“Well, well — another blond hair ... Conducting a little more ‘research’ with that Jane Goodall tramp?”
Pathology of the Integumentary System

Lecture 5
Endocrine / Miscellaneous / Neoplasia (web)

Paul Hanna Fall 2017
ENDOCRINE SKIN DISEASE

• hormones act on skin & other organs by modifying existing physiological processes

**Gross**

1. Bilateral symmetrical alopecia (nonpruritic)
2. Hyperpigmentation
3. Secondary seborrhea and/or pyoderma
Histology → Atrophic Dermatosis

1. Hyperkeratosis
2. Epidermal melanosis
3. Follicular changes - eg catagen / telogen predominance, keratosis, atrophy
4. Sebaceous gland atrophy

Hyperkeratosis with increased melanin

Dilated, atrophic follicle filled with keratin

Atrophic sebaceous gland
<table>
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<th>Diagnosis</th>
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<tr>
<td>① History and clinical signs / lesions</td>
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<td>② Skin biopsies → atrophic dermatosis</td>
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<td>③ Hormone assay &amp;/or response to therapy</td>
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HYPOTHYROIDISM

- the most common endocrinopathy causing skin disease of dogs
- $[T_3 / T_4]$ affects basal metabolic rate

**Gross**
- typical endocrine changes
- +/- thickened skin due to dermal myxedema

Dog with hypothyroidism showing bilateral symmetrical alopecia

Some hypothyroid dogs have thickened skin due to excess dermal mucin (ie myxedema); which can give dog “tragic expression”. 
**Histology**

- typical atrophic dermatosis pattern
- often hyperplasia of epidermis / follicular infundibulum
- +/- increased dermal mucin (= myxedema)

In some cases of hypothyroidism there is an increase in dermal mucin (myxedema) as seen in this photo. This slide is stained with Alcian blue which is specific for glycosaminoglycans (GAG's), ie stains them blue. Note GAG's are the molecules of dermal mucin).
HYPERADRENOCORTICISM

- second most common endocrinopathy of dogs
- increased endogenous or exogenous glucocorticoids

Gross
- typical endocrine changes
- often thin, hypotonic, poor healing skin
- +/- calcinosis cutis & comedones

Bilaterally symmetric alopecia in a dog with hyperadrenocorticism
HYPERADRENOCORTICISM

Calcinosis cutis in dog with Cushings disease. Note, white to dark plaque-like areas on the skin of the ventral abdomen; which would be firm / hard on palpation.

Alopecia & comedones (inset, close up of comedones)
**Histology**

- atrophic dermatosis pattern
- +/- epidermal / dermal atrophy
- +/- follicular keratosis (comedones)
- +/- dystrophic mineralization (calcinosis cutis)

Epidermis reduced to 1 cell layer in some areas

Dilated, atrophic follicle filled with keratin (comedone microscopically)
Histology

- atrophic dermatosis pattern
- +/- epidermal / dermal atrophy
- +/- follicular keratosis (comedones)
- +/- dystrophic mineralization (calcinosis cutis)

Histologic section from an area of calcinosis cutis, showing aggregates of dark purple-blue staining mineralized collagen fibers (H&E)
SOME OTHER ENDOCRINE SKIN DISEASE

Gonadal Hormone Imbalance

Alopecia X (growth hormone / castration responsive dermatosis)

Equine Pituitary (pars intermedia) Adenoma

Hirsuitism (hypertrichosis) due to pituitary adenoma of pars intermedia
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<th>Nutritional Skin Disease</th>
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<td>Zinc deficiency / Zinc-responsive dermatosis</td>
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<td>2</td>
<td>Copper deficiency</td>
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<td>3</td>
<td>Nutritional panniculitis / steatitis</td>
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<td>4</td>
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<td>Protein-calorie deficiency</td>
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MISCELLANEOUS SKIN DISEASES

Seborrhea

- broad classification for scaling / crusting, +/- greasiness (1\textsuperscript{o} vs 2\textsuperscript{o})

- defect in cornification (+/- abnormal sebum production)

- 3 main abnormalities: ① altered keratinization $\rightarrow$ scaling / crusting
  ② altered surface lipids $\rightarrow$ ↑ FFA, ↑ Chol, ↓ diester waxes
  ③ bacterial & yeast flora $\rightarrow$ altered species and ↑ numbers
a) Primary Seborrhea

• esp dogs; heritable / breed specific disorders of cornification

• clinical subtypes:
  ① seborrhea sicca
  ② seborrhea oleosa
  ③ seborrheic dermatitis

b) Secondary Seborrhea

• occurs with a multitude of unrelated disease processes
seborrhea sicca (dry)

seborrheic dermatitis

seborrhea oleosa (greasy)
NEOPLASTIC SKIN DISEASES

- most common site of neoplasia in most domestic species

**Etiopathogenesis**

- damage to the genome (UV light, viral, etc)
- influenced by genetics, hormones, etc

