

# Cover Sheet: Request 11400

## VEM 5XXX - Small Animal Dermatology

### Info

Process	Course New Ugrad/Pro
Status	Pending
Submitter	Carter, Sharon W swcarter@ufl.edu
Created	1/11/2017 3:28:43 PM
Updated	2/15/2017 6:19:56 PM
Description of request	Small Animal Dermatology (elective)

### Actions

Step	Status	Group	User	Comment	Updated
Department	Approved	VM - Small Animal Clinical Sciences 312809000	MILNER, ROWAN JAMES		1/11/2017
Added R1.CVM_syllabus_SA Dermatology.pdf					1/11/2017
Added notes.elective2016.withschedule.pdf					1/11/2017
College	Approved	VM - College of Veterinary Medicine	Thomas Vickroy		1/12/2017
No document changes					
University Curriculum Committee	Comment	PV - University Curriculum Committee (UCC)	Case, Brandon	Added to the February agenda.	1/23/2017
No document changes					
University Curriculum Committee	Pending	PV - University Curriculum Committee (UCC)			1/23/2017
No document changes					
Statewide Course Numbering System					
No document changes					
Office of the Registrar					
No document changes					
Student Academic Support System					
No document changes					
Catalog					
No document changes					
College Notified					
No document changes					

# Course|New for request 11400

## Info

**Request:** VEM 5XXX - Small Animal Dermatology  
**Description of request:** Small Animal Dermatology (elective)  
**Submitter:** Carter, Sharon W swcarter@ufl.edu  
**Created:** 2/1/2017 9:06:14 AM  
**Form version:** 2

## Responses

**Recommended Prefix**VEM  
**Course Level** 5  
**Number** XXX  
**Category of Instruction** Advanced  
**Lab Code** None  
**Course Title** Small Animal Dermatology  
**Transcript Title** SA Dermatology  
**Degree Type** Professional

**Delivery Method(s)** On-Campus  
**Co-Listing** No

**Effective Term** Fall  
**Effective Year** 2017  
**Rotating Topic?** No  
**Repeatable Credit?** No

**Amount of Credit** 2  
**If variable, # min** 0  
**If variable, # max** 0  
**S/U Only?** No  
**Contact Type** Regularly Scheduled  
**Weekly Contact Hours** 2

**Course Description** The goals: are to provide advanced knowledge on how to logically and systematically approach small animal dermatological diseases with particular emphasis on problem based approach. This course will include information regarding the clinical presentations, diagnostic approach and treatment of allergic, infectious, autoimmune and immune-mediated skin diseases of small animals.

**Prerequisites** Only students with the major code VM

**Co-requisites** No

**Rationale and Placement in Curriculum** Offered in Fall for 4th year students in advanced didactic courses.

**Course Objectives** The specific objectives are for the students to become familiar with a problem based approach and learn how to approach cases in a logical step-by-step manner both in terms of diagnosis and management.

Additional objectives are to provide the students with knowledge on the pathogenesis and clinical signs of skin diseases of dogs and cats that are encountered in clinical practice and were not addressed in the core dermatology course (VEM 5387).

Besides providing lectures, this course also provide opportunities for case discussion in which 3 instructors (Drs. Santoro, Gram and Marsella) will encourage students to participate in discussing clinical cases. This approach has the aim to encourage application of knowledge and open discussion of the pros and cons of different approaches that could be taken on various clinical cases. There will be no laboratory time in this course.

By the end of the coursework, the student will be able to explain the necessary types of diagnostic tests and the reasons for performing them when evaluating your patients. The

student will be able to discuss pros and cons of different therapy approaches for various diseases and customize the recommendations to individual cases.

**Course Textbook(s) and/or Other Assigned Reading** SCAVMA notes provided by Dr. Marsella

Recommended/ Reference texts British Small Animal Veterinary Association manual of Dermatology of dogs and Cats, 3rd Edition.

Additional Resources/ equipment: SCAVMA notes provided for the sophomore core dermatology course

### **Weekly Schedule of Topics** 1. Introduction to Problem Based Dermatology

2. Diagnostic approach to Pruritus
3. Management of Pruritus.....
4. Steroid therapy
5. Approach to Macular/Papular Pustular/Dermatoses
6. Approach to Crusting Scaling Dermatoses
7. Approach to nodular dermatitis
8. Approach to Alopecia (focal/multifocal)
9. Approach to Alopecia (symmetric)
10. Endocrine Interpretation / Tests...
11. Approach to Erosive Ulcerative Dermatoses
12. Approach to Pigmentary Abnormalities
13. Regional Dermatoses 1 (perineal, pinnae, claws)
14. Regional Dermatoses 2 (nose, footpad)
14. Approach to otitis
15. Antimicrobial Resistance
17. Discussion of clinical cases
18. Discussion of clinical cases
19. Discussion of clinical cases
20. Discussion of clinical cases
21. Discussion of clinical cases
22. Discussion of clinical cases
23. Discussion of clinical cases
24. Discussion of clinical cases
25. Discussion of clinical cases
26. Discussion of clinical cases
28. Discussion of clinical cases
29. Review
30. Review

**Links and Policies** For more information, please refer to:

<https://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>.

The student's grades will be posted on the course's E-Learning site. The students will be notified as soon as the grades become available.

There will be no practical assessment of clinical skills

#### **Class Attendance and Make-Up Policy**

Class attendance is strongly encouraged. Excused absences are consistent with university policies in the undergraduate catalog (<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>) and require appropriate documentation. A makeup final exam will be provided for students who miss either exam due to extreme, documented circumstances. Students should arrange with the instructor for makeup material.

#### **Students Requiring Accommodations**

Students with disabilities requesting accommodations should first register with the Disability Resource Center (352-392-8565, [www.dso.ufl.edu/drc/](http://www.dso.ufl.edu/drc/)) by providing

appropriate documentation. Once registered, students will receive an accommodation letter which must be presented to the instructor when requesting accommodation. Students with disabilities should follow this procedure as early as possible in the semester.

#### Course Evaluation

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://evaluations.ufl.edu>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu/results/>.

#### Class Demeanor

Students are expected to arrive to class on time and behave in a manner that is respectful to the instructor and to fellow students.

#### University Honesty Policy

UF students are bound by The Honor Pledge which states, "We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment." The Honor Code (<https://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/>) specifies a number of behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obligated to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the instructor

#### Counseling and Wellness Center

Contact information for the Counseling and Wellness Center:

<http://www.counseling.ufl.edu/cwc/Default.aspx>, 392-1575; and the University Police Department: 392-1111 or 9-1-1 for emergencies.

**Grading Scheme** The final grades assigned for this course will be based on the percentage of total points earned. The UF grading scheme will be used for this course.

Percent

#### Grade Grade Points

93.4-100	A	4.00
90.0-93.3	A-	3.67
86.7-89.9	B+	3.33
83.4-86.6	B	3.00
80.0-83.3	B-	2.67
76.7-79.9	C+	2.33
73.4-76.6	C	2.00
70.0-73.3	C-	1.67
66.7-69.9	D+	1.33
63.4-66.6	D	1.00
60.0-63.3	D-	0.67
0-59.9		

E 0.00

**Instructor(s)** Dr. Rosanna Marsella (Courses Coordinator)

Dr. Dunbar Gram

Dr. Domenico Santoro

**Small animal dermatology - elective course 2016**

**Course Coordinator: Dr. Rosanna Marsella**

**Participants: Drs. Dunbar Gram, Rosanna Marsella, and Domenico Santoro**

Topic	Instructor	Date	Day and time	Page
1. Introduction to problem based dermatology	Marsella	8.23.16	Tue 10:30-11:30	3
2. Approach to macular/papular/pustular dermatoses	Marsella	8.23.16	Tue 11:30-12:20	17
3. Approach to focal/multifocal alopecia	Marsella	8.24.16	Wed 10:30-11:30	34
4. Approach to nodular dermatoses	Marsella	8.24.16	Wed 11:30-12:20	55
5. Diagnostic approach to pruritus (Endocrine diseases)	Gram	8.30.16	Tue 10:30-11:30	75
6. Management of pruritus	Santoro	8.30.16	Tue 11:30-12:20	89
7. Steroid therapy	Gram	8.31.16	Wed 10:30-11:30	94
8. Approach to symmetric alopecia	Gram	8.31.16	Wed 11:30-12:20	103
9. Regional dermatoses (perineal, pinnae, claws)	Santoro	9.6.16	Tue 10:30-11:30	122
10. Regional dermatoses (nose, footpads)	Santoro	9.6.16	Tue 11:30-12:20	126
11. Approach to otitis	Santoro	9.7.16	Wed 10:30-11:30	129
12. Antimicrobial resistance	Santoro	9.7.16	Wed 11:30-12:20	132
13. Endocrine tests interpretation	Gram	9.8.16	Thu 10:30-11:30	See endocrine lecture -75
14. Approach to crusting and scaling dermatoses	Santoro	9.8.16	Thu 11:30-12:20	136

