NORMAL STRUCTURE AND FUNCTION (background information only)
- the skin is the largest organ of the body and consists of the following components:
  1. **Epidermis**
     - is composed of several cell types, ie keratinocytes, melanocytes, Langerhans cells, Merkel cells.
  2. **Adnexa** (appendages of the skin)
     - hair, glands (sebaceous, apocrine, eccrine; also circumanal, tail, anal), claws / nails and hooves.
  3. **Dermis**
     - consists of **fibers** (collagen, reticulin, elastin), **ground substance** (glycosaminoglycans, proteoglycans), **cells** (fibroblasts, mast cells, histiocytes, smooth muscle), **vessels** (blood, lymph), **nerves**.
  4. **Hypodermis** (subcutis)
     - consists of **lipocytes** (panniculus adiposus, digital cushion), **fibers** (collagen, elastin), **vessels**, **nerves**.
- epidermis is continuously renewed (~22 days in dogs); keratinocytes arising from stem cells in the basal layer differentiate as they move through the spinous, granular & corneum layers and are then shed from the surface.
- **keratinocytes** are tightly bonded to each other by spot-like adhesion structures called desmosomes; the cell adhesion molecules desmogleins & desmocollins are the transmembrane components of desmosome.
  - the basal keratinocytes are adhered to the underlying basal lamina (basement membrane zone) by hemidesmomes; the basal lamina is attached to the underlying dermis by anchoring fibrils.
  - the thickness of the stratum spinosum is inversely proportional to the thickness of the hair coat; ie very thin epidermis in dogs and cats, thicker in horses and cattle and thickest in pigs and humans.
- **melanocytes** are typically scattered throughout the basal layer of the epidermis (& hair bulbs) where they inject melanin pigment granules into keratinocytes (& hair) to provide coloration and protection against UV-light.
- **Langerhans (dendritic) cells** are antigen processing & presenting cells scattered throughout the epidermis.
- **Merkel (tactile) cells** have both mechanoreceptor and neuroendocrine functions.
Hair
- hair is produced in hair follicles by matrix cells overlying the dermal papillae in the bulb region of the follicle.
- each hair shaft has an inner (medulla), middle (cortex), and outer (cuticle) layer.
- two main types of hair; ie long, coarse primary (guard) hairs of the outercoat and shorter, finer secondary hairs that form an undercoat.
- each primary follicle has an attached arrector pili muscle, sebaceous and apocrine gland, while secondary follicles may have only sebaceous glands.
- dogs & cats have compound follicles; varying numbers (ie 5-20 secondary to 1 primary follicle) and length of secondary follicles accounts for the breed variation of coats; eg compare coat of Doberman to Golden retriever.
- horses & cattle have evenly distributed simple primary follicles; pigs have simple follicles grouped in clusters.
- sheep have simple follicles in hair-growing areas and compound follicles in wool-growing areas.

The Hair Cycle
- hair growth is not continuous; it occurs in phases, ie anagen (growth), catagen (transition) & telogen (resting)
  - in anagen, hair is produced by mitosis of the hair matrix cells which surround the dermal papilla in the bulb.
  - catagen is a short regressing stage, which indicates the end of active growth and the formation of a “club” hair.
  - telogen is the resting stage, during which the non-growing club hair remains attached for a variable period of time before it falls out and is replaced by an underlying new anagen follicle.
  - average human head has 100,000 hairs with ~ 90% of head hair in anagen which can last for 2-6 yrs (genetically determined) and ~10% in catagen / telogen for 2-6 months (randomly distributed so you don’t notice loss of fifty to 100 club hairs per day).
  - in dogs, anagen can be 3-4 months in short-coated & 18 months in long-coated breeds; telogen phase can range in various breeds from months to years.
  - in dogs, and many other mammals, the hair cycle can be somewhat synchronized (ie shedding) which is influenced by genetics, photoperiod, temperature, nutrition, health status & hormones.
  - with severe illness many hairs can synchronously be “pushed” into telogen and then can be shed together; called telogen defluxion or telogen effluvium.
  - since hair is predominantly protein, malnutrition can cause a poor quality haircoat, ie dull, dry, brittle &/or thin.

GENERAL FUNCTIONS
① Enclosing barrier - prevents loss of especially water, and also electrolytes, macromolecules
② Protection - protective against physical, chemical, microbiological agents
③ Sensory perception - touch, temperature, pressure, pain, itch
④ Temperature & blood pressure regulation - via hair coat, sweat glands, blood vessels
⑤ Storage - water, electrolytes, vitamins (eg vit D production), fat, carbohydrates, proteins, etc
⑥ Adnexa - production of hair, claws / hooves, horn, etc
⑦ Pigmentation of skin & hair - provides UV protection and distinguishing coat coloration
⑧ Antimicrobial action - the surface has antibacterial and antifungal properties
⑨ Immunoregulation - skin cells (esp Langerhans cells & lymphocytes) provide immunosurveillance capability
⑩ Indicator - the skin can be an important indicator of general health / internal disease.

RESPONSE OF SKIN TO INJURY
Because the skin is the largest organ of the body and is in direct contact with both the external and internal environments, it is susceptible to a wide range of insults. The skin has a limited range of responses, thus histopathology of punch biopsies and other ancillary tests are often required to determine the etiology.
GROSS MORPHOLOGY OF SKIN LESIONS

Primary Lesions - are the direct result of the underlying disease process; most important diagnostically

a) Macule - a circumscribed, area of discoloration (e.g. pigmentation, hemorrhage) up to 1 cm in diameter.
b) Patch - a macule over 1 cm in size.
c) Papule - a small (<1 cm diameter) solid elevation of the skin.
d) Plaque - a larger, flat-topped elevation formed by the extension or coalescing of papules.
e) Nodule - a circumscribed, solid elevation >1 cm in diameter that usually extends into the deeper layers.
f) Tumor - a large mass (neoplasia implied) that may involve any structure of the skin or subcutis.
g) Cyst - an epithelial lined cavity in the dermis or subcutis containing fluid or semisolid material.
h) Vesicle - a well circumscribed, <1 cm diameter, elevation of the epidermis, filled with clear fluid.
i) Bulla - a vesicle (blister) >1 cm diameter.
j) Pustule - a small, circumscribed, pus filled elevation of the epidermis.
k) Abscess - a well demarcated fluctuant lesion resulting from dermal or subcutaneous accumulation of pus.
l) Wheal - a sharply circumscribed, raised lesion due to dermal edema; will blanch with pressure.

