Pathology of the Endocrine System

Lecture 3
Parathyroid glands
Pancreatic islets
(Web Review)
Thyroid C (Parafollicular) Cells

**STRUCTURE AND FUNCTION**

- C cells derived from neural crest
- calcitonin protects against hypercalcemia by:
  i) inhibiting bone resorption
  ii) diuresis of Ca\(^{2+}\)
Thyroid C (Parafollicular) Cells

1) Thyroid C Cell Hyperplasia

2) Thyroid C Cell Adenoma

3) Thyroid C Cell Carcinoma:
   • all three seen in aged bulls
   • possible excessive dietary Ca\(^{++}\) for bulls on cow diet; ie prolonged stimulation of C cells

Figure 12-46 (McGavin).  C-cell carcinoma and metastases, thyroid and cervical lymph nodes, Holstein bull. Note the swellings in the neck (arrows) as a result of lymphadenopathy of the cranial cervical lymph nodes from metastases.
Parathyroid Glands

STRUCTURE AND FUNCTION

- morphology, # & location varies with species.
- single type of secretory cells (chief cells)
Parathyroid Hormone (PTH)

- minute-to-minute, fine regulation of [Ca$^{2+}$].

- PTH level controlled by direct feedback system based on [Ca$^{2+}$/Ph].

- protects against hypocalcemia by:
  i) stimulating bone resorption of Ca$^{2+}$
  ii) enhancing renal reabsorption of Ca$^{2+}$
  iii) ↑ intestinal absorption of Ca$^{2+}$ (with Vit D$_3$)
Figure 12-14 (Zachary). Interrelation of parathyroid hormone (PTH), calcitonin (CT), and 1,25-dihydroxycholecalciferol (1,25-[OH]2 VD3) in hormonal regulation of calcium and phosphorus in extracellular fluids (ECF).

- PTH and CT act in concert to keep [Ca$^{2+}$] in ECF within narrow limits
- Ca$^{2+}$ involved in: muscle contraction, nerve transmission/excitability, blood coagulation, enzyme activity, hormone release, etc
Hypoparathyroidism

1) Lymphocytic parathyroiditis
   • rare in dogs; believed to be autoimmune

2) Parturient Paresis (Milk Fever)
   • cows fed a high Ca\textsuperscript{2+} diet before parturition \(\rightarrow\) increased CT secretion & inactive parathyroids
   • onset of lactation (esp with concurrent anorexia) \(\rightarrow\) delayed response of parathyroids to sudden Ca\textsuperscript{2+} loss in milk \(\rightarrow\) progressive hypocalcemia, hypophosphatemia & paresis

3) Other causes include:
   • destruction of the parathyroids by neoplasms
   • accidental removal during thyroid surgery
   • atrophy after long-term hypercalcemia from calcinogenic plants
Hyperparathyroidism

FIGURE 21-29 (modified from Rubin's Pathology, 5th edition). Major pathogenetic pathways leading to clinical primary and secondary hyperparathyroidism (in humans).
Primary Hyperparathyroidism

- due to functional parathyroid adenomas or carcinomas
- produce excess PTH in spite of –ve feedback by high [Ca$^{2+}$]
- see hypercalcemia, PU/PD, weakening of bones (ie fibrous osteodystrophy)

Normal parathyroids, canine

Parathyroid adenoma, canine. Note single large parathyroid adenoma (top) with atrophy of remaining parathyroids.
Figure 12-46 (Zachary). Adenoma, parathyroid gland, dog. The adenoma consists of closely packed chief cells arranged in small groups separated by fine fibrous septa containing capillaries (arrowheads). It is partially encapsulated and has compressed the adjacent, nonneoplastic parathyroid tissue (arrows), which has undergone trophic atrophy. H&E stain.
Secondary Hyperparathyroidism

a) **Secondary to Nutritional Imbalances**
- cats, dogs, horses, nonhuman primates, birds and reptiles
- in response to excess dietary Phos & low Vit D<sub>3</sub> (normal or low Ca<sup>2+</sup>)
- horses on high-grain / poor quality roughage diet
- dogs & cats on all-meat diets

b) **Secondary to Renal Disease**
- response to hypocalcemia resulting from:
  i) progressive hyperphosphatemia due to ↓ GFR
  ii) impaired activation of Vit D<sub>3</sub>

• in both, renal and nutritional secondary hyperparathyroidism:
  i) hypertrophy & hyperplasia of chief cells → bilateral enlargement (hyperplasia) of parathyroids
  ii) excess PTH (in both 1<sup>o</sup> & 2<sup>o</sup>) → generalized fibrous osteodystrophy
Diffuse parathyroid gland hyperplasia, dog with renal secondary hyperparathyroidism. Note, all 4 parathyroid glands are symmetrically enlarged.
Fibrous osteodystrophy, mandibles, dog with renal secondary hyperparathyroidism. Note some dogs with hyperparathyroidism and fibrous osteodystrophy can get soft, pliable mandibles, that bend like rubber (so-called “rubber jaw”); as in photo above.

