hyperplasia. Note that the severity of the syndrome bears no relation to the size of the primary tumour. Less common cause is a functional adrenal gland neoplasia. The pathogenesis involves effects on gluconeogenesis, protein catabolism, lipolysis and anti-inflammatory caused by the glucocorticoids:

- Weakening of muscles – lordosis, pendulous abdomen, atrophy of temporal muscles – excessive protein catabolism combined with decreased protein synthesis.
- Hepatomegaly – due to “steroid hepatopathy” – increased deposits of glycogen and lipid.
- Skin lesions – atrophy of epidermis and adnexae, cutaneous calcification – “calcinosis cutis”.
- Calcification in lungs, muscle (especially intercostal muscles) and stomach wall.
- Increased appetite – direct effect of cortisol and/or destruction of appetite centre in hypothalamus.

Adrenal hyperplasia

Nodular hyperplasia of cortex – Common – usually multiple and bilateral (dog, cat, horse).

Diffuse hyperplasia – Functional tumours of pituitary gland.

Adrenal neoplasia

Cortical adenomas – Often incidental findings. May arise in glands with existing nodular hyperplasia.

Cortical carcinomas – Less common than adenomas. Cattle and dogs. If functional, these tumours will result in marked atrophy of the contralateral gland. Clinical signs as described for Cushing's disease plus the potential for invasion of major vessels and distant metastasis.

Medullary pheochromocytoma: Cattle and dogs. Can be large and invade locally to caudal vena cava plus distant metastasis. Some may be functional with signs relating to adrenaline (epinephrine)/noradrenaline (norepinephrine) excess.

ENDOCRINE PATHOLOGY (2)

ENDOCRINE PANCREAS

Diabetes mellitus

Aetiology

- Relative or absolute lack of insulin from pancreatic β cells (i.e. hypofunction) – common in the dog and more common in females.
 - Destruction of islet cells secondary to pancreatitis.
 - Amyloid deposition in the islets of Langerhan – cats.
 - Idiopathic pancreatic atrophy.
 - Hypoplasia.

Pathology

- Reduced availability of insulin → hyperglycaemia.
- Impaired leucocyte function – reduced resistance to infection.
- Hepatic fatty change.
- Cataracts → bilateral lens opacity (sorbitol pathway metabolism of glucose by lens).
- Renal glomerular sclerosis – deposits of glycoprotein in glomeruli.

Note: **Diabetes insipidus**: unrelated to the pancreas. Animals with diabetes insipidus have marked polyuria and polydipsia. It can be a disorder of either:

- Central (neurohypophyseal) diabetes insipidus – inadequate antidiuretic hormone (ADH) production by the neurohypophysis – due to neoplasms, cysts, inflammatory lesions, trauma
- Peripheral (nephrogenic) diabetes insipidus – renal epithelial cells are unable to respond adequately to ADH
 - Congenital absence of ADH receptors
 - Blockage of ADH receptors by autoantibodies

Endocrine pancreatic neoplasia

Insulinoma

- Neoplasia of pancreatic β cells.
- Carcinomas are more common than adenomas.
- Usually functionally active → hypoglycaemia.

Gastrinoma

- Rare.
- Gastrin → hypersecretion of gastric acid → Ulceration of gastrointestinal mucosa.

Glucagonoma

- Rare.
- Glucagon → hyperglycaemia.

THYROID GLAND

Developmental disorders

Accessory thyroid tissue

- Relatively common.
- Remnants of embryological development of thyroid gland.
- Usually in the mediastinum, often in heart base area.
- Can develop into neoplasia.

Thyroglossal duct cysts

- In ventral cervical region; fluctuant cysts.
- Can become neoplastic

Hypothyroidism

- Important in the dog; otherwise hypothyroidism is not common in other species.
 - **Idiopathic follicular atrophy:** Progressive replacement by adipose tissue.
 - **Lymphocytic thyroiditis:** Lymphocytic infiltration into the gland as a consequence of autoantibody formation.
- Reduced basal metabolic rate.
- Bilaterally symmetrical alopecia – hyperkeratosis, hyperpigmentation, myxoedema.
- Reduced spermatozoa count; anoestrus.
- Increase in cholesterol levels → atherosclerosis.

Hyperthyroidism

- Common in the cat.
- Even with functional thyroid neoplasia, it is uncommon to see hyperthyroidism in the dog, since this species is more able to excrete excess thyroid hormones.
- Polyuria, polydipsia, polyphagia; weight loss; hyperexcitability; heat intolerance.
- Hypertrophic cardiomyopathy.

Thyroid gland hyperplasia

Goitre

- Non-neoplastic/non-inflammatory enlargement of the thyroid gland.
- Diffuse goitre occurs in animals with an iodine deficient diet.

Nodular hyperplasia

- Multiple small nodules within the gland.
- Usually functional in the cat (hyperthyroidism).
- Rarely functional in other species.

Thyroid gland neoplasia

Follicular adenoma

- Discrete capsule and usually solitary (compare with nodular hyperplasia).
- More common in the cat (see hyperthyroidism above)

Follicular carcinoma

- More common in the dog.
- Locally invasive and often metastasise.
- Can arise in extrathyroidal tissue.

C-cell neoplasia

- C cells are present in the interstitial tissue and secrete calcitonin into interfollicular capillaries in response to hypercalcaemia.
- C-cell neoplasia is most common in bulls.
- These tumours may be found in association with pheochromocytomas and pituitary adenomas – “multiple endocrine neoplasia” (MEN).

PARATHYROID GLANDS

Hyperparathyroidism

Primary hyperparathyroidism

- Chief cell neoplasia.
- Adenoma more common than carcinoma.
- More common in the dog than in other species.
- These tumours are often functional, causing bone resorption and hypercalcaemia due to increased levels of parathyroid hormone (PTH).
- May cause pathological fractures of the bones.

Secondary hyperparathyroidism

- Renal secondary hyperparathyroidism.
- Nutritional secondary hyperparathyroidism (low calcium and/or high phosphorus).

Pseudohyperparathyroidism

- Humoral hypercalcaemia of malignancy, e.g. apocrine adenocarcinoma of anal sac, lymphosarcoma, metastatic neoplasia to the bone.

Hypoparathyroidism

- More common in small breed dogs than in other species.
- Usually caused by lymphocytic thyroiditis.
- Note also potential to remove these glands during thyroid surgery.
- Progressive decrease in serum calcium concentrations – neuromuscular excitability.

CHEMORECEPTOR ORGANS

Present at several sites – including carotid and aortic bodies, although chemoreceptor tissue is present in many other areas of the body. ‘Heart base’ tumours are most frequent.

Aortic body adenoma and carcinoma

- Most common in dogs, especially brachycephalic breeds.
- Adenomas are more common than carcinomas
- Mass around base of the heart.
- Carcinomas can invade the pulmonary artery or atria; distant metastases uncommon.
- Non-functional but can cause problems due to their space occupying effect.

Carotid body adenoma and carcinoma

- Arise near bifurcation of common carotid artery.

Multicentric tumours of chemoreceptor tissue occur, especially in brachycephalic breeds.