Skin Lesions That May Be Primary or Secondary

a) Scale - an accumulation of loose fragments (flakes / dandruff) of cornified skin;
   can be primary (e.g. primary seborrhea) or secondary (e.g. chronic inflammation).
b) Crust - accumulation of dried material (e.g. exudate, blood /serum, scale, medication) on skin surface;
   can be primary (e.g. zinc-responsive dermatosis) or secondary (e.g. self-trauma, pyoderma, etc).
c) Comedo - a hair follicle lumen plugged with cornified cells and sebaceous material;
   can be primary (e.g. Cushing’s disease) or secondary (e.g. demodecosis).

d) Abnormalities of hair
   Alopecia - partial to complete loss of hair (baldness); can be primary (e.g. endocrine disease, follicular dysplasia) or secondary (e.g. with self-trauma or inflammation).
   Hypotrichosis / atrichia - less hair than normal or absence of hair (i.e. failure to develop).
   Effluvium / defluxion - excessive shedding or falling out of the hair.
   Hypertrichosis (hirsutism) - excessive growth of hair.

e) Abnormal Pigmentation or Coloration
   Red (erythema) - inflammation / vasodilation
   Black - melanoderma (hypermelanosis) / melanotrichia
   White - leukoderma / leukotrichia / hereditary hypopigmentation (e.g. albinism)
   Red-purple-brown-black - macular hemorrhage < 1 cm (petechiae /purpura); > 1 cm = ecchymoses
   Yellow - icterus
   Blue - cyanosis

Secondary Lesions - evolve from primary lesions, via self-trauma, altered keratinization, etc.
a) Epidermal collarette - a circular rim of keratin flakes following loss of the “roof” of a vesicle or pustule.
b) Erosion - a shallow epidermal defect that doesn't penetrate the basal laminar zone; heals without scarring.
c) Ulcer - a break in the epidermis with exposure of the underlying dermis; usually heals with a scar.
d) Excoration - erosions or ulcers caused by scratching, biting or rubbing, usually due to pruritus.
e) Scar - an area of fibrous tissue that has replaced the damaged dermis and/or subcutis.
f) Fissure - a linear cleavage of usually thickened, inelastic skin.
g) Lichenification - a thickening and hardening of the skin with exaggeration of the superficial markings.
h) Callus - a thickened, rough, alopecic, lichenified plaque that develops on the skin.
DISTRIBUTION OF SKIN LESIONS
Regional location and symmetry or asymmetry of skin lesions are important diagnostic aids.

AGE, BREED AND SEX PREDISPOSITIONS OF SKIN DISEASES
Many dermatologic disorders have predispositions:
    - **Age** (eg demodecosis, juvenile cellulitis),
    - **Breed** (eg primary seborrhea of Cocker spaniels, skin fold pyoderma of Shar pei’s)
    - **Sex** (eg estrogen-responsive or testosterone-responsive dermatoses).

VOCABULARY OF DERMATOHISTOPATHOLOGY (for information only)

**Epidermal Changes**
- **Hyperkeratosis** - increased thickness of stratum corneum; ortho- (anuclear) or para-keratotic (nucleated).
- **Epidermal hyperplasia** (acanthosis) - increased thickness of the noncornified epidermis.
- **Epidermal atrophy** - decreased thickness of the noncornified epidermis.
- **Intracellular edema** - cell damage leading to hydropic (vacuolar) or ballooning degeneration.
- **Intercellular edema** (spongiosis) - accumulation of edema fluid in the intercellular spaces.
- **Acantholysis** - loss of cohesion between epidermal cells leading to clefts, vesicles / bullae or pustules.
- **Exocytosis** - migration of inflammatory cells through the intercellular spaces of the epidermis.
- **Pustule (microabscess)** - microscopic or macroscopic cavities filled with inflammatory cells.
- **Crust** - surface accumulations of varying combinations of keratin, serum, cell debris, bacteria, etc.
- **Necrosis / apoptosis** - microscopic forms of keratinocyte death.
- **Dyskeratosis** - premature or abnormal keratinization in the viable layers of the epidermis.
- **Hyper- & hypopigmentation** - excessive or decreased amounts of melanin within the epidermis.

**Dermal Changes**
- **Dermal edema** - see widened spaces between dermal collagen, perivascular edema or lymphatic dilation.
- **Collagen changes** - including hyalinization, degeneration, mineralization, etc.
- **Fibroplasia / fibrosis / sclerosis** - formation and maturation of fibrous tissue, leading to scarring.
- **Pigmentary incontinence** - melanin granules free within the dermis or within dermal macrophages.
- **Follicular changes** - include atrophy, dilation, keratosis, dysplasia, inflammation, etc.
- **Glandular changes** - include inflammation, atrophy, hyperplasia, cystic change, etc.
- **Vascular changes** - include fibrinoid degeneration, vasculitis, thromboembolism, etc.

**Subcutaneous Fat Changes**
A variety of reactions (inflammation, necrosis, fibrosis, etc) can occur from the direct extension of similar changes in the overlying dermis or can occur in isolation from changes in the overlying skin.

HISTOPATHOLOGIC PATTERN-ANALYSIS
Dermatitis is not a particularly useful term from a diagnostic or therapeutic point of view, since the skin becomes inflamed in response to a myriad of causes. A method of pattern-analysis (at low magnification) of skin lesions has proved useful in relating inflammatory patterns to various types of skin diseases. With the addition of details observed at higher magnification, a specific diagnosis can often be made.
1) **Perivascular (Interstitial) Dermatitis**
   - the predominant inflammatory reaction is centered on the superficial and/or deep dermal vessels.
     1. **Perivascular (interstitial) dermatitis** (ie no significant epidermal changes)
        - especially hypersensitivities and urticaria.
     2. **Spongiotic perivascular (interstitial) dermatitis** (ie with epidermal spongiosis)
        - especially hypersensitivities, contact dermatitis, ectoparasitism, viral, dermatophytosis, Malasseziasis, etc.
     3. **Hyperplastic perivascular (interstitial) dermatitis** (ie with epidermal hyperplasia and hyperkeratosis)
        - common chronic dermatitis reaction of many causes which is mostly non-diagnostic.
        - seen especially in chronic hypersensitivities, altered keratinization, lick dermatitis, etc.

2) **Interface Dermatitis**
   - obscuring of the dermoepidermal junction by hydropic degeneration / apoptosis &/or a lichenoid infiltrate.
   - seen with a variety of immune-mediated and/or autoimmune skin diseases, drug reactions, some viral infections

3) **Vasculitis**
   - seen with a variety of infections (eg septicemias, RMSF, Equine viral arteritis), immune-mediated disease (eg drug reactions) and others; can be neutrophilic, lymphocytic, eosinophilic or mixed.

4) **Nodular and Diffuse Dermatitis**
   - can be granulomatous, pyogranulomatous, neutrophilic, eosinophilic, or mixed.
   - especially due to traumatic implantation of foreign material (eg hair, plant material) or a wide variety of bacteria, fungi or protozoa.
   - for identification of specific agents use polarization, special stains and microbial culture.

5) **Intraepidermal or Subepidermal Vesicular and Pustular Dermatitis**
   - vesicles are fragile and transient (esp in dogs & cats)
   - vesicles often evolve rapidly into pustules.
   - intraepidermal vesicles/pustules can result from:
     1. acantholysis (eg. neutrophilic proteolytic enzymes in bacterial infection, pemphigus autoantibodies)
     2. coalescing ballooning degeneration in viral dermatitis (eg pox viruses, vesicular viruses)
     3. intense intracellular and/or intercellular edema of the epidermis (with any severe dermatitis)
   - subepidermal vesicles can result from:
     1. genetically defective or autoimmune attack of adhesion molecules of D/E junction (eg bullous pemphigoid)
     2. severe subepidermal edema and/or cellular infiltration damaging the D/E junction (eg urticaria, cellulitis)

6) **Perifolliculitis / Folliculitis / Furunculosis**
   - especially due to bacteria (esp Staphylococcus), fungi (esp ringworm) or parasites (esp demodex).
   - **sebaceous adenitis, hidradenitis and bulbitis** are other occasional types of adnexal inflammation.

