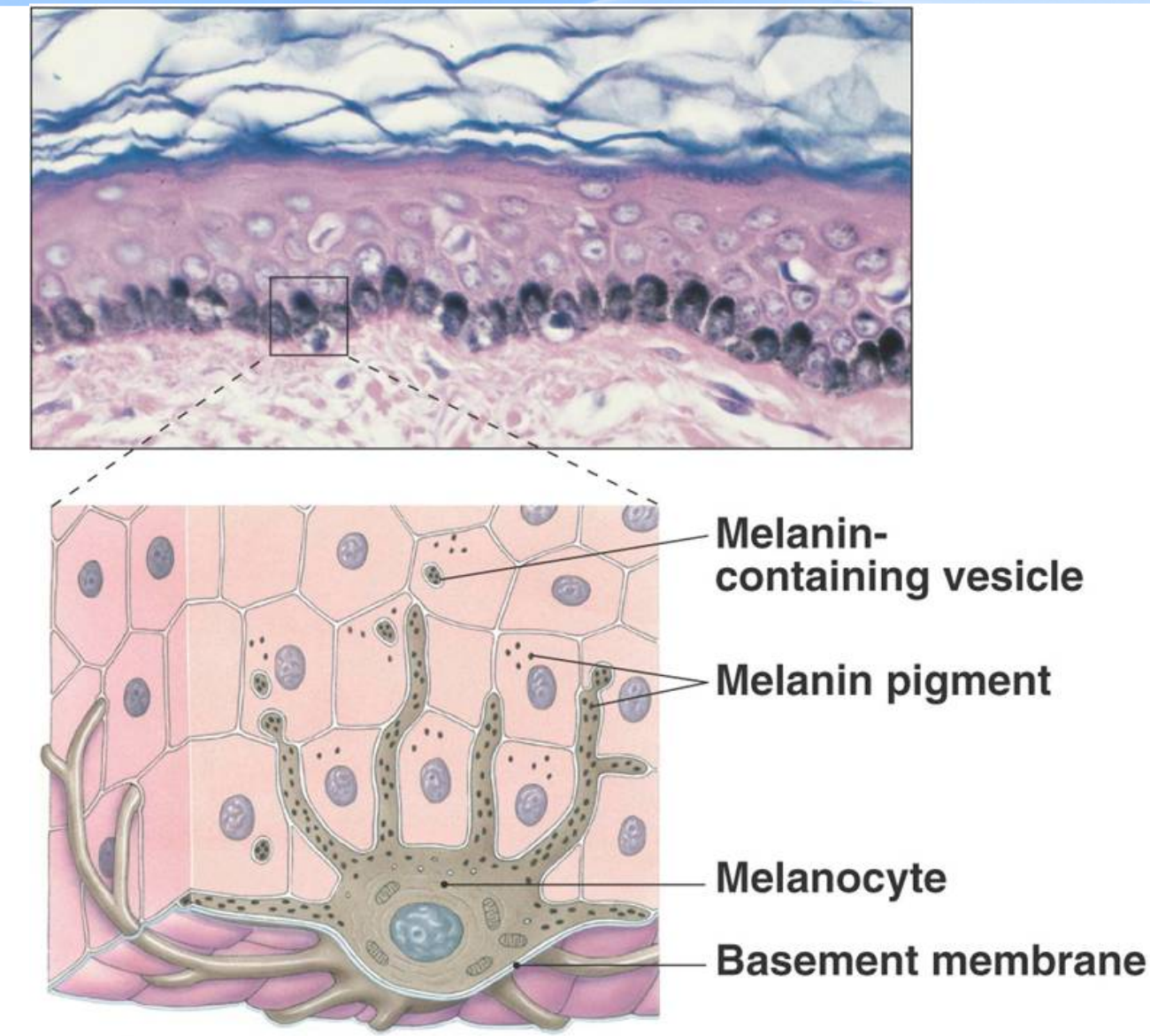
Nasal planum depigmentation – what can it be?

Ekaterina Mendoza-Kuznetsova, DipECVD, Tufts University, USA

Where does pigment come from and where is it stored?