15. Approach to erosive/ulcerative dermatoses	Marsella	9.9.16	Fri 10:30-11:30	141
16. Approach to pigmentary abnormalities	Marsella	9.9.16	Fri 11:30-12:20	158
17. Clinical cases	All 3	9.12.16	Mon 8:30-9:20	
18. Discussion	All 3	9.12.16	Mon 9:30-10:20	
19. Clinical cases	All 3	9.13.16	Tue 10:30-11:30	
20. Discussion	All 3	9.13.16	Tue 11:30-12:20	
21. Clinical cases	All 3	9.14.16	Wed 10:30-11:30	
22. Discussion	All 3	9.14.16	Wed 11:30-12:20	
23. Clinical cases	Gram	9.19.16	Mon 1:00-1:50	
24. Discussion	Gram	9.19.16	Mon 2:00-2:50	
25. Clinical cases	Santoro	9.20.16	Tue 1:00-1:50	
26. Discussion	Santoro	9.20.16	Tue 2:00-2:50	
27. Clinical cases	Marsella	9.21.16	Wed 1:00-1:50	
28. Discussion	Marsella	9.21.16	Wed 2:00-2:50	
29. Clinical cases	Gram	9.22.16	Thu 1:00-1:50	
30. Discussion	Gram	9.22.16	Thu 2:00-2:50	
31. Final exam		9.23.16	Fri 1:00-2:50	

## **Problem Based Dermatology**

Rosanna Marsella, DVM, DACVD

### **Introduction**

The purpose of this course is to apply previously learned information about dermatological diseases of dogs and cats to various types of clinical presentations. Thus, rather than to focus on specific diseases as we have done in the dermatology core we will focus on dermatologic signs (problem based approach) and formulate differential diagnoses and a diagnostic plan on how to approach the various types of clinical presentations. Thus we will be building on the basic knowledge obtained in the core and apply it to clinical cases. *Please review your SCAVMA notes from the dermatology core before the beginning of this course.*

You will notice that some information is repeated in multiple lectures. This is because the same disease can manifest with different types of lesions thus there is overlap in clinical presentations. You will also notice that different clinicians may have slightly different ways to approach cases. This is part of clinical practice and we plan to provide you with multiple viewpoints to broaden your knowledge about the various ways to approach certain clinical presentations and the pros and cons of the various approaches.

### **The importance of history taking**

In order to rank the various differential diagnoses it is important to obtain a thorough history which will help rule in or rule out certain diseases. A logical and systematic approach to dermatological cases is fundamental to successfully diagnose and manage them.

*1. Partial History:* This is often the type of history taken by practitioners but for dermatologic disease a more complete history is desirable. There are two occasions in which a partial history may be indicated.

a. When the diagnosis is quickly apparent as soon as the animal is seen and the owner mentions the problem. Examples would be a hot spot on an animal with fleas or a cat bite abscess on an animal after a fight.

b. The animal is a regular patient and the health history and record are well known to the veterinarian.

2. *Complete History*: This type of history supplies complete and full information about the general health of the animal and the specific dermatologic condition. It is best if this information is obtained at the onset of the skin disease but this is not always possible. Whenever a diagnosis is not made with ease, it is highly recommended that an extended appointment be used to get this complete history.

3. *Recheck History*: Focus here on if the treatment is working and whether there have been any adverse reactions or changes in the animal since the prior visit (s).

### **Obtaining a Complete History**

Patient details are multiple and should be recorded at time of visit if not before.

**Age**: The age of the animal is important and it is very useful to not the age of onset of the problem. Younger dogs are more likely to have genodermatoses. Other considerations for young dogs would include demodicosis, dermatophytosis, dermatomyositis, impetigo, juvenile cellulites, pituitary dwarfism, and histiocytoma. Dogs in the age range of 1-3 years for onset of dermatologic conditions would most likely include atopic dermatitis, primary seborrhea, histiocytoma, and zinc responsive or generic dog food disease. Middle aged to older dogs are more inclined toward endocrinopathy, autoimmune disorders, neoplasia, and systemic disease with cutaneous manifestations.

**Breed**: Many skin conditions have breed predilections. These will vary somewhat regionally dependant on the conditions of the champion breeding dogs in the area. Most dermatology textbooks provide listing of breeds and their reported potential problems.

**Origin**: The source of the animal and the length of time of ownership can be important when formulating a differential list for certain types of problems.



Rescue animals or feral/stray animals will be much more likely to have ecto and endo parasite problems. Infections and nutritional problems can also be seen in these pets. If the animal was acquired from a breeder it more likely that a complete family history can be obtained if deemed necessary.

**Vaccination and routine parasiticide (endo and ecto) status:** This information should be recorded as it can sometimes be useful in certain conditions. Skin conditions associated with endoparasites are rare but have been reported (heartworms). Viral conditions usually do not result in skin conditions but distemper virus can cause hyperkeratosis of footpads (hard pad disease), and skin conditions in the cat may occur with herpes virus, papiloma virus, and pox viruses. Pododermatitis is known to be rarely associated with migrating hookworm larva. It is very useful to know what type of parasite control is being used and how frequently. The systemic product selamectin is effective against many parasites and so some parasite infections can be eliminated or moved down the problem list dependant on the history. However, even though appropriate medications have been used, resistance may be a factor or compliance is always a potential problem. For example, lufenuron is not effective if it is vomited behind the sofa and doesn't enter the dog.

### **Owner's Complaint:**

**What are the major problems of the pet as perceived and reported by the owner?** The most common skin problems presented to the practitioner are alopecia, pruritus, lumps, and otitis. Dependant on the geographical location popular/pustular/macular lesions may be common or not. Excessive scaling, ulceration and drainage are less often the presenting dermatologic complaint but certainly can be.

**How long has the problem been present?** The appearance of the dog may be directly related to the length of time of the problem. When the skin is continual traumatized and there is persistent inflammation, chronic skin changes such as thickening (lichenification) and hyperpigmentation are common occurrences. In humid environments, oiliness may worsen on the skin as a response

to inflammation as well. It can be a challenge to try to determine what the primary lesions are once chronic changes have developed.

**What did the skin condition look like at the beginning?** This is especially useful information if the owner can describe for you clearly how it looked and what the clinical signs were in the early stages.

**Has the problem changed over time and if so, how?** It is useful to know when pruritus began in the chronological course of events. It is helpful to know if the problem has worsened slowly (allergy, endocrine) or more rapidly (infectious, parasitic). Likewise determining seasonality can be helpful if it exists.

### **Pruritus:**

One needs to know and to record information about pruritus including the distribution (front half/back half, ventral/dorsal, feet/face, etc.), the severity (it is often useful to have the owners grade the itch on a sliding numerical scale, and the onset of itch in relationship to the skin lesions.

**Distribution:** With some owners it is helpful to point to specific areas rather than simply asking, “where does the animal itch most?”

**Severity of itch:** There are a variety of ways to record itch in veterinary medicine. Some use simply the categories of mild, moderate and severe. Another method commonly employed at the VMC is to give a numerical score between 1-10.

**Is the condition contagious?** It is useful to ask if other pets in the household have similar lesions. Also discreetly inquire as to whether any humans in the home have skin disease that seems to relate to interaction with the pet?

**Is there a family history?** Are the dog's relatives affected with skin disease and if so, has a diagnosis been made.

**Have previous treatments been given and what kind of effect did they have on the skin?**

This is often very critical information but it also can be a large stumbling block for the owner and veterinarian. If the history is long, it is ideal to have an extended appointment. Going through the various treatments and other veterinarian's records is not nearly as helpful as going through the history with the owner and the pet. If there is a long history of treatment, it may be possible in "condense" the history to:

Has the pet been treated with antibiotics alone at the proper dosage? What happened?