7) **Panniculitis** (inflammation of the subcutis)
   - is often an extension an overlying nodular or diffuse dermatitis with similar inflammatory cell types.
   - other specific causes include nutritional steatitis, injection reactions and idiopathic.

8) **Atrophic Dermatosis**
   - usually due to endocrine disorders and less frequently nutritional or developmental dermatoses.
   - see varying combinations of orthokeratotic hyperkeratosis, epidermal melanosis, sebaceous gland atrophy, and follicular changes indicative of hair cycle arrest and/or atrophy (eg telogen predominance without hair shafts, dilation & keratin plugging of follicles, follicular atrophy).
Superficial perivascular dermatitis

Spongiotic perivascular dermatitis

Hyperplastic perivascular dermatitis

Interface dermatitis with hydropic degeneration and lichenoid infiltrate

Vasculitis

Nodular dermatitis

Diffuse dermatitis

Intraepidermal vesicular and pustular dermatitis

Subepidermal vesicular and pustular dermatitis

Perifolliculitis

Folliculitis

Furunculosis

Panniculitis

Atrophic dermatosis
CONGENITAL AND HEREDITARY SKIN DISEASE

- note the difference between the terms **congenital** (present at birth; can be hereditary or acquired), **hereditary** (genetically determined) and **acquired** (environmental, eg viral, toxic, etc).

1. **Congenital Hypotrichosis**
   - reported in all domestic species (variety of heritable syndromes in many breeds), but most common in calves.
   - absence of hair follicles or abnormal follicular development (follicular dysplasia).

   **Cattle:**
   - **hereditary** - several modes of inheritance in different breeds.
   - **acquired** - causes include: intrauterine BVD infection, iodine deficiency and goitre, adenohypophyseal hypoplasia in Guernsey and Jerseys and maternal ingestion of *Veratrum album*.
   - rule-out:
     1. **Telogen effluvium (defluxion)** - various stresses (eg febrile illness, parturition, surgical shock) can prematurely push many hairs into the telogen phase with subsequent massive shedding of hair.
     2. **Anagen effluvium (defluxion)** - damage to and rapid loss of hair in the anagen stage of growth due to chemotherapy, radiation or catastrophic disease.

   **Dogs and Cats:**
   - several hereditary forms of hypotrichosis have been reported.
   - some forms have been selected for, eg Chinese Crested and Mexican Hairless dogs and Sphinx cat.

2. **Hereditary Collagen Dysplasia (for information only)**
   - known by several names, ie Ehlers-Danlos syndrome, dermatosparaxis, cutaneous asthenia, etc.
   - is the most commonly recognized connective tissue disorder reported in humans and most domestic species.
   - collagen is the major structural component of the dermis and abnormalities in collagen results in changes that vary from hyperextensibility to skin that is easily torn with routine handling, play with littermates, scratching.
   - light microscopic changes in dermis (eg thin, pale, haphazardly arranged collagen fibers) are seen in some cases, but diagnosis usually requires electron microscopic examination.

3. **Mechanobullous disease / Epidermolysis bullosa (for information only)**
   - inherited structural defects in the basement membrane zone (BMZ) leads to blistering (bullae) and ulceration of the skin and mucus membranes.
   - three broad groups seen in humans, ie **epidermolysis bullosa simplex** (defect in cytokeratins 5 & 14 of basal cells), **junction epidermolysis bullosa** (defect in anchoring filament-hemidesmosome complexes), and **dystrophic epidermolysis bullosa** (defect in anchoring fibrils)
   - these groups of EB are rarely seen in various domestic animals, for example junctional epidermolysis bullosa has been reported in dogs and horses (esp Belgians).

4. **Some Other Congenital / Hereditary Skin Diseases (for information only)**
   - **Ichthyosis in many species**
   - **Pattern Baldness of dogs / Alopecic Breeds**
   - **Canine Dermatomyositis**
ENVIRONMENTAL INDUCED SKIN DISEASE

1. Actinic (Sun) Injury
- the amount of light reaching skin is determined by:
  1. Environmental Factors
  2. Host Factors
- visible light range is ~ 400-700 nm; longwave UV is ~ 320-400 nm (UV-A), damaging portion is by middlewave UV ~ 290-320 nm (UV-B) which represents ~ 1% of the light reaching the skin.
- ozone strongly absorbs shortwave UV < 290 nm (UV-C) which is very damaging.
- UV-B light energy is absorbed by some molecules in the skin → electron transfer with the generation of free radicals → damage to nucleic acids, proteins & lipid membranes → cell injury / death.
- also causes mutagenesis (tumorigenesis)
  1. pyrimidine dimer formation has been shown to occur in mutation “hot spots” on P53 gene (tumor suppressor gene) in basal epidermal cells.
  2. cells with mutated P53 have an impaired ability to: i) delay replication until any DNA damage is repaired, and ii) undergo apoptosis when DNA is damaged beyond repair.
  3. UV can also be a promoter, in that health cells which are damaged by UV light and undergo apoptosis, can be preferentially replaced by cells with mutated P53 (which are resilient to UV induced apoptosis).

2. Sunburn and Solar Dermatosis / Dermatitis
- due to:
  1. direct endothelial damage
  2. damage to keratinocytes with release of inflammatory mediators.
- acutely see initial redness (sunburn erythema), followed by pain, ± edema, blistering, etc
- chronically see thickened inflamed skin (solar dermatitis) with possible development of dysplasia / neoplasia.

2. Photosensitization
- when photodynamic substances in skin are activated by UV-A (normally not harmful) or visible light.
- the absorbed energy creates free radicals which damage the skin.
  1. Type I - exogenous origin of photodynamic agents, especially certain plant toxins and drugs
  2. Type II - aberrant endogenous heme pigment synthesis, ie porphyrias
  3. Type III (hepatogenous type) - failure to remove phylloerythrin a photoreactive metabolite of chlorophyll
  4. Type IV - unknown etiology / pathogenesis
- gross lesions occur in areas with poorly pigmented hair & skin (ie white haired regions) or where hair coat is sparse; initially see edema with possible vesicles / bullae followed by exudation, necrosis and sloughing.

II. Chemical Injury
Local application - agent must penetrate hair & stratum corneum; enhanced by moisture &/or skin damage.
Systemic absorption - ingestion of toxins with systemic effects on the skin and usually other organs.

1. Primary Contact Irritant Dermatitis
- skin contact by substances expected to cause irritation, ie caustic chemicals (eg acids, alkalies), concentrated drugs (eg insecticides), soaps/detergents, body excretions (eg anal sac, urine), etc.