Other dogs, with the same disease, can get symmetrical enlargement of the head due to swelling of the maxillae and mandibles, often with displacement of the teeth (photo to the right). The swelling is due to excessive proliferation of poorly mineralized woven (immature) bone and fibrous tissue.

In this latter case the excessive proliferation may be in response to the mechanical stresses of mastication on these already weakened bones.
Fibrous osteodystrophy, dog. Note thickened maxilla and displacement of teeth (above). On cut surface (above right) note fibro-osseous enlargement and distortion of maxilla compared with normal amount of maxillary bone (below right).
Histologically there is prominent osteoclastic resorption of bone (arrows) with surrounding proliferation / replacement by fibrous tissue.

Figure 12-52 (McGavin). Primary hyperparathyroidism, humerus, dog. Severe thinning of cortical bone and large resorptive cavities (arrow) have resulted from localized resorption of bone by osteoclasts.
Pseudohyperparathyroidism (= HHM = humoral hypercalcemia of malignancy)

- type of paraneoplastic syndrome
- tumor secretes humoral factors (PTH-RP) → hypercalcemia / hypophosphatemia
- eg apocrine gland adenocarcinoma of anal sac & lymphosarcoma

Figure 12-60 (Zachary). Adenocarcinoma, apocrine glands of right anal sac, anus, dog. The right perianal region is distended by an adenocarcinoma (arrow), which has compressed the right side of the anus. It also projects as two nodules (arrowhead) on the dorsolateral margin of the anus. T, Tail; A, anus

Figure 12-61 (Zachary). Adenocarcinoma, apocrine glands, anal sac, dorsal plane, formalin fixed specimen, dog. A 1-cm-diameter nodule (arrows) derived from apocrine glands of the wall of the right anal sac (glands of the perianal sinus) protrudes into the lumen of the right anal sac. Anal sacs (A) are present on both sides of the rectum (R).
Pancreatic Islets

Serous acinus (exocrine)

Islet of Langerhans (endocrine)

Pancreatic acinus

Blood capillary

Pancreatic islet cells

- Alpha cell
- Beta cell
- Delta cell
- F cell

Basic Histology
FIGURE 24–26D&E (Robbin’s)  Hormone production in pancreatic islet cells. D, Electron micrograph of a β cell shows the characteristic membrane-bound granules, each containing a dense, often rectangular core and distinct halo. E, α cell also shows granules, but with closely apportioned membranes and dense, round center.
Diabetes Mellitus

**Type I diabetes mellitus**
- destruction of beta cells → complete loss of insulin secretion
- insulin-dependent from time of Dx

**Type II diabetes mellitus**
- characterized by insulin resistance
- over time develop into insulin-dependent DM
Type II diabetes mellitus

**FIGURE 24–31 (Robbin’s)**
Development of type 2 diabetes. Insulin resistance associated with obesity is induced by adipokines, free fatty acids, and chronic inflammation in adipose tissue. Pancreatic β cells compensate for insulin resistance by hypersecretion of insulin. However, at some point, β-cell compensation is followed by β-cell failure, and diabetes ensues.
Secondary diabetes mellitus

• reflects antagonism in peripheral tissues between insulin and other hormones:
  
  progesterone
  
  glucagon
  
  growth hormone

  *glucocorticoids*
In dogs:

- common endocrinopathy of dogs (1:200); females more frequent than males
- most clinically like type I diabetes
- associated with the following lesions:
  i) destruction of islets concurrent with exocrine pancreatic disease
  ii) aplasia / hypoplasia of pancreatic islets
  iii) immune destruction of beta cells?
Figure 12-49 (Zachary). Chronic relapsing pancreatitis, pancreas and duodenum, cross section, dog. The pancreas is multinodular and firm with areas of hemorrhage (arrow), fibrosis, and necrosis. D, Duodenum.