Has the pet received anti-inflammatory doses of steroids? What type of change was noted? Has the dog been treated for Scabies or has it been ruled out? Of all the various treatments that you have given your pet, what do you think has given the most benefit?

**What does the animal eat?** The diet can be a reason for skin disease and thus it is useful to record what and how much the pet eats. Food intolerances are possible as well as some nutritional dermatoses which are rare. Remember to include the less frequently ingested "foods" like treats, rawhide chews, pig's ears, and table food.

**Where does the animal live?** Veterinarians should be familiar with conditions more common in their geographical area. There are many examples of this: Fleas are in the warm humid areas of the world, blastomycosis is seen in the Mississippi river valley regions, cheyletiella is regional in the US.

## PHYSICAL EXAMINATION

One must do a thorough and complete examination of the skin. Use a technician to hold the dog either in the company of the owner or not, dependant on whether the history has been gathered separately. Ideally it is helpful if the veterinarian has the owner at hand so that he/she can point to lesions or affected areas and ask appropriate questions about duration, degree of itch, prior response to therapy etc. Some goals of the physical examination include: the detection of any visible parasites, the identity of any lesions present and to determine the distribution of lesions. One should not forget that the mucous membranes, interdigital spaces, unguis folds, claws and footpads are all part of the examination.

Primary lesions: direct result of the disease process

Secondary lesions: occur from progression of the disease or from self-trauma.

Review the primary and secondary lesions from your core notes.

Loss of hair

Changes in skin color

Rashes

Scaling

Changes in thickness of skin

Draining tracts

Defects in integrity of skin

Abnormal components on the surface

Lumps and swellings

**Loss of hair:** This is a common clinical sign in both dogs and cats. It may occur spontaneously or be created by self trauma. Spontaneous hair loss is a sign of a disorder of the hair follicle such as one would see with infection, follicular parasite, or hormonal alteration. When hair loss is due to pruritus the hair can be removed by a variety of animal means (scratching, rubbing, biting, licking).

**Alopecia** means loss of hair

***Focal alopecia*** – a single, small patch of alopecia

***Multi-focal*** – multiple, small, circular patches of alopecia giving the coat a moth eaten appearance

***Regional alopecia*** – affecting just one region of the body e.g. leg

***Symmetrical alopecia*** – has same distribution on both halves of the body

***Hypotrichosis*** - less than normal amount of hair, in veterinary dermatology the term is used primarily for congenital or inherited hair loss.

***Defluxion/effluvium*** – a sudden widespread loss of hair

***Easy epilation*** – the ability to easily remove excessive quantities of hair with little resistance.

This can be physiologic or pathologic. If the epilation leads to a bald spot then this is not normal. However, remember that on most dogs the majority of hairs are in the telogen or resting stage of hair growth. Breeds that require frequent clipping like poodles, OESD, lhasa apsa and shitzu have most hairs in anagen (like your scalp hair)

Scar – the abnormal skin at the site of a healed area. Scars usually have a lack of hair and a lack of pigment. They are generally shiny and raised. Scars lack hair follicles so hair will never grow there.

### **Changes in color of skin:**

***Erythema*** – skin that is redder than normal, usually suggesting the skin is inflamed

Occurs most often in allergy, parasites, infections and immune mediated skin conditions.

Erythroderma means generalized erythema.

***Hyperpigmentation*** – skin darker than normal

Excessive pigment in the epidermis makes the skin appear black colored. This occurs most often with chronic skin conditions and with hormonal effects in endocrine conditions.

Excessive pigment in the dermis leads to a grey-blue appearance to the skin. This occurs most often in demodicosis. Sometimes many comedones will make the skin appear grey.

**Hypopigmentation** – skin or hair lighter than normal

Loss of pigment can occur from hereditary, autoimmune, nutritional, neoplastic, and idiopathic diseases

**Macules** – circular flat areas of discoloration in the skin

**Erythematous macules** - common in staphylococcal pyoderma and FAD. They are seen in contact allergic dermatitis and erythema multiforme (EM).

**Hemorrhagic macule (ecchymosis)** - seen with vasculitis and coagulopathies. One should use diascopy (the application of a glass slide to see if the condition blanches (not hemorrhage but erythema) to differentiate hemorrhage from erythema.

**Hyperpigmented macules**- common with staphylococcal pyoderma. Some dogs have normal “freckles” or hyperpigmented macules on their ventral abdomens. Other dogs (Irish Setters, Schnauzers) will develop these as they age and in these cases they have no pathology.

**Hypopigmented macules** - seen in vitiligo.

### **Erythematous maculo-papulo-pustular eruption (rash)**

Erythematous macules (see above)

**Papules**: small red raised lesions (dot like)

They are common in staph, FAD, scabies, atopic dermatitis and contact dermatitis. Be sure to look at the edges of erythematous macular areas to see if papules are present.

**Pustules** – red circular spots containing a central blip of pus (neutrophilic )

Crusted papules and pustules often are seen in conjunction with the above primary lesions. Crusted pustules are very common in dogs and cat’s skin because the fragility of these lesions does not allow them to remain intact for any period of time.

Staphylococcal collarette lesions ; this is a central circular area of alopecia which may be centrally pigmented surrounded by erythema and a ring of external scaling.

### **Scaling:**

**Scale** – visible accumulations of corneocytes (dandruff). Any condition that disrupts the normal process of keratinization has potential to result in scale.

**Seborrhea** – a descriptive clinical term for an animal with excessive scale or greasiness.

**Exfoliation** – shedding of skin in larger flakes over much of the body

**Hyperkeratosis**- this is really a term for pathologists but is sometimes used to describe a thick crust in a clinic patient

**Comedone** – keratin or other debris contained within a hair follicle (blackhead). Comedones occur with demodicosis, endocrine and keratinization defects.

**Follicular cast** – a adherent sheath of scale surround a hair shaft above the skin. This lesion occurs with follicular hyperkeratosis and is found with keratinization defects.

### **Changes in skin thickness:**

**Lichenification** - marked thickening of the skin due to a dramatic increase in the epidermis. This visibly appears to be exaggeration of the skin marking so that the skin looks like an elephant or armadillo. It is an attempt of the body to protect itself from further injury for forming a thicker barrier. It often occurs in conjunction with hyperpigmentation which is another defensive mechanism of the skin. Lichenification occurs most often with chronic pruritus.

**Plaque** – a localized patch of thickened skin with a flat surface. Plaques can be caused by thickening of the epidermis or by infiltration of inflammatory or neoplastic cells.

**Callus** – a thickened, rough, alopecid, lichenified plaque that forms over pressure points

**Myxedema** – puffy, thickening of the skin caused by excess mucin in the dermis. This is a feature of rare cases of hypothyroidism and is commonly seen in the shar pei dog.

**Cutaneous atrophy** – skin that is visibly thinner than normal. This usually is accompanied by easily wrinkled skin with vessels easily visible. It can be seen with hyperadrenocorticism and iatrogenic Cushing's.

## **Draining tracts**

*Furunculosis* - rupture of the hair follicles beneath the skin surface. This is usually the result of demodicosis or bacterial infection or both.

*Sinus* – an opening between the dermis and subcutis. These usually are associated with deep infections.

## **Defects in skin integrity**

*Erosion* - a shallow defect in the epidermis

*Ulcer* – a deeper defect where the epidermis is absent. Ulcers can be caused by autoimmune, infections, self trauma, neoplasia, burns.

*Vesicle* – a blister which is small. These occur from the lack of cohesion between the epidermis and dermis. There is fluid in the in-between space.

*Bulla* – a large blister, not seen in dogs and cats.

*Excoriation* - a scratch in the skin caused by trauma or self trauma

*Fissure* – spontaneous occurring linear split in the epidermis which allows the dermis to show. These usually occur on the pinna, footpads, of nasal pad.

## **Abnormal components in the skin surface**

*Exudate* – fluids and cells on the skin surface

*Crust* – stratum corneum and serum blood or pus dries on the skin surface

*Hyperhidrosis* – excessive sweat on the skin surface. Hyperhidrosis can be seen with various inflammatory skin diseases but it most often present in AD (Atopic dermatitis)

*Calcinosis cutis* – deposition of calcium into the dermis. It presents as white, chalky pieces of grit-like material in the skin. It is seen with steroids.