2. Some Other Chemically Induced Skin Diseases (for information only)
  Gangrenous Ergotism and Fescue Toxicosis
  Inorganic poisons, eg thallium, selenium, mercury, arsenic, etc
III. Physical Injury

1. Acral Lick Dermatitis
   - a relatively common psychogenic dermatitis of dogs, especially large active breeds and often young (< 5 yrs).
   - focal self-trauma, typically found on the dorsal surface of a distal limb region.
   - see a well delineated, plaque of alopecia and ulceration; often see peripheral hyperpigmentation during healing.

   Etiopathogenesis
   - psychogenic disorders (ie emotional / psychological); similar to obsessive-compulsive disorders of humans
   - usually results from: ① boredom - alone during day.
     ② anxiety - new home, pet, baby, etc. / loss of companion, etc. / any other stress.

2. Some Other Physically Induced Skin Diseases (for information only)
   Abrasion, Laceration, Ulceration and Foreign Bodies
   Extremes in Temperature - cold (frostbite) vs thermal injury (eg flame, scald, electrical, lightning, etc)
   Callus / Hygroma
   Feline psychogenic dermatitis (one cause of feline symmetric alopecia)
   Radiation

INFECTIOUS SKIN DISEASE

I. Viral Skin Diseases

1) Local viral infection of the skin
   - intact skin is resistant to locally infecting viruses (eg papillomaviruses & parapoxviruses).
   - local infection requires abrasion or arthropod bite for the virus to gain entry into the skin.

① Contagious pustular dermatitis [= Contagious ecthyma = "Orf"]
   - a common parapoxvirus infection (world wide distribution) in young sheep & goats.
   - occasionally affects humans, cattle, dogs, others.

   Etiopathogenesis
   - typical pox phases (ie hydropic / ballooning degeneration of keratinocytes with cytoplasmic inclusion bodies → vesiculation → intraepidermal pustules → crust); but is much more proliferative (hyperplastic) than most other poxvirus infections.
   - lesions most commonly on the lips, especially commissures of mouth (initiated by abrasions from pasture / forage), may see involvement of eyelids / feet / oral cavity and rarely GI tract / viscera.

2) Systemic viral infection with skin involvement
   - more common are viral infections that target the skin in the viremic phase of a systemic infection.
   - eg’s: ① epitheliotropic viruses, eg poxviruses, vesicular viruses (FMD, VS, VE, SVD), BVD / MCF
     ② pantropic viruses, eg canine distemper, hog cholera
     ③ other, eg pruritus caused by scrapie or pseudorabies

   Diagnosis
   - history & clinical signs / lesions.
   - skin biopsy - mostly vesicular to pustular dermatitis, ± viral inclusion bodies.
   - serology / virus isolation / virus identification (eg PCR, EM)
Some other Viral Dermatitides (for information only)

DOGS
Canine papillomavirus - (see Neoplasia)
Canine distemper virus - dogs (also wolf/coyote, ferret/mink, raccoon, others)

CATS
Feline Herpesvirus 1

CATTLE
Bovine mammallitis virus (bovine herpes 2)
Lumpy skin disease (caused by LSD virus, capripoxvirus)
Bovine papillomavirus - (see Neoplasia)

SHEEP & GOATS
Sheeppox and Goatpox

SWINE
Swinepox (Suïspox): common, cosmopolitan, usually mild

HORSES
Equine molluscum contagiosum
Equine papillomavirus (see Neoplasia)

II. Bacterial Skin Diseases (Pyoderma)

Etiopathogenesis
• healthy skin is resistant to infection by pathogenic bacteria because of:
  1. lack of moisture
  2. stratum corneum forms an impermeable barrier that undergoes continuous desquamation
  3. antibacterial substances in sebum / sweat and competitive inhibition by normal skin microflora
• factors assisting bacterial colonization / proliferation include:
  1. moisture and dirt lead to dilution of lipid barrier and abrasion of cornified layer
  2. altered cornification (eg seborrhea, endocrine skin diseases)
  3. physical damage (eg parasites or allergies ➔ self-trauma, etc.)
• result then depends on pathogenicity of the agent and the defense mechanisms of the host.
• bacterial skin diseases are common in dogs, especially when compared to other species.

Diagnosis
• history & clinical signs / lesions.
• bacterial culture
• skin biopsy

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<th>PRIMARY PYODERMA</th>
<th>SECONDARY PYODERMA</th>
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<tbody>
<tr>
<td>SKIN</td>
<td>otherwise healthy (esp young)</td>
<td>not healthy (eg parasites, etc)</td>
</tr>
<tr>
<td>BACTERIA</td>
<td>one species</td>
<td>&gt; one species</td>
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<tr>
<td>PATTERN</td>
<td>characteristic</td>
<td>not characteristic</td>
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<tr>
<td>ANTIBIOTICS</td>
<td>successful</td>
<td>not successful</td>
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A Small Selection of Bacterial Dermatitides

CANINE

1 Pyotraumatic dermatitis ("hot spots" or "acute moist dermatitis")
- a rapid onset superficial pyoderma due to intense pruritus (esp fleas; also other parasites, allergies, etc) → self-trauma → secondary bacterial infection.

2 Impetigo
- a primary superficial pustular dermatitis that occurs mostly commonly in dogs (ie puppy pyoderma), especially due to coagulase-positive Staphylococcus, occasionally Streptococcus.
- predisposing factors include, moist / dirty environments, abrasions, parasitism, poor nutrition.

3 Skin fold pyoderma (Intertrigo)
- predisposed by friction / moisture in skin folds, eg’s facial, lip, vulvar, tail-fold and body-fold dermatitis.

FELINE

Subcutaneous Abscesses
- especially bite wounds in cats (P. multocida, β Streptococcus, Bacteroides spp, etc).

RUMINANTS

1 Papillomatous Digital Dermatitis ("hairy heel warts")
- initially an erosive / ulcerative plaque-like lesion, which is intensely painful and progresses to a proliferative / papillomatous (with long, thin papillae), less painful lesion bordering the interdigital space at back of foot.
- thought to be polymicrobial; see increased numbers of intralesional spirochetes (esp Treponema spp)

2 Dermatophilosis (cutaneous streptothricosis, strawberry foot rot, rain scald, etc)
- a superficial exudative dermatitis due to D. congolensis, especially ruminants & horses; rare in dogs, cats, etc.
- seen worldwide, but most common in hot, humid regions with heavy rainfall.

HORSES

Staphylococcal Folliculitis / Furunculosis
- usually secondary to trauma; seen especially in saddle & tack areas.
- typically see papules that may enlarge to nodules (~1cm) often with a central ulcer that can discharge exudate.
- also one cause of “pastern dermatitis”, a dermatitis affecting the caudal aspect of the pastern / fetlocks.
PORCINE

1. Exudative Epidermitis (Greasy Pig Disease)
   - an acute, rapidly spreading, often fatal exudative superficial pyoderma seen in suckling to weaners (5-35 days).