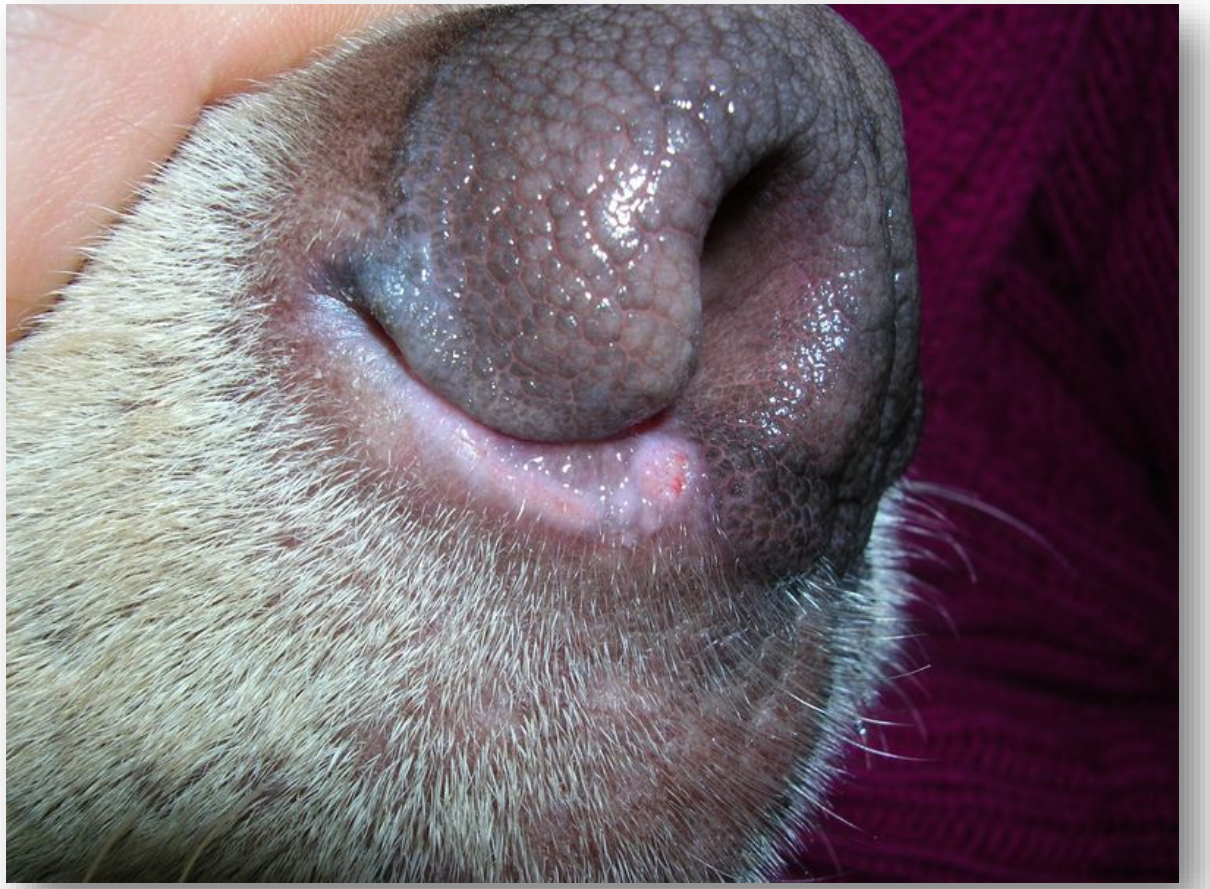
Mechanisms of nasal depigmentation

- Mechanical damage up to the basal layer in depth
- Selective destruction of melanocytes / melanin
- Destruction of the basal / spinous layer of the epidermis
  - Infiltration by inflammatory cells
  - Infiltration by neoplastic cells
  - Exfoliation / vesiculation inside of the deep layers of the epidermis
  - Autoimmune attack on melanocytes / melanin / keratinocytes of the epidermis.

Mucocutaneous pyoderma: clinical presentation

- Distribution of the lesions:
  - Nasal planum, lips, prepuce/vulva, anus, eyelids
- German Shepherd dogs and their crosses are predisposed
- Type of lesions:
  - Crust
  - Vertical fissures

Mucocutaneous pyoderma: clinical presentation



- Distribution of the lesions:
  - Nasal planum, lips, prepuce/vulva, anus, eyelids
- German Shepherd dogs and their crosses are predisposed
- Type of lesions:
  - Crust
  - Vertical fissures
  - Ulcers, erosions, depigmentation.

Mucocutaneous pyoderma: differential diagnoses

- Discoid / cutaneous lupus (DLE)
- Mucocutaneous lupus (MCLE
- Mucous membrane pemphigoid (MMP)
- T-cell epitheliotropic lymphoma (TCL)
- SCC
- …

Mucocutaneous pyoderma: diagnostics

- Clinical presentation
- Cytology
  - Neutrophils, bacteria
- Response to the AB treatment
- Skin biopsy.

Distinctive features of the muco-cutaneous pyoderma

- Crust
- Lesions first, depigmentation usually follows.
- Vertical fissures
- Changes of the structure / architecture are present only at the site of lesions and around.
- More often lesions are on the wings (ala) of the nose than in the center.