## **Lumps and swellings**

*Abscess* – cavity in the skin filled with pus (usually are infections but can be sterile)

*Hematoma* – a cavity in the skin filled with blood

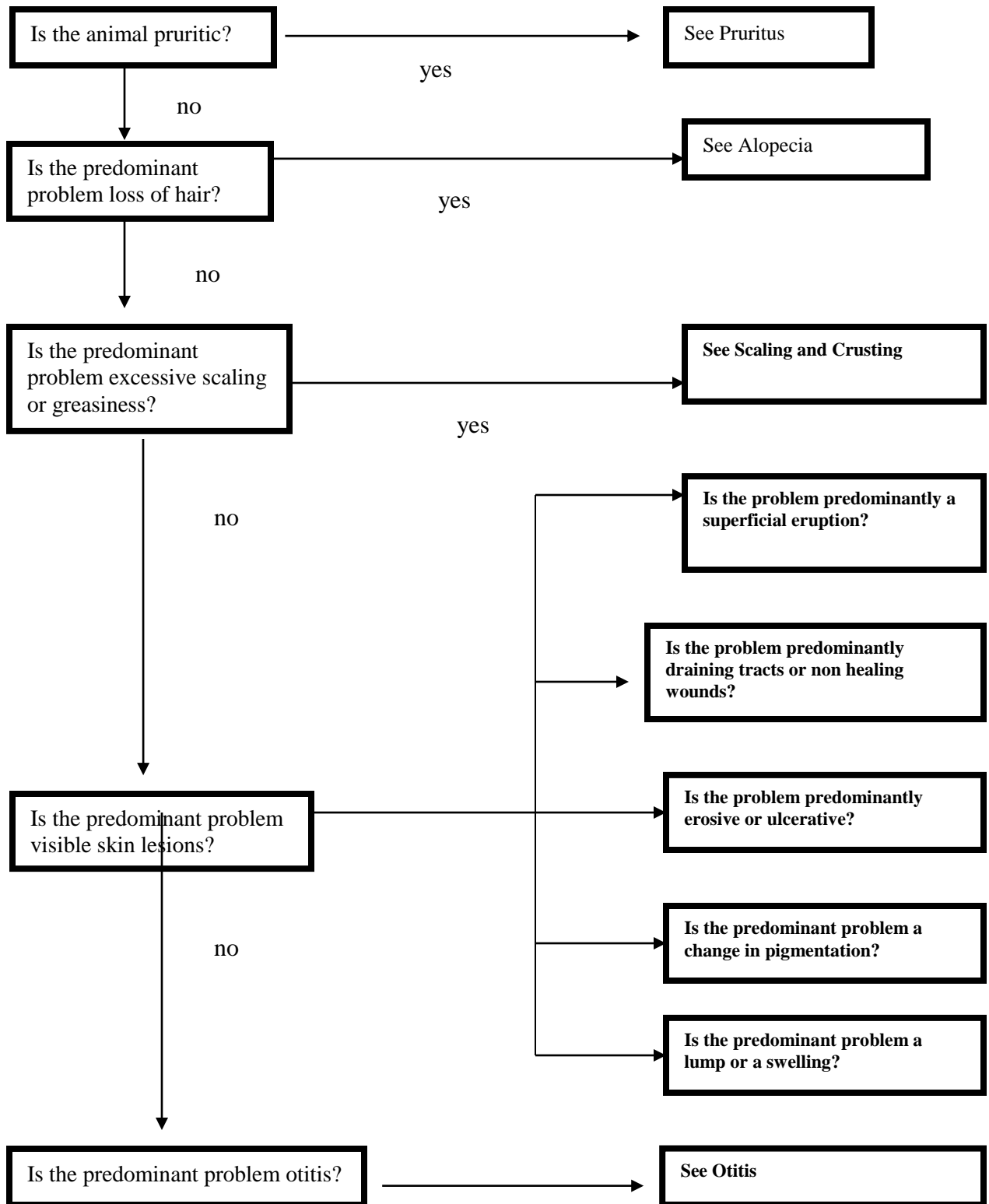
*Wheal* – circumscribed, circular, raised area of skin caused by edema



***Cyst*** – an epithelial lined cavity filled with skin components such as keratin, corneocytes, hair or sebum

***Nodule*** – a firm solid cutaneous swelling caused by inflammatory or neoplastic cells

***Tumor*** – a solid mass of tissue caused by neoplastic cells



## DERMATOLOGY CONSULT, DOG

Owner: \_\_\_\_\_ Date: \_\_\_\_\_

Dog ID: \_\_\_\_\_ Breed: \_\_\_\_\_

Age: \_\_\_\_\_ Sex: \_\_\_\_\_

### General information

How old was the dog when you got it? \_\_\_\_\_

Does your dog drink more than usual? \_\_\_\_\_

Does your dog urinate more than usual? \_\_\_\_\_

Does your dog eat with the same appetite as usual? \_\_\_\_\_

How many times per day does your dog need to go to the bathroom? \_\_\_\_\_

Does your dog have intestinal problems (vomiting, loose stool, gas)? \_\_\_\_\_

What does your dog eat, or put into the mouth?

Food: \_\_\_\_\_

Treats: \_\_\_\_\_ Other: \_\_\_\_\_

What type of food and water bowl does your dog have? \_\_\_\_\_

Does your dog's relatives have any skin disorders? \_\_\_\_\_

Where does your dog sleep? \_\_\_\_\_

**Dermatology history, dog**

Describe the problem: \_\_\_\_\_

At what age did your dog first show evidence of skin problem? \_\_\_\_\_

Did it start suddenly? \_\_\_\_\_ Gradually? \_\_\_\_\_

Does your dog have pruritus skin lesions coat changes:  
sneezing running eyes \_\_\_\_\_

If your dog is itchy (licks, chews, scratches) what came first, itching or skin lesions? \_\_\_\_\_

Where are problems noticed? Face Paws Ears Neck Back Sides  
"Arm pits" Groin Legs Rear end Tail

Is the problem constant or is it sometimes better? \_\_\_\_\_

Is there any seasonal difference? \_\_\_\_\_

Compared to when first noticed, is the problem?  
Worse Better No difference

How often is your dog bathed? \_\_\_\_\_

Shampoo \_\_\_\_\_ Conditioner \_\_\_\_\_

Is flea or tick prevention used? If so, what and how often?

Has any diagnostic test been done?

Test \_\_\_\_\_ Result \_\_\_\_\_

Test \_\_\_\_\_ Result \_\_\_\_\_

Test \_\_\_\_\_ Result \_\_\_\_\_

Has any treatment been tried?

Medicine \_\_\_\_\_ When? \_\_\_\_\_ Dose? \_\_\_\_\_ Effect? \_\_\_\_\_

Medicine \_\_\_\_\_ When? \_\_\_\_\_ Dose? \_\_\_\_\_ Effect? \_\_\_\_\_

Medicine \_\_\_\_\_ When? \_\_\_\_\_ Dose? \_\_\_\_\_ Effect? \_\_\_\_\_

## **APPROACH TO MACULAR/PAPULAR/PUSTULAR DISEASE**

Rosanna Marsella, DVM, DACVD

### **MACULES**

Macules are flat areas of skin of different color. Macules can be erythematous, hyperpigmented, or depigmented. Macules are rarely present as the only manifestation of skin disease.

### **PAPULES**

Papules are small solid elevations of the skin. Papules are erythematous due to the infiltration of inflammatory cells. They can be follicular or non-follicular and depending on whether they are focused on follicles or not different diseases should be considered. In the identification of the disease responsible for the papular eruption it is important to know whether pruritus is present or not.

### **PUSTULES**

Pustules are small skin elevations filled with pus. Pustules start as papules and then progress into epidermal collarettes. Cytology of a pustule is important to provide information regarding the type of inflammatory cells, the presence of bacteria and/or acantholytic cells.

### **CLINICAL APPROACH TO A MACULAR/PAPULAR/PUSTULAR CASE**

- Consider presence or absence of pruritus
- Response to previous treatments
- Waxing and waning (typical of autoimmune diseases)
- Distribution of lesions and whether different stages of development of lesions are present in the same animal (e.g. papules and epidermal collarettes). For example bacterial pyoderma is mostly a truncal disease and various lesions at different stage of development are visible; while pemphigus foliaceus tends to start on the face and ears and during flare ups lesions appear to go in waves and have similar stage of development.