**Diagnosis**

- +/- distinct gross morphology and location
- definitive diagnosis by cytology / histology of biopsies
- occasionally requires cell markers (IHC) or EM
• Ectodermal: tumors of the epidermis and adnexa
• Melanocytic: tumors of melanocytic origin
• Mesodermal: tumors of mesenchymal or round cell origin
EPITHELIAL NEOPLASMS / TUMORS

Epidermal Tumors
Cutaneous horn of feline pawpad
Pawpad keratoma
Linear epidermal hamartoma
Dermoid cyst
Squamous papilloma
Viral papilloma
Canine pigmented viral plaque
Feline viral plaque
Actinic keratosis
Bowenoid in situ carcinoma
Squamous cell carcinoma
Basal cell carcinoma
Basosquamous carcinoma

Follicular Tumors
Follicular hamartoma
Fibroadnexal hamartoma
Follicular cyst
Dilated pore
Warty dyskeratoma
Trichofolliculoma
Trichoepithelioma
Infundibular keratinizing acanthoma
Tricholemmoma
Pilomatrixoma
Trichoblastoma
Malignant trichoepithelioma
Malignant pilomatrixoma

Sebaceous Tumors
Sebaceous duct cyst
Nodular sebaceous hyperplasia
Sebaceous hamartoma
Sebaceous nevus
Sebaceous adenoma
Sebaceous epithelioma
Sebaceous carcinoma
Nodular perianal gland hyperplasia and perianal gland adenoma
Perianal gland epithelioma
Perianal gland carcinoma

Sweat Gland Tumors
Apocrine cyst
Canine apocrine cystomatosis
Feline ceruminous cystomatosis
Apocrine cystadenoma
Apocrine secretory adenoma
Apocrine ductular adenoma
Apocrine secretory adenocarcinoma
Apocrine ductular carcinoma
Eccrine carcinoma

Nailbed Epithelial Tumors
Nailbed epithelial inclusion cyst
Nailbed inverted squamous papilloma
Nailbed keratoacanthoma
Nailbed squamous cell carcinoma
Nailbed basal cell carcinoma
Metastatic pulmonary carcinoma in cats
Squamous Cell Carcinoma (SCC)

- relatively common neoplasm
- strongly associated with UV light damage

**Gross:**
- location often head (eye / ear / nose); esp unpigmented areas
- firm, poorly demarcated mass, +/- ulcerated or proliferative / papillary
- locally invasive with tissue destruction & slow to metastasis

SCC’s develop in unpigmented areas and if untreated the primary tumor often becomes large / invasive / disfiguring (right)
SCC’s typically metastasize quite late and can become very large if left untreated.
Microscopically squamous cell carcinoma is characterized by downgrowth of proliferating cords and nest (asterisks) of neoplastic squamous epithelium; some of which have keratinized central areas.

Digital SCC’s often originate from subungual (nailbed) epithelium, and are usually solitary, ulcerative and expansile. They are locally invasive (ie 80% invade bone of P3) and have low to moderate metastatic potential.
Papilloma (warts)

- see in all domestic and many non-domestic animals
- most caused by host-specific and often site-specific papillomaviruses
- most undergo spontaneous regression; but some can progress to SCC

Gross:
- exophytic masses with finger-like fronds
**Papilloma (warts)**

**Histopath:**
- Proliferation of epithelium (squamous papilloma) or epithelium & fibroblasts (fibropapilloma)
- When viral induced → viral cytopathic effects +/- intranuclear inclusion bodies

*Squamous papilloma.*
Note extensive papillary proliferation of epithelium.
MELANOCYTIC NEOPLASMS

Melanocytoma / Melanoma

- common in dogs, gray horses, some swine breeds

**Gross**
- dark brown-black macules $\rightarrow$ papules $\rightarrow$ nodules $\rightarrow$ tumors

**Histopath**

Microscopically see proliferation of neoplastic melanocytes; most skin melanomas have at least some melanin (when compared to many in the oral cavity which are amelanotic)
# Melanocytoma / Melanoma

## Biologic Behaviour

1. **Dogs**
   - eyelid or skin (< 2 cm) → mostly benign*
   - skin (> 2 cm) or digits / nailbed or oral cavity → mostly malignant*

*use histologic criteria of malignancy

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**Fig 14-152 (Sm An Derm) Cutaneous Melanocytoma.** A pigmented nodule in close proximity to the nasal planum of an adult dog.