Histopathological investigation

Veterinary Dermatology 2004, **15**, 341–348

A retrospective study comparing the histopathological features and response to treatment in two canine nasal dermatoses, DLE and MCP

S. P. WIEMELT*, M. H. GOLDSCHMIDT†, J. S. GREEK‡, J. G. JEFFERS§, A. P. WIEMELT¶ and E. A. MAULDIN†

- The histological picture of mucocutaneous pyoderma and (localized) discoid lupus was often similar.
- In most cases, histological changes did not correlate with the response to antimicrobial treatment.

Mucocutaneous pyoderma: treatment

- Topical antibiotics (ABs)
  - Mupirocin (reserved AB, unique mechanism of action)
  - Systemic ABs of the first choice for 3-4 weeks
    - Cephalexin 22-30 mg/kg BID
    - Amoxicillin-clavulanate 20-30 mg/kg BID
    - Clindamycin 11 mg/kg SID
  - Sometimes anti-inflammatory doses of steroids may be required.
    - Prednisone/Prednisolone 0.25-0.5 mg/kg SID 1-3 weeks of topical steroids.

Localized discoid lupus erythematosus (DLE)

Localized discoid lupus erythematosus (DLE)

- No systemic signs
- Photosensitivity is present in 50% of cases
- Infiltration of the skin mainly by plasma cells
  - Unlike people
  - In humans, DLE has infiltration mainly with T-helper cells.

Localized discoid lupus: clinical presentation (dogs)

- No sex or age predisposition
- Breed predisposition: collie, German Shepherd, Husky, German Pointer.
- Depigmentation, erythema, scales, loss of nasal planum architecture
- Later lesions: erosion, ulcers and crust
- Lesions can be also in the mouth, on the lips, around the eyes, on the pinnae
- Pain and pruritus can be seen in some cases.

Localized discoid lupus: diagnostics

- Blood tests are usually non-informative
- Antinuclear antibodies negative or low
- Histopathology: interface cytotoxic dermatitis (lichenoid or hydropic), pigment incontinence, basement membrane zone thickening, accumulation of mononuclear and plasma cells around the vessels and glands, apoptosis of basal cells, basal keratinocyte hydropic degeneration.
- IgA, IgM, IgG and complement deposition along the basal membrane.

Localized DLE: diagnostic criteria (T. Olivry)

- Depigmentation, erythematous and atrophic skin changes on the nasal planum and surrounding skin
- Characteristic changes in histopathology
- ± Immunofluorescence

Distinctive features of localized DLE

- Early diffuse depigmentation, then crust and ulceration
- Loss of nasal planum architecture.

Treatment of localized DLE

- The prognosis is good, but life-long treatment is often required.
- UV light avoidance
- Topical corticosteroids
- Tacrolimus
- Vitamin E 400-800 IU per day
- Omega-3 and omega-6 fatty acids
- Tetracycline + niacinamide (250-500 mg of each TID)
- A short course of prednisolone 2.2 mg/kg SID for a month, then topically.

Mucocutaneous lupus erythematosus (MCLE)

Vet Dermatol 2015; **26**: 256–e55 DOI: 10.1111/vde.12217

Mucocutaneous lupus erythematosus in dogs (21 cases)

Thierry Olivry*†, Michael A. Rossi‡, Frane Banovic*† and Keith E. Linder†§

- 52% of dogs – German Shepherds or their crosses
- Lesions on the nose are much less common than lesions of the genitals and anus (19% vs. 57%)
- Symmetrical lesions
- More often 2 or more affected areas
- No systemic symptoms
- No spontaneous resolution is described.

Mucocutaneous lupus erythematosus (MCLE)

Diagnostics

- Clinical picture
- Histopathology - interface cytotoxic dermatitis
- Immunofluorescence:
  - Immunoglobulins and complement deposition along the basal membrane
- ANAs negative or low in rare cases.

Treatment

- Niacinamide + tetra or doxycycline
- Glucocorticoids (GCS) systemic / topical
- Cyclosporine
- Tacrolimus
- Combinations of options
- Clinical remission:
  - On average, after 30 days using systemic GCS
  - On average, after 60 days with other treatment options without oral GCS.
- Relapse after discontinuation of treatment – in majority of the cases.

Distinctive features of MCLE

- Lesions are not limited to the nose, almost all dogs with affected nose also have lesions on the genitals or on the anus
- Main lesions - ulcers and erosions, depigmentation is less common.

Vitiligo

Tham *et al. BMC Veterinary Research* (2019) 15:251
https://doi.org/10.1186/s12917-019-2003-9

BMC Veterinary Research

REVIEW Open Access

Autoimmune diseases affecting skin melanocytes in dogs, cats and horses: vitiligo and the uveodermatological syndrome: a comprehensive review

Heng L. Tham[1], Keith E. Linder[2,3] and Thierry Olivry[2,4*]

Vitiligo

- Often in young dogs (median 2 y.)
- Rottweilers, Dobermans, Collies and Siamese cats may be predisposed (USA)
- The etiology is not clear:
  - Autoimmune attack to melanocytes
  - Genetic predisposition
  - Neurogenic theory
  - Theory of melanocyte oxidative damage.