### **MOST IMPORTANT DIFFERENTIAL DIAGNOSES FOR ERYTHEMATOUS MACULES**

- Superficial pyoderma
- Atopic dermatitis
- Contact allergy
- Food allergy
- Erythema multiforme (target lesions)\*
- Cutaneous lymphoma
- Mastocytosis
- Vasculitis\*
- Urticaria

\*more info on the bottom of the notes

## DIFFERENTIAL DIAGNOSIS FOR PAPULAR/ PUSTULAR ERUPTION

### Follicular

- Demodex
- Dermatophytes
- Staphylococcus

### Non follicular

- Flea bites and other insect bite hypersensitivities
- Sarcoptes
- Contact
- Malassezia dermatitis
- Atopic dermatitis (very small papules are sometimes present)
- Food allergy
- Impetigo
- Chin acne
- Pemphigus complex (foliaceous and erythematous)
- Systemic Lupus
- Canine familial dermatomyositis\*
- Sucorneal pustular dermatitis\*
- Sterile eosinophilic pustular dermatitis\*
- Idiopathic Linear Pustular Acantholytic Dermatitis\*
- Drug eruptions (e.g. reactions to shampoos or dips)
- Juvenile cellulitis
- Mast cell tumors
- Calcinosis cutis (dogs)
- Miliary dermatitis in cats

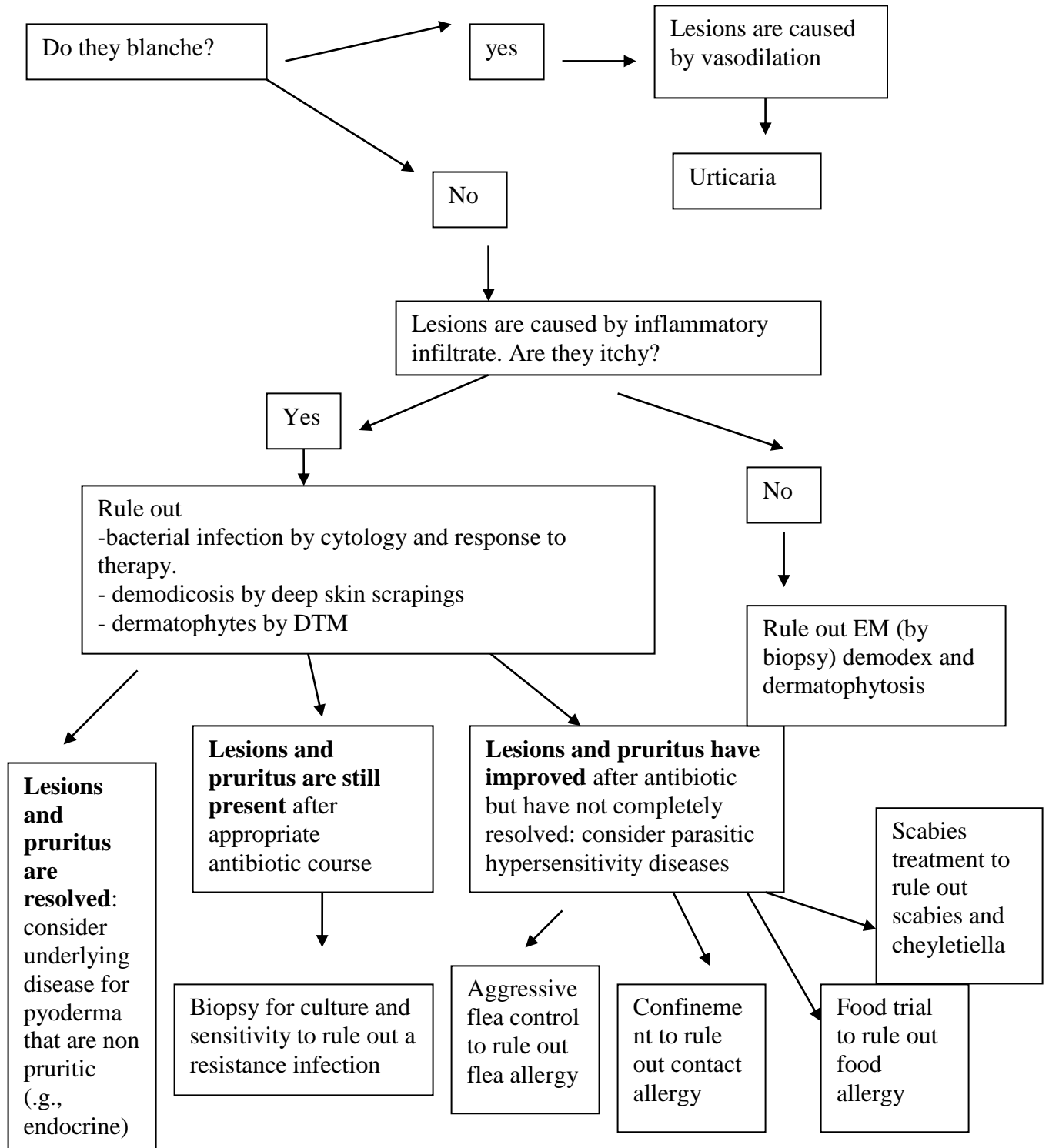
#### Underlying causes include

- ❖ Bacterial, yeast and viral infections
- ❖ Ectoparasites (e.g. fleas, lice, Cheyletiella, Notoedres)
- ❖ Allergic (Flea, atopy, food, contact)
- ❖ Cutaneous lymphoma
- ❖ Immune-mediated (e.g. pemphigus)
- ❖ Manifestations of internal disease (e.g. hyperthyroidism)

### Minimum data base includes:

- Cytology
- Superficial and deep skin scrapings
- Fungal culture in all feline cases
- Prescribe antibiotic therapy in all canine cases and in feline cases of miliary dermatitis
- Step up flea control; Treat for yeasts if necessary and reassess primary eruption +/- pruritus.
- Based on history of age of onset and distribution of lesions consider additional therapies and/or biopsy to investigate autoimmune, immune mediated or neoplastic disease

**LOGICAL APPROACH TO MACULES AND PAPULES**



## **FOR DOGS THAT HAVE RECURRENT PYODERMA it is important to identify the underlying cause**

- Pruritic causes
  - ◆ Allergic
    - ☞ Flea allergy
    - ☞ Atopic dermatitis
    - ☞ Food allergy
    - ☞ Contact allergy
  - ◆ Parasitic
    - ☞ Scabies
    - ☞ Cheyletiella
    - ☞ Demodex
    - ☞ Hookworm dermatitis
- Non pruritic causes
  - ◆ Endocrine
    - ☞ Hypothyroidism
      - Rapid deep pyoderma
    - ☞ Hyperadrenocorticism
    - ☞ Sex hormone imbalances
  - ◆ Dz. keratinization
    - ☞ Primary seborrhea
  - ◆ Parasitic
    - ☞ Demodex
  - ◆ Chronic steroid use
  - ◆ Idiopathic

### **Diagnostics at first visit**

- ◆ Cytology
  - ☞ Determine morphology of bacteria, types of cells
    - Intracellular/extracellular, yeasts, acantholytic cells
- ◆ Deep skin scraping
  - ☞ Limitations
    - Pododermatitis
    - Fibrotic tissue
    - Shar-pei
- ◆ DTM
- ◆ 4-6 weeks of antibiotic, good flea control and then re-evaluate
  - ☞ Longer times are necessary if steroids have been used or with Cushing's

### **At recheck visit**

- Pyoderma has resolved
  - How long did it take to clear? Add 7-10 days
  - Is it itchy? Evaluate residual pruritus and relapse time (see list of pruritic diseases)



- If there is no residual pruritus, consider underlying diseases that are not itchy (e.g. endocrine, metabolic, diseases of keratinization, food allergy)
  - Pyoderma has improved but not resolved
    - Continue antibiotic for 2 weeks past the resolution of clinical signs
  - Pyoderma lesions have not improved – possible resistant infection
    - Stop AB for 3-5 days; then do biopsy for culture and sensitivity
    - Consider other differential diagnoses (see list for papular/pustular eruption). In doing this consider the presence of pruritus and the distribution of lesions
      - If primary lesions are present, options are:
        - Treat for scabies
        - Food trial
        - Confinement to R/O contact
        - Biopsy to address possible PF, MF
-