Etiopathogenesis
   - infection with *Staphylococcus hyicus*, which contain several exfoliative exotoxins.
   - predisposing factors include: ① immature protective mechanisms
     ② skin abrasion
     ③ poor nutrition
     ④ concurrent infections

2. Bacterial sepsis
   i) *Salmonella* - lesions are the result of endotoxemia (ie venous thrombosis / infarction of extremities).
   ii) "Diamond Skin Disease" (usually Swine Erysipelas, rarely *Actinobacillus suis*) - lesions are the result of localized vasculitis and thrombosis.

III. Mycotic Skin Diseases

Diagnosis
   - history & clinical signs / lesions.
   - fungal identification (UV light, direct exam, smears) and/or culture.
   - skin biopsy.

1. Cutaneous (Superficial) Mycoses - restricted to keratinized tissues, ie stratum corneum, hair, nails.

   ① Dermatophytosis (Ringworm)
      - common in all domestics (esp cats and cattle; zoonotic), worldwide but especially in hot, humid environments.
      - can see classical expanding circular patches of scaling / alopecia to papules / pustules / furunculosis / crusting.
      Etiopathogenesis
      - due to infection with keratinophilic fungi, primarily in the genera of *Microsporum* or *Trichophyton*; (note, *Epidermophyton spp* are adapted to humans and rarely infects animals).
      - young animals are more susceptible and severe disease occurs in immunocompromised animals.
      - predisposing factors: overcrowding, high humidity, poor sanitation and poor nutrition.
      - highly contagious; transmission of infectious arthrospores can be direct or by fomites (esp. stabled animals).
      - attacks keratinized layers with enzymes (keratinase, collagenase, and elastase) and an inflammatory reaction develops to these proteases as they diffuse into the adjacent dermis.

   ② Malasseziasis
      *Malassezia pachydermatis* is a yeast of the normal microflora and its overgrowth associated with dermatitis is thought to be secondary to underlying skin disease, eg allergies, seborrhea, etc (similar to secondary pyoderma)
      - grossly see erythema, alopecia, scale, greasy (rancid odor); if chronic see lichenification & hyperpigmentation.

   ③ Candidiasis (*Candida* spp)
      - rare opportunistic skin infection, especially when immunocompromised or on long-term antibiotics.

   ④ Cutaneous Mycoses of Wildlife
      - in the last several years there has been an emergence of several important cutaneous mycoses of wildlife, many of which are causing serious population declines.
      - some important eg’s: *Chytridiomycosis* of frogs & salamanders
        *White-nose syndrome* of bats
        *Snake fungal disease*
2. Subcutaneous Mycoses

- infections of the skin / subcutis typically due to traumatic implantation of a wide variety of saprophytic fungi.
- some lesions are caused by specific agents and others caused by a group of related agents; eg’s
- terminology for the subcutaneous mycoses can be contradictory, confusing, and frequently changing, eg’s:
  - **Eumycotic mycetoma** (see clinical triad of tumefaction, draining tracts, and tissue grains), **Chromomycosis** (pigmented fungi), **Pythiosis** (eg Florida horse leeches), **Sporotrichosis**, etc.

3. Systemic Mycoses

- systemic fungal infections which can involve the skin (esp Blastomycosis & Cryptococcosis).
- frequently seen in animals with compromised resistance to infection.

IV. PARASITIC SKIN DISEASES

- ectoparasitism (live on body surface) vs. endoparasitism (live within the body).
- note, infestation (cutaneous habitation by ectoparasites) vs infection (invasion and multiplication of microorganisms in tissues, causing cell damage and inflammation).
- parasites cause disease directly by:
  1. inflammation → pruritus / self-trauma, ± hypersensitivity reaction
  2. blood sucking → eg fleas & ticks
  3. toxin injection → eg. tick paralysis
     - results in: annoyance, reduced production and unthrifty / blemished hides.
- parasites cause disease indirectly by:
  1. important vectors of a wide variety of agents; viruses (eg WNV), rickettsia (eg RMSF), bacteria (eg Lyme disease), protozoa (eg Leishmaniasis) and helminths (eg dirofilariasis).
  2. predisposing to pyoderma, myiasis or local viral infections.

Diagnosis

- history & clinical signs (esp pruritus) / lesions
- parasite identification (eg. visual exam, scrapings)
- skin biopsy

1. Mites

   ① Demodectic Mange (Demodicosis)
   - seen mainly in dogs (breed/familial predispositions); occasionally in other species.
   - **Etiopathogenesis**
   - *Demodex spp.* are part of the normal microfauna of most species; transmitted from dam to neonates.
   - see disease in dogs with genetic predisposition and selective or partial states of immunodeficiency.
   - ① **Localized form** - young dogs, 3-10 months, usually self-limiting.
     - 1 to 5 patchy areas of alopecia, with variable erythema, scaling & hyperpigmentation.
   - ② **Generalized form** - in juvenile dogs; ~ 10% with localized form progress to generalized form.
   - when see demodicosis in older dogs (> 1yr), usually have serious internal disease &/or immunosuppression.
   - on histology see massive proliferation of mites → perifolliculitis / folliculitis / furunculosis, 2° pyoderma.

   ② Sarcoptic Mange (Scabies)
   - most frequent in pigs > dogs > ruminants, horses; little breed or age predisposition.
   - **Etiopathogenesis**
   - highly contagious, host-adapted varieties (eg. *S. scabiei var. suis; var. canis*, etc).
   - people readily parasitized by animal adapted species, but these don't usually complete life cycle.
   - in normal host, male and females mites mate near surface then females burrow deeper and lay eggs.
• lesions due to:
  1. mechanical damage from burrowing in epidermis
  2. irritation from mite saliva and excreta
  3. severe self-trauma due to hypersensitivity to mite products
• the variability in individual reactions relate to the degree of the hypersensitivity response and the ability hosts immune response to limit mite replication (ie chronic, severe scabies seen in immunosuppressed individuals).
• initially see erythematous macules / papules / scale; with pruritus see excoriations / alopecia / hemorrhagic crusts; chronically lichenification / crusting.

3. Some other mites
   Notoedric Mange (Notoedres cati) - primarily cats ("Feline Scabies") and rabbits
   Cheyletiellosis (Cheyletiella spp) - so-called “walking dandruff” seen primarily cats, dogs, and rabbits
   Otodectic Mange (Otodectes cynotis) - ear mite of carnivores
   Psoroptic Mange (Psoroptes sp) - many species, especially ears of goats and rabbits
   Chorioptic Mange (Chorioptes spp) - ruminants and horses
   Psorergatic Mange (Psorergates ovis) - of sheep
   Trombiculidiasis - "chiggers"- larvae of trombiculid mites

2. Ticks
   • two families:
     1. Hard ticks (Ixodidae)
        - most of pathogenic species, eg Ixodes spp. (Lyme disease vector), Rhipicephalus spp, Dermacentor spp
     2. Soft ticks (Argasidae)
        - contains the “spinose ear-tick” (Otobius megnini) and many important bird ticks.
   • are important as vectors for many viral, bacterial & protozoal diseases of domestic animals.
   • also cause disease by local damage (+/- secondary infections or hypersensitivity reactions), anemia (from bloodsucking) or paralysis (some have neurotoxin in saliva).