Vitiligo: clinical presentation

- Areas of leukoderma and leukotrichia
  - Usually well demarcated
  - Without tissue structure changes
  - Without noticable inflammation
- More often affected areas are lips and nose
- Association with diabetes and hypoadrenocorticism described in dogs.

Vitiligo: differential diagnoses

- Alopecia areata
  - Vitiligo does not cause alopecia
- Uveodermatologic syndrome
  - Breed, lack of uveitis and lack of inflammation
- Other pathologies
  - No changes in tissue structure.

Distinctive features of vitiligo

- Very clear demarcation of the depigmented area
  - With the exception of "snow nose"
- No tissue structure changes or crust
- More often in young animals
- Usually complete depigmentation
  - With the exception of "snow nose"

Vitiligo: diagnostics and treatment

- Diagnostics:
  - Clinical presentation
  - Histological confirmation

- Treatment:
  - Cosmetic problem
  - Usually doesn't require treatment
  - In humans: calcineurin inhibitors (tacrolimus, cyclosporine)
  - No effective treatment in animals described
  - Spontaneous remission is possible.

Uveodermatological syndrome (VKHL syndrome)

Tham *et al. BMC Veterinary Research* (2019) 15:251
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Autoimmune diseases affecting skin melanocytes in dogs, cats and horses: vitiligo and the uveodermatological syndrome: a comprehensive review

Heng L. Tham[1], Keith E. Linder[2,3] and Thierry Olivry[2,4*]

Uveodermatological syndrome (VKHL syndrome)

- Autoimmune attack to melanocytes or melanocyte-associated antigens
- There is a genetic predisposition in Akitas (haplotype DQA1*00201, DLA II)
  - Akitas (about 66% of cases), Samoyeds and Huskies are predisposed
- Reported in many breeds and mongrels
- Immune attack on melanocytes / melanin
- Median age of onset is 3 years
- Female-to-male ratio is 0.6.

Uveodermatological syndrome (VKHL syndrome)

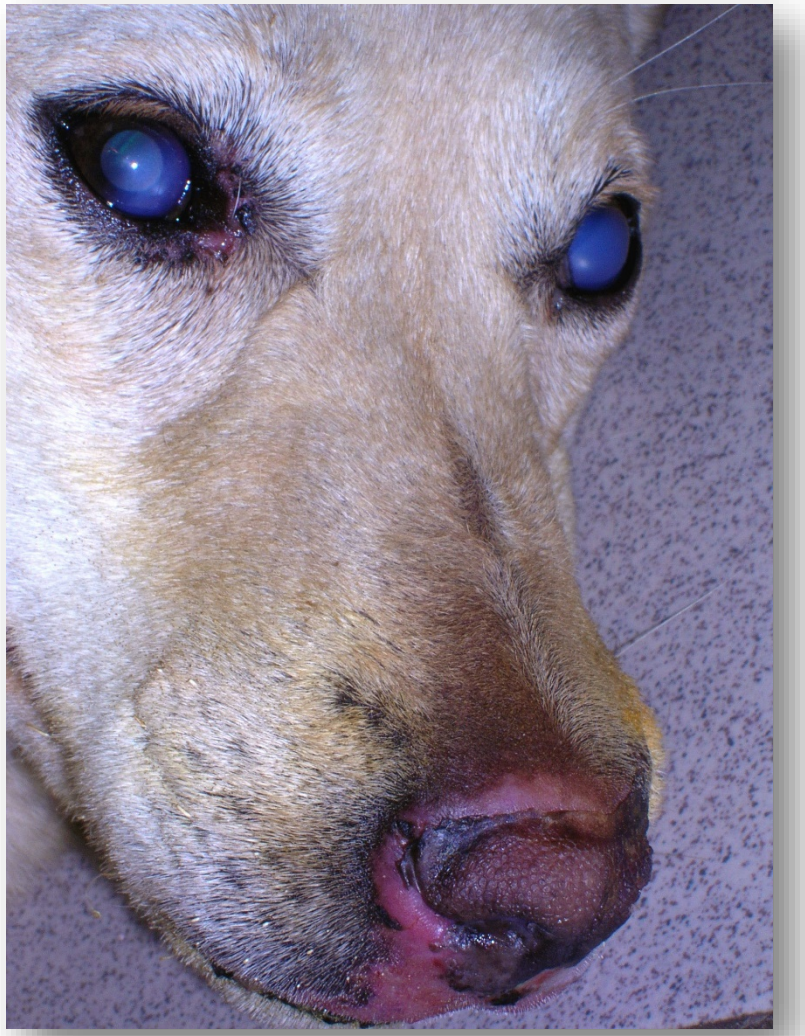
A. Markina's patient

- In humans: flu-like symptoms → eyes → skin
- In 85% dogs: eyes → skin → (?) nervous system
- Only one eye can be affected
- Skin lesions:
  - Always on the face (nose) or head
  - Depigmentation (leukoderma and leukotrichia)
  - Erosions, ulcers.