## DISEASES NOT EXTENSIVELY COVERED IN THE CORE THAT MAY PRESENT WITH MACULES/PAPULES/PUSTULES

### ERYTHEMA MULTIFORME (EM)

#### KEY FACTS ABOUT EM:

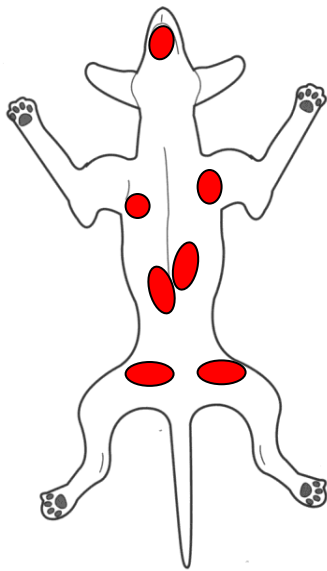
**Lesions:** Macules, target lesions, ulcerative lesions

Ventral distribution

In some cases also oral cavity and feet are affected

**Diagnosis:** biopsy

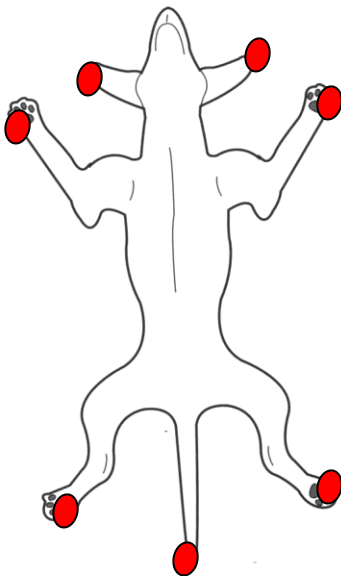
**Treatment:** identification of triggering cause + supportive care



EM is described as an acute, self-limited inflammatory condition that affects the skin and, in some cases, the mucous membranes. EM is not a specific diagnosis. It is the description of a syndrome that can have a variety of underlying causes. In dogs EM has been recognized in association with drugs (aurothioglucose, cephalosporins, levamisole, sulfonamides), infections and neoplasia. Lesions include erythematous macules or papules that spread peripherally and clear centrally producing arciform lesions (target lesions). Plaques, vesicles and bullae can also be seen. Bullous and ulcerative lesions of the oral cavity, pinnae, axillae and groin and footpads may be present. Affected animals are systemically ill, febrile and anorectic. When it affects the mucous membranes it is called EM major or Stevens-Johnson syndrome. Erythema multiforme may have a variable course. Some cases will regress while others will continue and animals with extensive lesions may die.

Diagnosis is made by clinical signs and biopsy. Suggestive changes include apoptotic keratinocytes at various levels of the epidermis and lymphocytes migrating in the epidermis. Once a diagnosis is made the offending drug should be discontinued and avoided in the future. Discontinuation of the medication results in complete clearing of the lesions in some cases. In some cases, however, topical and systemic supportive therapy is needed. Topical therapy is done to control the secondary bacterial infection, remove crusts and speed up the healing process. Systemic antibiotic should be used in severe drug reactions due to the loss of barrier function of the skin and the potential for life-threatening sepsis. Topical antibiotic (e.g. silver sulfadiazine cream) may be used on necrotic areas as blood supply is insufficient and systemic antibiotic may not achieve high enough concentrations. Fluid therapy may be needed to compensate the loss of fluids, electrolytes and proteins through the skin. The use of systemic glucocorticoids is controversial as they may predispose to more severe secondary bacterial infections. Generally in severe cases that are progressively deteriorating, the use of steroids is indicated for shock and to decrease the immunological reaction. Recovery, depending on the severity of the disease, should occur within 4 weeks.

## VASCULITIS



### KEY FACTS ABOUT VASCULITIS

**Lesions:** haemorrhagic macules, ulcers

**Distribution:** tip of the ears, tip of tail, center of footpads

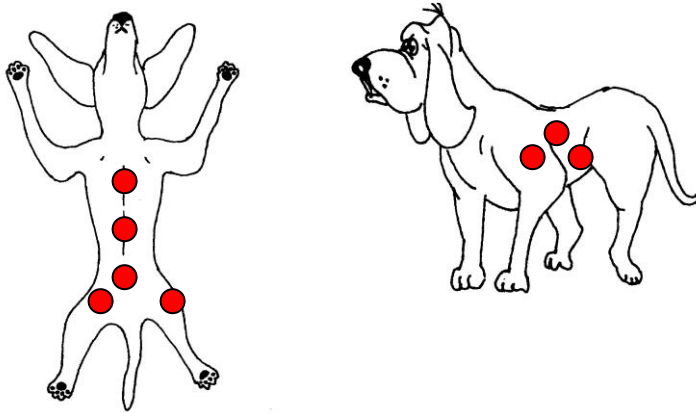
**Diagnosis:** biopsy

**Treatment:** identification of triggering cause+ pentoxifylline or other anti-inflammatory therapies (e.g., glucocorticoids, topical tacrolimus)

It represents type III hypersensitivity and can be secondary to a variety of antigenic stimulations (e.g. infectious, drugs, autoimmune). Affected dogs may present with cutaneous signs and or systemic signs depending on the extent of vasculitis. Cutaneous signs include

erythematous macules that progress into necrotic lesions due to impaired tissue oxygenation. Areas typically affected are the tips of the ears, tail, the center of the footpads. Edema may be present when vasculitis affects the distal limbs. Diagnosis is made by biopsy. It is important to pursue an underlying cause to correct it, whenever possible. Symptomatic therapy for vasculitis includes systemic pentoxifylline at 15-20mg/kg TID with food. Topically tacrolimus (Protopic) has been helpful to decrease the inflammatory response.

### **SUBCORNEAL PUSTULAR DERMATOSIS (SPD)**



#### **KEY FACTS ABOUT SPD**

Rare disease

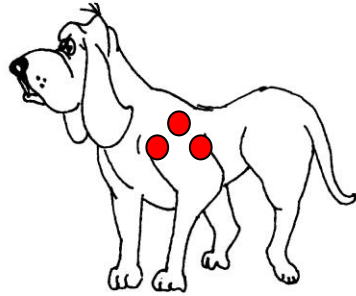
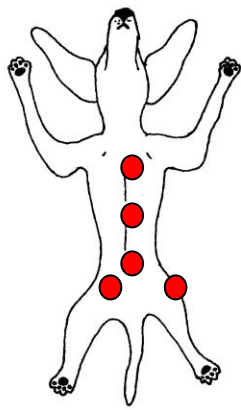
**Lesions:** pustules, epidermal collatettes, scaling

**Distribution:** head and trunk

Rule out more common diseases (e.g., bacterial infections, pemphigus)

This is a rare and idiopathic disease. Miniature Schnauzer may be predisposed to this condition. Affected dogs have multifocal to generalized pustular eruption. Pustules are non follicular and large. Scaling and crusting is common since pustules are transient. Pruritus is variable. Dogs appear to be healthy otherwise. It is important to rule out other more common causes of pustular eruption in dogs. Cytology is negative for bacteria and so are bacterial cultures. Acantholysis is minimal. The condition is usually resistant to antibiotics and glucocorticoids. Dapsone has been used in the past to control this condition but due to the severe adverse effects, both hematologic and hepatic, this drug is not commonly prescribed.

### **STERILE EOSINOPHILIC PUSTULAR DERMATITIS (SEPD)**



### **Key facts about SEPD**

Rare

Lesions: papules and pustules +/- pruritus

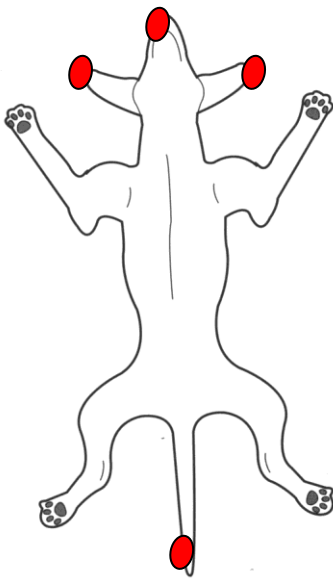
Distribution: mostly trunk

Rule out more common diseases

Responsive to glucocorticoids

Sterile eosinophilic pustulosis is a rare dermatosis of dogs and humans. In some cases it can be related to insect bites or drug reactions. The disease is characterized by a moderately generalized, pruritic, sterile, follicular and non-follicular papulo-pustular dermatitis. The onset of the lesions is usually acute and blood and tissue eosinophilia are usually present. Cytology and cultures are negative for the presence of bacteria. Most dogs respond to systemic glucocorticoids and since the disease is chronic relapses are frequent and long term therapy is necessary. It may be helpful to combine glucocorticoid therapy with essential fatty acids or antihistamines.