Figure 12-50 (Zachary). Chronic pancreatitis, pancreas, dog. The pancreas (P) is markedly atrophied and its parenchyma almost completely replaced by fibrous connective tissue in “end-stage” pancreatitis. D, Duodenum.
Diabetes Mellitus

In cats:
• also relatively common; most cases resemble type II diabetes

Figure 12-52 (Zachary). Amyloidosis, pancreatic islets, cat. Note the deposits of amyloid (A) and degeneration and loss of islet cells. H&E stain.

Figure 12-51 (Zachary). Hydropic (“vacuolar”) degeneration, pancreatic islet, cat. Discrete vacuoles (arrowheads) are present in the cytoplasm of β cells. E, Exocrine pancreas. H&E stain.
**Diabetes Mellitus**

**Clinical Signs & Lesions**

- **hyperglycaemia and glycosuria** - decreased insulin or insulin resistance
- **polydipsia / polyuria** - glucosuria → osmotic diuresis with compensatory polydypsia
- **polyphagia** - affect on satiety center
- **loss of weight** - glucosuria & generalized ↑ catabolism
- **weakness** - ↓ tissue/muscle glucose, protein catabolism ± polyneuropathy
- **hepatic lipidosis** - increased lipolysis in adipose tissue → excess fatty acids to liver
- **bilateral cataracts** - excess glucose to polyol pathway causing:
  - ↑ osmotic sorbitol → hydropic degeneration of lens fibers
  - glutathione depletion → oxidative damage of lens fibers
- **recurrent infections** - ↓ leukocyte kinetics and ↑ glucose substrate
- **vascular damage** - glomerulo-sclerosis and retinopathy
- **neuropathies** - peripheral demyelinating neuropathies
Diabetes Mellitus

- Bilateral diabetic cataracts, dog

Diabetic neuropathy, cat. Note plantigrade stance

Hepatic lipidosis is common in diabetic animals
Neoplasia of Pancreatic Islets

1) Beta Cell Neoplasms

- often functional, producing excess insulin (insulinomas)

- adenomas encapsulated vs carcinomas (larger / locally invasive / may metastasize)

- if functional → severe hypoglycemia → weakness, fatigue, CNS signs (ataxia, seizures)

- Dx → high serum insulin, low blood glucose and one or more nodules in the pancreas

- rare, malignant variety more frequent

- one hormone is usually dominant, esp insulinomas
1) Beta Cell Neoplasms

Figure 12-53 (Zachary). β-Cell adenoma, pancreatic islet, dog. A solid islet adenoma, surrounded by a fibrous capsule of variable thickness has compressed the adjacent exocrine pancreas (arrow). H&E stain. [Note, if there was no clinical history, immunohistochemical staining for insulin would have to be done to confirm this was an insulinoma]
1) Beta Cell Neoplasms

Fig. 12-54 (Zachary) β-cell carcinoma, pancreatic islet, dog.

A, The whitish-red carcinoma (CA) is well demarcated from the lobular exocrine pancreas (P).

B, The β-cell carcinoma (right side of figure) has metastasized to the liver and has expanded to compress adjacent hepatic parenchyma and invade sinusoids. H&E stain.
Neoplasia of Pancreatic Islets

2) Non-beta Cell Neoplasms:

Glucagonomas

- rare (dogs)
- excess glucagon → secondary diabetes mellitus, +/- superficial necrolytic dermatitis

**Crusted footpads, dog.** Note thickening and crusting of foot pads, which can be seen with glucagonomas (note can also see crusted pads with other diseases, eg hepatic disease, canine distemper, pemphigus)
Chemoreceptor Organs

STRUCTURE AND FUNCTION

• also called nonchromaffin paraganglia → esp aortic & carotid body
• chemoreceptors that sense change in pH, [CO$_2$] & [O$_2$]
Chemoreceptor Neoplasms

- also called chemodectomas or non-chromaffin paragangliomas
- esp brachycephalic dogs

1) Aortic Body Adenomas / Carcinomas

- more common than carotid body tumors
- rarely functional → usually heart failure due to space-occupying nature
- "heart-base tumor" (R/O ectopic thyroid tumor)
Aortic body tumor (right) surrounding and compressing the aorta at the base of the heart.

Figure 12-55 (Zachary). Carcinoma, aortic body, dog. Note the large mass (C) at the base of the heart (H). Contiguous portions of the right-middle and diaphragmatic lung lobes are atelectatic. L, Lungs.