Distinctive features of uveodermatological syndrome

- Usually uveitis first
- Breed predisposition (?)
- Young age (?).

Uveodermatological syndrome : diagnostics



- Clinical presentation + breed
- Histological examination - necessary
  - Depigmented skin areas
  - Better early lesions + fully depigmented
  - It better to avoid taking biopsy from erosions and ulcers, or try to take the erosion edge.

Uveodermatological syndrome: treatment

- Systemic agressive immunosuppressive aggressive treatment.
- 60% to achieve clinical remission if initiate the treatment in 1 month from the first clinical sign (20% - if after 2 months)
  - Prednisolone ≥ 2 mg/kg SID
  - Prednisolone + azathioprine 2 mg/kg SID or cyclosporine ≥ 5 mg/kg SID
- Topical eye treatment
- Prognosis is cautious
  - Lifetime treatment may be required.
  - Changes in the eyes may be irreversible
  - No spontaneous remission is reported.

Epitheliotropic T-cell lymphoma (TCL)

- Infiltration and destruction of the epidermis and / or follicles by neoplastic T-lymphocytes (γδ)
- Usually the second half of life (mean 11 years)
- Female/male ratio 1.5:1
- There are several clinical forms:
  - "Mycosis fungoides" – plaques, nodules
  - Exfoliative erythroderma
  - Mucocutaneous form
  - Oral ulceration
  - Sézary syndrome.