### **DERMATOMYOSITIS (DM)**



### **KEY FACTS ABOUT DM**

**Lesions:** macules, crusting, scaling, alopecia

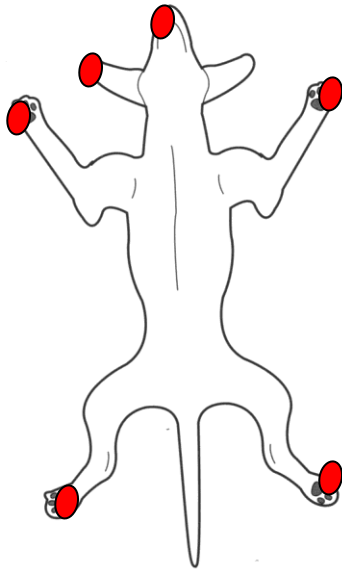
**Distribution:** most commonly on tip of ear, tip of tail, face  
Sometimes also on feet, oral cavity,

**Diagnosis:** biopsy

**Treatment:** variable depending on the severity (most commonly involving pentoxifylline and other anti-inflammatory therapies)

Dermatomyositis is an inflammatory condition of the skin and muscle in dogs. Skin lesions usually appear in dogs less than 6 months of age and as early as the 7th week of life. Skin lesions are most common on the face, ears, feet, and tip of the tail. The lesions usually consist of patchy hair loss, redness, scaling, and mild crusting. Some dogs may exhibit ulcers. The mouth, the footpads, and the nails may be affected. The muscle involvement is often seen months after the skin lesions are first seen. Some dogs, particularly those with mild skin lesions, may not exhibit symptoms of muscle involvement. When present, the nature and severity of muscle involvement are variable. Atrophy of the muscles of the legs and head is common. Another common finding is a "dirty" waterbowl containing food particles that are not completely swallowed by the dog while eating. Some dogs walk abnormally. More severe muscle involvement can result in difficulty chewing, drinking, swallowing, and walking. The diagnosis is most often made by biopsy of the skin, and may be supported in some cases by biopsy of the muscle and muscle testing. Because the severity of the disease is so variable, treatment is not always needed. Some dogs with mild disease heal rapidly without progression of the skin disease, although some have permanent scarring. In most cases, skin lesions are fully developed by 1 year of age, and do not progress significantly after that time. The skin lesions are easier to control than the associated muscle lesions. Unfortunately, some dogs with severe muscle involvement become extremely debilitated despite therapy. Therapy for the skin lesions may consist of vitamin E, fatty acid supplements, and occasionally prednisone (a corticosteroid). The use of prednisone should be minimized due to its numerous side-effects. Pentoxifylline (Trental®) can be very helpful in controlling the skin lesions of dermatomyositis. Because the disease is hereditary in Shetland Sheepdogs and Collies, affected dogs, their siblings, and their parents should not be used for breeding. It is hoped that scrupulous elimination of even mildly affected animals and their relatives from the breeding program may reduce the incidence of this common condition.

#### **PEMPHIGUS FOLIACEOUS AND MANAGEMENT OF AUTOIMMUNE CASES**



“butterfly”  
distribution  
of lesions  
on face

#### **KEY FACTS ABOUT PF**

Autoimmune disease

Lesions: pustules, crusting, scaling

Distribution: face, ear, feet

Diagnosis: biopsy

Treatment: immunosuppressive therapy (glucocorticoids combined with a steroid sparing agent)

Pemphigus is a cell adhesion autoimmune disease caused by circulating antibodies directed against desmosomal (molecules that mediate adhesions among keratinocytes) antigens. Desmosomes are defined as disc-like structures where plasma membranes of the cells attach to each other. Typically autoimmune diseases such as pemphigus, affect middle age animals. The disease has a waxing and waning course, usually starting on the head and then spreading to the rest of the body. Animals may be systemically ill during a flare up of the disease. Flare ups are worsened by stressful situation. In some cases the autoimmune disease is not idiopathic but triggered by antigenic stimulation, such as infections, drugs, or neoplasia. Diagnosis is obtained by combining clinical signs, histopathology findings and results of immunology tests (e.g. direct immunofluorescence and immunohistochemistry for the detection of antibody deposition in the skin).

Therapy for autoimmune skin diseases includes the use of glucocorticoids in combination with other immunosuppressive agents (steroid sparing agents).<sup>1</sup> Combination therapy may prolong remission and reduce side effects due to glucocorticoid therapy. Immunosuppressive drugs can be non cytotoxic (e.g. glucocorticoids) or cytotoxic (e.g. azathioprine, chlorambucil). Azathioprine is commonly used in dogs while chlorambucil is most commonly used in cats.

#### **Glucocorticoids**

Systemic glucocorticoids are the most common therapy. They are seldom used as single therapy. Induction dose for prednisone is 2.2-6.6mg/kg q12h for dogs and 4.4-8.8 mg/kg for

cats. Methylprednisolone can be used to reduce PU/PD and induction dose is 0.8-1.5mg/kg q12h. Induction usually lasts from 10 to 14 days, depending on the severity of the case. Once the disease is in remission (e.g. no new lesions are found on physical examination), the dose is slowly tapered until an alternate day administration is obtained. Tapering to a long-term maintenance dose is best achieved over 8-10 week-period. For a dog of 80# of body weight the tapering is initially done at a rate of 10-20mg/week until an alternate day regimen is achieved and then more slowly at 5-10mg/week until the maintenance dose is reached. At that point dose reduction should be much slower (5-10mg reduction/week). Most dogs will require a maintenance dose of prednisone from 0.5 to 1.1mg/kg q48 hours.

Alternatively, triamcinolone at 0.2-0.3mg/kg q12h or dexamethasone at 0.1-0.2mg/kg q12h could be used for induction with tapering to 0.1-0.2 mg/kg q48-72h (triamcinolone) and 0.05-0.1mg/kg q48-72h (dexamethasone). Glucocorticoid pulse therapy is reserved for very severe cases. In dogs intravenous administration of methylprednisolone (sodium succinate) is given at 11 mg/kg/day, over a 3-hour period for 1 to 3 days. Once remission is obtained, intermediate to low-dose, oral glucocorticoid therapy is started in conjunction with other immunosuppressive drugs. Topical glucocorticoids can be used for localized lesions. The main adverse effect of high doses of glucocorticoids is gastro-intestinal ulcers. Other adverse effects include secondary hyperadrenocorticism, diabetes mellitus, hepatopathy, nephropathy, hypertension, electrolyte disturbances, and secondary infections (e.g. skin and urinary tract infections). Dogs may also develop generalized demodicosis secondary to the immunosuppressive therapy. Owners should be warned about the possibility of the development of GI ulcers and careful monitoring of bowel movement is recommended.

### **Azathioprine**

Azathioprine (Imuran®, 50mg scored tablets) is usually the first choice of immunosuppressive therapy for autoimmune skin diseases in dogs. It is a purine analog that interferes with nucleic acid synthesis (both DNA and RNA) and is cytotoxic to T cells. It is effective in suppressing T cell function (depresses cell mediated immunity) and T cell dependent antibody production (depresses humoral immunity). After oral administration azathioprine is rapidly converted in the liver into 6-mercapto-purine (6-MP). As the bio-transformation of azathioprine occurs in the liver, its immunosuppressive effects are reduced in animals with hepatic insufficiency. 6-MP is oxidized and methylated to various derivatives by 3 competing enzyme pathways: thio-purine-methyltransferase (TMPT), xanthine oxidase and hypoxanthine-guanine-phosphoribosyl-transferase. Of these pathways, only the last one leads to the production of active metabolites. Human patients that are deficient of TMPT have an increased production of active metabolites leading to increased toxicity.<sup>2</sup> It has been reported that, in a normal population, 88.6% of people are homozygous for an allele for high TPMT activity, where as only 0.3% are homozygous for the low activity allele and 11.1% are heterozygotes. A recent study in veterinary medicine revealed that dogs might have a similar distribution of this enzyme.<sup>3</sup> It is also important to note that when a xanthine oxidase inhibitor is used (e.g. allopurinol) the dose of this drug should be reduced to ¼.