3. Fleas
   • the single most important cause of skin disease in small animals.
   • in dogs and cats Ctenocephalides felis most common, also C. canis.
   • flea infestation can cause skin irritation / pruritus, anemia (esp puppies & kittens), vectors for infectious agents (eg tularemia, bubonic plague) and hypersensitivity reactions.
   • in dogs and cats, can be clinically manifest as:
     1. asymptomatic carriers
     2. flea-bite dermatitis (papular / crusting dermatitis, ± pruritus / self-trauma)
     3. flea allergy dermatitis (see Immune-mediated skin disease)

4. Lice (Pediculosis)
   1. Sucking lice (eg Linognathus spp., Hematopinus spp.) feed on blood and tissue fluids.
   2. Biting lice (eg Damalini spp., Trichodectes spp.) feed on exfoliated epithelium and debris.

5. Flies
   • flies can cause disease by annoyance (“fly-worry”), localized skin damage / pruritus, +/- hypersensitivity, anemia, direct toxicity (eg black fly toxin), vectors for infectious agents and myiasis.
   1. Fly bite dermatitis - due to biting flies (eg horse flies, horn flies, stable flies, black flies, etc)
   2. Myiasis = the infestation of living animal tissues with fly larvae (maggots / grubs).
Warbles (*Hypoderma*)
- primarily cattle; occasionally horses and others.
- eggs laid on hair (esp legs) → larva burrow into skin → migrate & overwinter in epidural fat or esophagus → in spring migrate to subQ along back & form nodules → mature larvae emerge & pupate on soil.

Cuterebriasis
- typically small wild mammals (rodents, rabbits), but occasionally infest cats and others.

Screwworm myiasis
- obligate parasites that invade the edges of fresh, uncontaminated wounds.

6. Helminth Disease

1. Cutaneous larval migration
   - adults live in non-cutaneous sites while larval stages migrate through skin.

Cutaneous Habronemiasis (“summer sores”)
- common disease in horses due to aberrant deposition & migration of *Habronema* & *Draschia spp* larvae.
- larvae normally deposited near mouth by flies → swallowed and complete life cycle in the stomach.
- when larvae deposited on moist skin (esp eyelid or prepuce) &/or wounds by house or stable fly → larval migration results in an ulcerative papular to nodular dermatitis.
- often require biopsy / histology since gross lesions can look like squamous cell carcinoma, ulcerated sarcoid, exuberant granulation tissue, etc
- histologically see eosinophilic granulomatous inflammation which often contain segments of *Habronema* larvae within areas of necrosis.

Others: Hookworm dermatitis in dogs and ruminants, Pelodera dermatitis in dogs, ruminants, horses, Strongyloidiasis ruminants and horses, Parelaphostrongylosis of goats, etc

2. Filarial Dermatitis
   - adults or microfilaria spend some time in the skin.
   - eg’s: Onchocerciasis - in horses, Stephanofilariasis of ruminants, Dirofilarial dermatitis in dogs, etc

7. Protozoal Diseases
   - Leishmaniasis in humans, dogs, rodents and others
   - Sarcocystosis in cattle
   - Besnoitiosis in wild ungulates, cattle and horses

IMMUNE-MEDIATED SKIN DISEASE

1. Hypersensitivity Reactions
   **Definition**
   - a reaction that develops in response to normally harmless foreign compounds (ie exogenous antigens).
   - most cutaneous HS's are mediated by types I &/or IV HS reactions.
   - pruritus is a feature common to most HS's.
   **Diagnosis**
   - history and clinical signs (esp pruritus) / lesions.
   - skin biopsy (often non-specific; compatible with many HS's and/or other etiologies).
   - intradermal skin testing, elimination of offending antigens and/or clinical response to therapy.
1. **Atopic Dermatitis**
   - **Etiopathogenesis**
     - complex type I (and some type IV) HS to normally innocuous environmental antigens
     - current evidence supports an epidermal barrier dysfunction that results in a variety of predominately transepidermally absorbed allergens (eg house dust mites, pollen).
     - subsequent immune response with switching from $T_1$ to $T_2$ production of proinflammatory cytokines (eg IL-31) and overproduction of specific IgE (mast cell degranulation / inflammatory mediator synthesis).
   - **Gross**
     - primary lesions not seen; secondary lesions are due to self-trauma: erythema, excoriation and alopecia; over time develop hyperpigmentation and lichenification.
     - starts on face, feet, ventral abdomen, perineum; with chronicity can become generalized.
   - **Histology (non-diagnostic)**
     - early: superficial perivascular dermatitis, often just edema. (non-specific!)
     - later: hyperplastic perivascular / interstitial dermatitis
     - changes are often complicated by secondary pyoderma &/or Malasseziasis.
   - **Differential Diagnosis**
     - especially other allergies (flea, food, etc.) and ectoparasitism (scabies, fleas, etc.).

2. **Flea-bite hypersensitivity** *(Flea Allergy Dermatitis)*
   - most common hypersensitivity of cats & dogs in flea-endemic regions.
   - **Etiopathogenesis**
     - mediated by combination of types I & IV HS reactions to antigens in flea saliva.
     - once sensitized, few fleas are needed to initiate severe reaction.
     - intense pruritus ~ self-trauma / secondary infections.
   - **Gross**
     - primary lesion is an erythematous papule or wheal, however self-trauma quickly leads to alopecia, excoriations and crusts; with chronicity see hyperpigmentation and lichenification.
     - in dogs, lesions usually on lumbosacral regions, caudomedial thighs and caudoventral abdomen; can become generalized in severely affected individuals.
     - in cats, lesions (esp crusted papules = so-called "Miliary Dermatitis") usually occur on head and neck but in some cases see alopecia along trunk and lumbosacral regions associated with excessive grooming.
   - **Histology (non-diagnostic)**
     - perivascular / interstitial dermatitis with predominance of eosinophils & mast cells early and mononuclear inflammatory cells later.
     - may see spongiotic perivascular dermatitis with eosinophils; +/- eosinophilic microabscesses (flea nibbles).

3. **Food Hypersensitivity** *(Cutaneous adverse food reaction)* *(for information only)*
   - reported to be the third most common hypersensitivity of dogs; relatively common in cats as well.
   - suggested IgE-mediated HS reaction to food allergens (eg beef, soy, chicken, wheat, dairy/egg, etc).
   - the most consistent clinical sign is pruritus; can be localized (esp face/ears/feet/perianal) or generalized.
   - primary lesions in dogs are erythema, papules, urticaria/angioedema; often quickly obscured by self-trauma, ie alopecia, excoriations, scale/crust; and with chronicity hyperpigmentation / lichenification.
   - in cats, can see similar lesions &/or miliary dermatitis; esp on head / face.
   - as with other allergies, the histology is non-diagnostic, see superficial perivascular / interstitial dermatitis, often spongiosis, often mixture of eosinophils & mononuclear inflammatory cells.
4. Some Other Hypersensitivity Reactions (for information only)

Urticaria (hives or wheals) / Angioedema (edematous swellings)

Allergic Contact Dermatitis [Contact HS]

Equine Insect (Culicoides) Hypersensitivity

II. Autoimmune Reactions

- diseases that develop when autoantibodies or T cells react against self rather than foreign antigens.
- autoimmune diseases are relatively rare in domestic animals, seen in dogs > horses, cats > others.
- most have a hereditary predisposition with some likely triggering factors, eg underlying neoplasia, drug therapy, infections, tissue injury.