T-cell lymphoma: clinical presentation

- The beginning is gradual, may resemble folliculitis

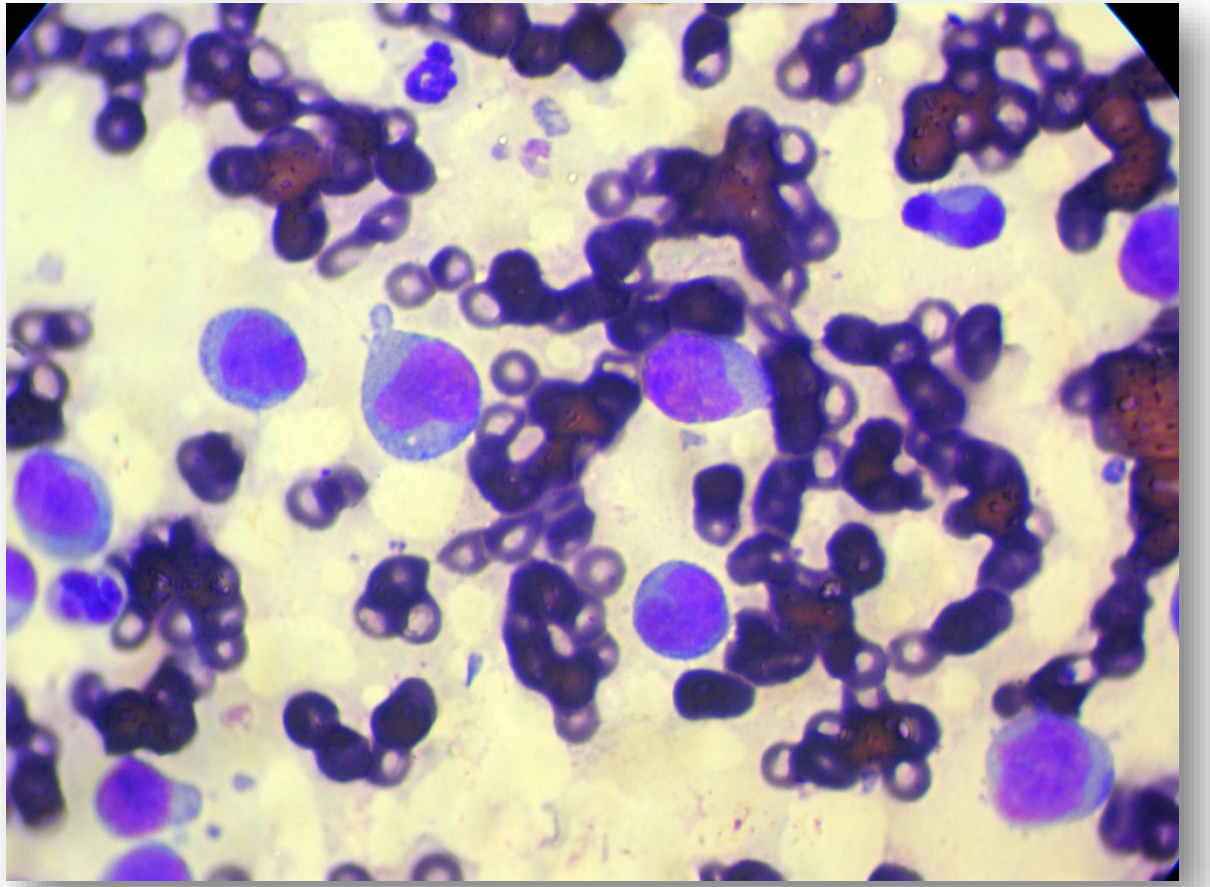
T-cell lymphoma: clinical presentation

- The beginning is gradual, may resemble folliculitis
- Often – a combination of skin and mucosal lesions
- Skin – hyperpigmentation, mucosal – depigmentation
- More often non-pruritic, but it can be very pruritic.

Distinctive features of TCL:

- Older / old animals
- Existing lesions never heal
  - Unlike pyoderma lesions
- The tissue structure is always changed
- Over time, alopecia often develops into dense plaques
- Lesions on the nose are commonly asymmetrical and of irregular shape
- Commonly these is a combination of skin and mucosal lesions.

T-cell lymphoma: diagnostics



- Cytology – lymphocytes predominate, often atypical
- Confirmation – biopsy
- Sometimes required:
  - Immunohistochemistry (CD3)
  - Clonality analysis.

T-cell lymphoma: prognosis

- Median survival time for dogs – 264 days
  - Cutaneous form: 130 days.
    - Multiple skin lesions are associated with the shorter survival time
  - mucocutaneous/mucosal forms: 491 days.