**Malignant melanoma from dog digit (Noah Archive).** Note, some melanomas have minimal to no pigment (amelanotic).
Melanocytoma / Melanoma

② Gray-White Horses
- common at 6 yrs, 80% in aged population (> 15 yrs)
- especially on perineum / genitalia
- most benign; occasionally show local invasion and metastasis to viscera

In most case the tumors are benign, ie melanocytomas

However in a few cases they are, or can progress to, malignancy, ie melanomas
Melanocytoma / Melanoma

Large black mass (ie melanoma) on shoulder region of pig.
1) MESENCHYMAL NEOPLASMS / TUMORS
(modified from Gross et. al, Skin Diseases of the Dog & Cat)

Fibrous Tumors
Collagenous hamartoma
Canine nodular dermatofibrosis
Acrochordon and acrochordonous plaque
Dermatofibroma
Nodular fasciitis
Fibroma
Canine keloidal fibroma
Fibrosarcoma
Myxoma
Myxosarcoma
Equine / Feline sarcoids

Vascular Tumors
Angiomatosis
Hemangioma
Lymphangiomatosis
Hemangiosarcoma
Lymphangiosarcoma

Perivascular Tumors
Glomus tumor
Hemangiopericytoma

Cutaneous soft-tissue sarcoma

Lipocytic Tumors
Lipomatosis
Lipoma
Spindle cell lipoma
Infiltrative lipoma
Liposarcoma

Smooth and Skeletal Muscle Tumors
Leiomyoma
Leiomyosarcoma
Canine skeletal muscle hamartoma
Rhabdomyosarcoma

Neural and Perineural Tumors
Traumatic neuroma
Merkel cell tumor
Benign peripheral nerve sheath tumor
Malignant peripheral nerve sheath tumor

Other Mesenchymal Tumors
Vaccine-induced sarcoma
Transmissible venereal tumor
Ganglion
Granular cell tumor
Anaplastic sarcoma with giant cells
Cutaneous Soft-tissue Sarcomas

- grouping of some spindle cell tumor types with similar behavior / prognosis
- common in dogs; less in cats, sporadic horses, rare in others

Gross

- firm to gelatinous, gray-white nodular masses
- single or multinodular, any site (esp limbs)
Biologic Behaviour

- locally invasive with frequent local recurrence (due to histologic microinvasion)
- behaviour correlates to anaplasia, esp mitotic count (low vs high grade)

Microscopically see variably dense aggregates of spindloid cells, often with whorling or “fingerprint” patterns.
Vaccine-associated sarcoma of cats

Firm nodular tumor developing at the site of prior vaccination
Vaccine-associated sarcomas (aka postvaccinal fibrosarcoma) are extremely invasive neoplasms with a high rate of local recurrence.

Microscopically, vaccine-associated sarcomas most often consist of interwoven bundles of neoplastic spindle cells with multinucleate tumor giant cells.

Vaccine-associated sarcoma of cats
Equine Sarcoid

- occult (flat) form
- verrucose (warty) form
- nodular form
- fibroblastic (proud flesh-like) form
Feline Sarcoid


Fig 20-27 (Miller) Feline sarcoid. Well-circumscribed nodule on face.

Feline sarcoid. Note the exophytic mass present on the nasal philtrum of this cat. Compend Contin Educ Vet. 2013; 35(7)
Lipoma

A particularly large lipoma in the hind limb of a dog
2) ROUND CELL NEOPLASMS / TUMORS

**Mast Cell Tumors**
Canine mast cell tumor
Feline mast cell tumor
Cutaneous mastocytosis

**Histiocytic Tumors**
Canine cutaneous histiocytoma
Reactive fibrohistiocytic nodule
Feline progressive dendritic cell histiocytosis
Histiocytic sarcoma

**Lymphocytic Tumors**
Epitheliotropic lymphoma
Non-epitheliotropic lymphoma
Cutaneous plasmacytoma
Cutaneous lymphocytosis
Chronic lymphocytic leukemia with cutaneous lesions
Mast Cell Tumor

- common in dogs (mean age 8 yrs)

**Gross**
- single or multiple, edematous nodular masses
- often hairless and ulcerated in late stages
**Mast Cell Tumor**

**Biologic Behaviour**

- most frequent potentially malignant skin tumor of the dog
- in dogs, behaviour correlates with histologic criteria of malignancy

Microscopically see proliferation of neoplastic mast cells with infiltration of many eosinophils (due to degranulation of neoplastic mast cells which contain inflammatory mediators including chemotactic factors for eosinophils)

Special staining is often helpful to confirm mast cells; note: metachromatic staining of mast cell cytoplasmic granules with toluidine blue stain.
Cutaneous histiocytomas are a common, benign, spontaneously regressing tumor, typically seen in young dogs.
Cutaneous lymphoma (lymphosarcoma) in a cow. One of the sporadic (non BLV associated) forms of bovine lymphoma.
Cutaneous lymphoma, mycosis fungoides variant, in a dog. In the skin epitheliotropic lymphoma is more common than non-epitheliotropic forms. Mycosis fungoides is the most common variant (shown here) which typically presents with early plaque-like tumors (above left), that progressively enlarge over a few months (below left) and then has lymph node (above right) and/or systemic involvement in the late stages. Note, the term epitheliotropic refers to the microscopic affinity of the tumor cells to infiltrate epithelium.