1. Pemphigus

- autoantibodies to desmosomal proteins (esp desmogleins & desmocollins) → loss of cohesion (acantholysis) & activation of inflammatory mediators → neutrophilic infiltration → intraepidermal pustules.
- grossly in pemphigus foliaceus (PF), the most common form, see fragile pustules which rupture to form scale/crust & in the rare pemphigus vulgaris (PV) see vesicles/bulla which rupture to form erosions/ulcers.
- histologically, see subcorneal to intragranular pustules with numerous acantholytic cells in PF and suprabasilar vesicles / bullae with few acantholytic or inflammatory cells in PV.
- diagnosis typically confirmed by demonstration of intercellular deposition of IgG within the epidermis

2. Discoid (cutaneous) lupus erythematosus

- postulated that UV light alters keratinocyte Ag’s → autoimmune response → interface dermatitis.
- may not be related to SLE and thus the new term photosensitive nasal dermatitis has been proposed.
- in dogs, see erythema, alopecia with scaling / crusting and depigmentation, especially on the nasal planum, often also around eyes / mouth and on ears.

3. Autoimmune subepidermal blistering diseases (AISBDs) (for information only)

- a group of diseases with autoantibodies against components of the basement membrane.
- some examples include Bullous pemphigoid (autoAb to collagen XVII), Epidermolysis bullosa acquisita (autoAb to collagen VII), Mucous membrane pemphigoid (autoAb to variety of BM components)
- grossly see vesicles / bullae which often rupture to leave ulcers; on skin (esp face / ears, axilla, groin, paws), mucocutaneous junctions and mucus membranes (esp oral cavity).

Diagnosis

- history and clinical signs / lesions.
- skin biopsy of fresh lesions; especially showing specific vesicular / pustular and interface dermatitis.
- immunologic tests, especially immunohistochemistry.

III. Some Other Immune-mediated Disorders (for information only)

Immune-mediated Vasculitis (type 3 HS reaction following infections, drugs)

Erythema Multiforme (most commonly associated with drugs and infections)

Toxic Epidermal Necrolysis (most commonly associated with drugs and infections)

Vogt-Koyanagi-Harada-like syndrome [cutaneous depigmentation and uveitis in dogs]

Plasma Cell Pododermatitis of cats

Cutaneous Amyloidosis

Etc
ENDOCRINE SKIN DISEASE

- hormones act on skin & other organs by modifying existing physiological processes.
- endocrine disorders often affect the skin, but the resulting skin lesions are usually not specific for any particular endocrinopathy.

Gross
  ① Bilateral symmetrical alopecia (nonpruritic) - also hair easily epilated and failure to regrow after clipping
  ② Hyperpigmentation
  ③ Secondary seborrhea and/or pyoderma

Histology (atrophic dermatosis pattern)
  ① Hyperkeratosis
  ② Epidermal melanosis (hyperpigmentation)
  ③ Follicular changes - catagen or telogen predominance, follicular dilation / keratosis / atrophy.
  ④ Sebaceous gland atrophy

Diagnosis
  ① History and clinical signs / lesions.
  ② Skin biopsies - usually atrophic dermatosis, ± lesions specific to a particular endocrine dermatosis.
  ③ Demonstration of hormone deficiency or excess and/or response to specific therapy.

1. Hypothyroidism
- the most common endocrinopathy causing skin disease of dogs (± other classical clinical signs).
- nearly all cases are primary hypothyroidism, mostly lymphocytic thyroiditis or idiopathic thyroid atrophy.

Gross
  typical endocrine changes; ± thickened skin due to cutaneous myxedema (tragic expression!).

Histology
  typical atrophic dermatosis pattern.
  often epidermal hyperplasia extending into infundibular (upper) region of follicle, ± increased dermal mucin.

2. Hyperadrenocorticism
- second most common endocrinopathy of dogs, with several breeds predisposed.
- increase in endogenous or exogenous (iatrogenic) glucocorticoids.(see endocrinology notes for details)

Gross
  typical endocrine changes, but skin is also often thin with decreased elasticity and poor wound healing.
  may also see calcinosis cutis (dystrophic mineralization of dermal collagen), and comedones.

Histology
  typical atrophic dermatosis pattern.
  often epidermal/dermal atrophy, ± marked follicular keratosis (comedones), ± mineralization (calcinosis cutis)

3. Some Other Endocrine Skin Disease (for information only)
   Alopecia X (growth hormone / castration-responsive dermatosis)
   Equine pars intermedia pituitary adenoma
   Gonadal Hormone Imbalances - eg female hyperestrogenism, sertoli cell tumor-associated skin disease.
   Etc.
NUTRITIONAL SKIN DISEASE (for information only)

1. **Zinc deficiency / Zinc-responsive dermatosis**
   - in swine, dogs, ruminants; see marked parakeratotic hyperkeratosis

2. **Copper deficiency (molybdenum toxicity)**
   - primarily ruminants; depigmentation (many other systems can be affected)

3. **Nutritional panniculitis / steatitis**
   - in cats, mink, foals and pigs; associated with high dietary levels of unsaturated fatty acid and/or vitamin E / selenium deficiency

4. **Vitamin E / Selenium Responsive Dermatosis**
   - in goats; scaling and alopecia of the coat along the back (marked hyperkeratosis)

5. **Protein-calorie deficiency**
   - hair growth & keratinization require ~25% of daily protein requirement; with starvation see thin, dull, dry, brittle hair coat

MISCELLANEOUS SKIN DISEASES

1. **Seborrhea**
   - broad classification for many clinical syndromes with scaling, crusting, +/- greasiness (1º vs 2º).
   - basic feature is defect in cornification (± abnormal sebum production); note, cornification includes all the processes that form the stratum corneum (eg keratinization, formation of lipid-rich intercellular domain, etc)
   - involves 3 main abnormalities:
     ① altered keratinization → scaling & crusting.
     ② altered surface lipids → increased free fatty acids & cholesterol and decreased diester waxes.
     ③ bacterial & yeast flora → altered species and/or increased numbers / unit area.

   ① Primary Seborrhea
   - primarily seen in dogs; heritable, breed specific disorders of cornification.
   - clinical subtypes (which may be intermixed):
     i) seborrhea sicca (dry) - especially German Shepherds, dachshunds, Doberman's
     ii) seborrhea oleosa (waxy/oily) - especially Cocker Spaniels, Springer Spaniels and Chinese Shar Pei
     iii) seborrheic dermatitis - likely due to secondary pyoderma &/or Malassezia infections.

   ② Secondary Seborrhea
   - see with a multitude of unrelated disease processes; eg endocrinopathy, dermatophytosis, ectoparasites, etc.