- Systemic retinoids or/and chemotherapy may increase the survival time in dogs with cutaneous form and multiple lesions
- In cutaneous form with the multiple lesions complete clinical remission may correlate with longer survival time
- It is unclear if chemotherapy influence a survival time for dogs with mucocutaneous/mucosal forms or with single cutaneous lesion.

T-cell lymphoma: treatment

- LOMUSTIN (70-90 mg/m2 every 3-4 weeks ± prednisone/prednisolone)
  - If monotherapy – only 10% achieved complete remission
- VELCAP-EL protocol
  - 38% achieved complete remission
- Systemic retinoids may increase the survival time in cutaneous form and multiple lesions
- Chemotherapy can reduce lesions and improve quality of life
- Side effects are common.

Pemphigus foliaceous (PF) and pemphigus erythematous (PE)

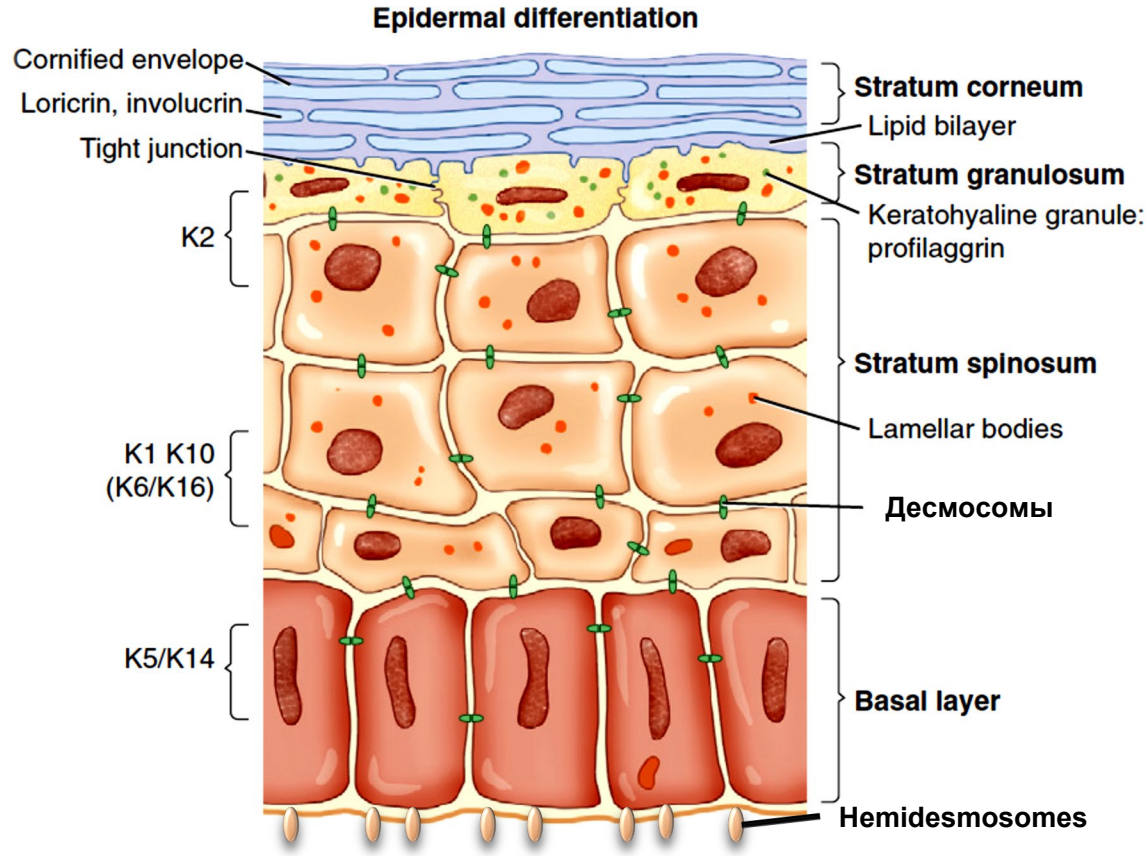
- Pemphigus foliaceous:
  - Autoimmune attack on desmosomes
  - Pustules and crust
- Pemphigus erythematosus:
  - Autoimmune attack on desmosomes (?) + on basal keratinocytes
  - The combination of pemphigus foliaceous and localized discoid lupus erythematosus.

Distinctive features of pemphigus foliaceous

- Abundant crust and pustules
- Superficial lesions
- Usually not only the nose is affected
- Depigmentation in the crusted area only
  - If there is no secondary pyoderma
- Pinnae and footpad lesions are very suspicious
  - In cats – purulent paronychia is very suspicious.

Pemphigoids / Autoimmune subepidermal blistering diseases

- Autoimmune attack on hemidesmosomes:



Pemphigoids / Autoimmune subepidermal blistering diseases

- Mucous membrane pemphigoid
- Bullous pemphigoid
- Epidermolysis bullosa acquisita.

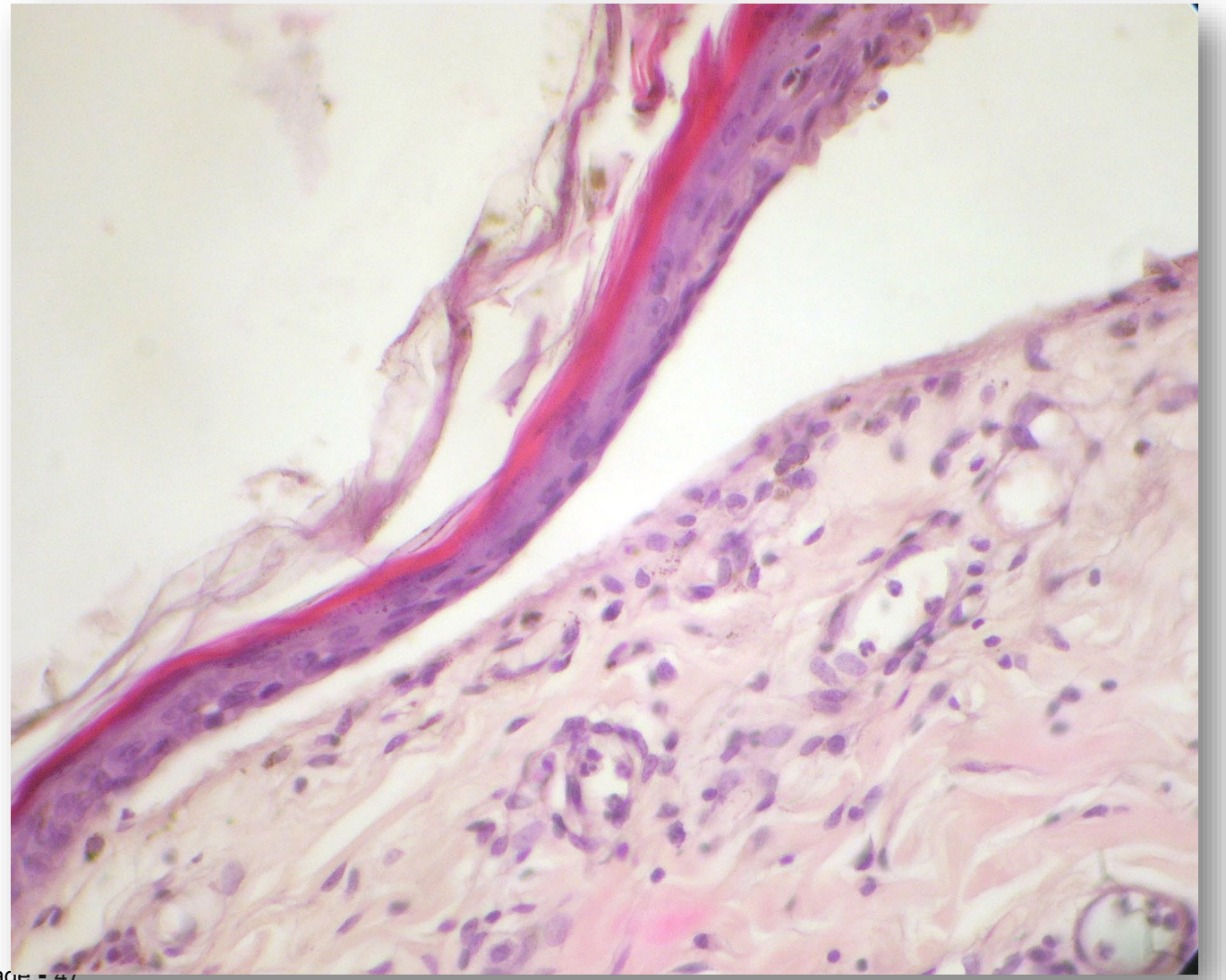
Pemphigoids: clinical presentation

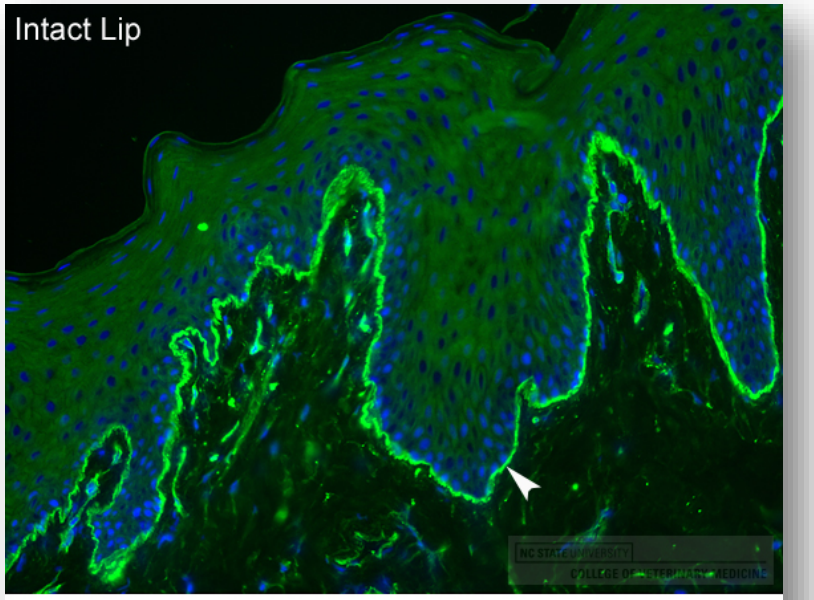
- May affect mucous membranes and skin.
  - Nasal planum, oral cavity, anus, prepuce / vulva, pinnae, footpads…
- The severity of the condition depends on the disease and the patient.
- Primary lesions: bullae
- Secondary: erosions and ulcers, epidermis exfoliation.

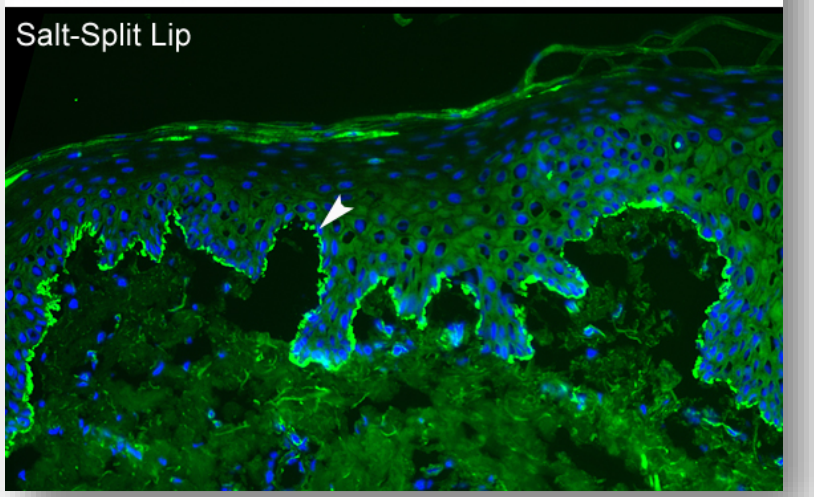
Distinctive features of pemphigoids

- Bullae and ulcers appear first, depigmentation follows
- Almost no crust
- Usually not only the nasal planum affected
  - Depends on the type of pemphigoid
- Lesions are deep
- Depigmentation is usually only around the ulcers or area of the ulcers.

Pemphigoids: diagnostics – biopsy ± IFA







Pemphigoids: treatment

- Treatment choice depends on the type of pemphigoid
- Tetracycline + niacinamide (250-500 mg TID)
- Immunosuppressive treatment:
  - Prednisolone 2 mg/kg SID
  - Prednisolone + azathioprine
  - Other immunosuppressive drugs
- Prognosis depends on the type of pemphigoid and the response to treatment.