2. **Some Other Miscellaneous Skin Diseases** (for information only)
   - there are a large number of species and/or breed specific dermatoses of usually poorly defined etiology, eg:

   Eosinophilic & Collagenolytic Dermatitides
   ① Feline Eosinophilic Granuloma Complex
      - Feline Eosinophilic Ulcer (feline indolent rodent, feline rodent ulcer)
      - Feline Eosinophilic Plaque
      - Feline Eosinophilic Granuloma (feline linear granuloma, feline collagenolytic granuloma)

   ② Canine Eosinophilic Granuloma

   ③ Equine Nodular Collagenolytic Granuloma (eosinophilic granuloma with collagen degeneration)

Cutaneous paraneoplastic syndromes
- Canine juvenile cellulitis (juvenile pyoderma, puppy strangles)
NEOPLASTIC SKIN DISEASES
- the skin is the most common site of neoplasia in most domestic species.

Etiopathogenesis (see general pathology)
- damage to the genome by radiation, viruses, chemicals, etc.
- influenced by genetics, hormones, etc.

Diagnosis
- distinct gross morphology and location often relate to identification and prognosis.
- definitive diagnosis by cytology / histology of biopsies ie. fine needle, punch, excisional, etc.
- specific categorization occasionally requires cell markers (immunohistochemistry) or electron microscopy.

Classification
- tumors derived from multipotential stem cells in skin which differentiate toward a variety of skin components
  - Ectodermal: tumors of the epidermis and adnexa.
  - Melanocytic: tumors of melanocytic origin.
  - Mesodermal: tumors of mesenchymal or round cell origin.

ECTODERMAL NEOPLASMS
- most neoplasms of the epidermis & adnexa, with the exception of squamous cell carcinoma, are benign.

1. Epidermal Origin

 Squamous Cell Carcinoma (SCC)
  - relatively common neoplasm; on poorly pigmented areas of cats, Hereford cattle, horses.
  - sunlight (UV-light) exposure is probably the most important carcinogenic stimulus for these tumors.
  - firm, poorly demarcated mass, ± ulceration or proliferative/papillary.
  - often located on head (eye / ear); especially unpigmented areas.
  - locally invasive with tissue destruction.
  - skin SCC’s have low metastatic potential & slow to metastasize (possible exception is canine nailbed SCC)

 Cutaneous Papillomas (warts)
  - papillomas are seen in all domestic and many non-domestic animals with most cases due to host-specific and often site-specific papillomaviruses; a low percentage are non-viral (spontaneous).
  - most papillomaviruses are highly species-specific (with exception of bovine papillomaviruses, see sarcoïds).
  - can induce either squamous papilloma or fibropapilloma (ie both epithelial & fibroblastic proliferation).
  - most undergo spontaneous regression due to cell-mediated immunity; however some can progress to SCC’s.
  - grossly: squamous papillomas are exophytic masses with finger-like fronds.
  - histologically: papillary proliferation of epidermis, with viral cytopathic effects and intranuclear inclusions.

 Many Other Epidermal Tumors
  - keratoma, actinic keratosis, basal cell carcinoma, etc.
2. Adnexal Origin

- **Hair follicle tumors** - eg trichoepithelioma, pilomatrixoma, etc.
- **Sebaceous gland tumors** - nodular hyperplasia to adenomas to carcinomas.
- **Perianal gland tumors** - nodular hyperplasia to adenomas to carcinomas.
- **Sweat gland (apocrine and eccrine) tumours** - nodular hyperplasia to adenomas to carcinomas.

MELANOCYTIC NEOPLASMS

1. Melanoma (Melanocytoma)
   - common in dogs, gray horses, some swine.
   - melanocytoma refers to the beign form; melanoma or malignant melanoma refers to malignancy.
   
   **Gross**
   - dark brown-black, macules, papules, nodules → tumors; usually single in the dog, multiple in horse.
   
   **Biologic Behaviour**
   
   ① Dogs
   - eyelid or skin, if < 2 cm → mostly benign*.
   - skin, if > 2 cm or digits / nailbed or oral cavity → mostly malignant*.
   *also use general histologic criteria of malignancy.

   ② Gray-White Horses
   - common at 6 yrs., 80% in aged population (> 15 yrs).
   - especially on perineum (in some cases tumors can enlarge to several kilos).
   - occasionally see local invasion and metastasis to viscera.

MESODERMAL NEOPLASMS

1. Mesenchymal Neoplasms

- **Cutaneous soft-tissue sarcomas (spindle cell tumor/sarcoma)**
  - grouping of some spindle cell tumor types that are common in dogs; esp schwannomas (= peripheral nerve sheath tumors), hemangiopericytomas, etc.
  - many forms are histologically interchangeable, require immunohistochemistry or EM to accurately classify.
  
  **Gross**
  - firm to gelatinous, gray-white nodular mass; single or multinodular, any site especially limbs.

  **Biologic Behaviour**
  
  - most are locally invasive with frequent local recurrence after removal (usually due to incomplete excision).
  - metastatic potential correlates to degree of histologic anaplasia (low grade vs high grade).

- **Vaccine-associated sarcoma of cats** (= postvaccinal fibrosarcoma = vaccine-site sarcoma)
  - highly invasive mesenchymal tumor occurring at sites of prior vaccination

- **Equine and feline sarcoids**
  - fibropapillomas resulting from infection with bovine papillomavirus.
Other Mesenchymal tumors
  Fat cell neoplasms - lipoma / liposarcoma.
  Fibroblastic tumors - fibroma / fibrosarcoma.
  Myxomatous tumors - myxoma / myxosarcoma.
  Tumors of blood vessel origin - hemangiom(a) (-sarcoma), lymphangioma (-sarcoma).
  Tumors of neural origin - eg benign peripheral nerve sheath tumor (schwannoma).
  Smooth muscle tumors - leiomyoma / leiomyosarcoma.

2. Round Cell Neoplasms

Mast Cell Tumors
  • common in dogs (mean age 8 yrs) and to a lesser extent in cats.
  Gross
  • single or multiple, edematous nodular masses.
  • often hairless and ulcerated in late stages.
  Biologic Behaviour
  • most frequent potentially malignant skin tumor of the dog.
  • in dogs, behaviour correlates with histologic criteria of malignancy (ie histologic grading system is used)

Histiocytic Neoplasms - some examples:
  ① Canine cutaneous histiocytoma - common benign tumor (Langerhans cells) of usually young dogs.
  ② Cutaneous & systemic reactive histiocytosis - dysregulated proliferation of dermal dendritic cells.
  ③ Histocytic sarcoma (malignant histiocytosis) - neoplastic proliferation of dermal dendritic cells.

Lymphocytic Neoplasms
  ① Epitheliotropic lymphoma - eg mycosis fungoides and others.
  ② Nonepitheliotropic lymphoma - dermal location.
  ③ Cutaneous plasmacytoma - extramedullary, ie only rarely associated with multiple myeloma.
  ④ Cutaneous lymphocytosis (pseudolymphoma) - focal dermal lymphoid hyperplasia in response to Ag.

Other Round cell Tumors:
  Transmissible venereal tumor
  Cutaneous neuroendocrine (Merkel cell) tumor