**Azathioprine has a slow onset taking 4 to 6 weeks to produce clinical effects** thus during that period of time the use of glucocorticoids is crucial to control the disease. In dogs, a dose of 1.5-2.5 mg/kg q 48 hours is commonly used. The dose of azathioprine is usually not



tapered, unless severe bone marrow suppression occurs. A common maintenance protocol is to administer azathioprine on days in which glucocorticoids are not given. Cats are very sensitive to the toxic effect of this drug so it is not recommended in this species. Adverse effects include myelosuppression, vomiting, diarrhea, pancreatitis, and hepatotoxicity. Initially, complete blood cell count (CBC) and platelet counts should be monitored every 2 weeks. If the white blood cell counts (WBC) decreases to less than  $4000/\text{mm}^3$  therapy should be discontinued. After the disease is in remission, the frequency of monitoring can be decreased to every 2-3 months. Hepatotoxicosis is a potential side effect of azathioprine therapy thus liver function should be monitored during administration of this drug.

### **Chlorambucil**

Chlorambucil (Leukeran®, 2 mg scored tablets) is an alkylating agent that causes DNA breaks and cross-links. Lymphocytes, especially B cells, are extremely sensitive to the effects of this drug. It is the immunosuppressive drug of choice for cats and it may be used as adjunctive immunosuppressive therapy in dogs that cannot tolerate azathioprine. Recommended dose is 0.1-0.2 mg/kg q 48 hours. It is rapidly and well absorbed after oral administration and is extensively bound to plasma and tissue proteins. It is rapidly metabolized in the liver. It has very low urinary excretion. **There is also a lag phase of 4-6 weeks before producing clinical effects.** It is the slowest-acting alkylating agent and for this reason is not considered a first choice in dogs. Adverse effects include hepatotoxicity and bone marrow suppression. Monitoring is similar to that with azathioprine. It should be discontinued if neutrophil count is less than 2,000/mcl or if platelet count is less than 80,000/mcl. Leukogram usually returns to normal within 10-14 days after discontinuation of therapy. It could lower the threshold of seizures in predisposed patients. Alkylating agents have the greatest potential to induce secondary neoplasms (especially lymphoreticular malignancies) with prolonged use.

### **Tetracycline and niacinamide**

Oral tetracycline and niacinamide have been used in dogs and people with pemphigus with variable success.<sup>4,5</sup> The rationale for this therapy is that tetracycline inhibits chemotaxis, complement, prostaglandin synthesis, lipases and collagenases, and that niacinamide inhibits mast cell degranulation and phosphodiesterase. Adverse effects in dogs include vomiting, diarrhea, anorexia, and increased liver enzyme activity. In dogs weighing more than 10 kg, 500mg of tetracycline and 500mg of niacinamide are given three times daily, while dogs weighing less than 10kg, should receive 250 mg of each. Dogs that show improvement with this therapy do so within the first one or two months of therapy. Once remission has occurred the dose may be gradually tapered to once daily administration.

### **General recommendations on Immunosuppressive therapy**

1. It is imperative to establish a firm diagnosis of autoimmune skin disease before considering the use of immunosuppressive therapy. Many inflammatory and infectious skin diseases may look like autoimmune skin disease and in those cases immunosuppressive therapy would be highly contraindicated. In addition, due to the waxing and waning course of autoimmune diseases it is crucial to use appropriate (e.g.

full dose) doses. Failure to do so because of a lack of diagnosis, may result in only partial improvement and lead to resistance to immunosuppressive therapy.

2. Diagnosis is made by biopsy (histopathological evaluation) for pemphigus and DLE and by biopsy and fulfillment of several criteria for SLE. Skin biopsies are best taken after a short course of antibiotics to minimize the effects of bacteria on histopathological changes. In addition, it is important to note that glucocorticoids may interfere with interpretation of histopathology thus biopsies should be taken before the beginning of steroid therapy.
3. Careful monitoring of CBC and platelet counts is recommended to prevent the occurrence of irreversible adverse effects. Monitoring of liver and renal function may also be necessary depending on the nature of the adjunctive immunosuppressive agent used.
4. Due to the existence of a lag phase for adjunctive immunosuppressive agents and due to the fact that it is very unusual to manage an autoimmune skin disease with only glucocorticoids, it is recommended to begin adjunctive therapy at the same time when glucocorticoids are started.
5. Concurrent antibiotic therapy is recommended for the first months of immunosuppressive therapy. Many dogs with autoimmune skin disease will have concurrent skin infections.
6. If sudden worsening of the skin condition is noted, it is important to consider the possibility of other concurrent diseases (e.g. superficial bacterial pyoderma, demodicosis and dermatophytosis) before an adjustment of the immunosuppressive regimen is recommended.
7. Prognosis varies according to the severity of disease in individual patients. As a general rule pemphigus vulgaris, bullous pemphigoid are extremely aggressive and animals rarely tolerate the doses of drugs required to keep the disease into remission. Pemphigus erythematosus and DLE are usually easily managed with topical steroids. Pemphigus foliaceus usually requires combination of glucocorticoids and other immunosuppressive agents.
8. The first 6 months of therapy are usually the most difficult due to the high incidence of side effects (e.g. GI ulcerations secondary to high doses of glucocorticoids and bone marrow suppression due to other immunosuppressive drugs) and higher probably of relapses.

Table 1. Suggested schedule for a 50 # dog diagnosed with Pemphigus foliaceus.

	<b>Sunday</b>	<b>Monday</b>	<b>Tuesday</b>	<b>Wednesday</b>	<b>Thursday</b>	<b>Friday</b>	<b>Saturday</b>
<b>Week 1</b>	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg Azathioprine 50mg Prednisone 50mg	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg	Prednisone 50mg  Prednisone 50mg
<b>Week 2</b>	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg	Prednisone 50mg  Prednisone 50mg	Prednisone 50mg <b>Azathioprine 50mg</b> Prednisone 50mg **
<b>Week 3</b>	Prednisone 50mg  Prednisone 50mg	Prednisone 40mg <b>Azathioprine 50mg</b> Prednisone 40mg	Prednisone 50mg  Prednisone 50mg	Prednisone 40mg <b>Azathioprine 50mg</b> Prednisone 40mg	Prednisone 50mg  Prednisone 50mg	Prednisone 40mg <b>Azathioprine 50mg</b> Prednisone 40mg	Prednisone 50mg  Prednisone 50mg
<b>Week 4</b>	Prednisone 30mg <b>Azathioprine 50mg</b> Prednisone 30mg	Prednisone 50mg  Prednisone 50mg	Prednisone 30mg <b>Azathioprine 50mg</b> Prednisone 30mg	Prednisone 50mg  Prednisone 50mg	Prednisone 30mg <b>Azathioprine 50mg</b> Prednisone 30mg	Prednisone 50mg  Prednisone 50mg	Prednisone 30mg <b>Azathioprine 50mg</b> Prednisone 30mg **
<b>Week 5</b>	Prednisone 50mg  Prednisone 50mg	Prednisone 20mg <b>Azathioprine 50mg</b> Prednisone 20mg	Prednisone 50mg  Prednisone 50mg	Prednisone 20mg <b>Azathioprine 50mg</b> Prednisone 20mg	Prednisone 50mg  Prednisone 50mg	Prednisone 20mg <b>Azathioprine 50mg</b> Prednisone 20mg	Prednisone 50mg  Prednisone 50mg

Table 1 continued.

	<b>Sunday</b>	<b>Monday</b>	<b>Tuesday</b>	<b>Wednesday</b>	<b>Thursday</b>	<b>Friday</b>	<b>Saturday</b>
<b>Week 6</b>	Prednisone 10mg <i>Azathioprine 50mg</i> Prednisone 10mg	Prednisone 50mg  Prednisone 50mg	Prednisone 10mg <i>Azathioprine 50mg</i> Prednisone 10mg	Prednisone 50mg  Prednisone 50mg	Prednisone 10mg <i>Azathioprine 50mg</i> Prednisone 10mg	Prednisone 50mg  Prednisone 50mg	Prednisone 10mg <i>Azathioprine 50mg</i> Prednisone 10mg
<b>Week 7</b>	Prednisone 50mg  Prednisone 50mg	<i>Azathioprine 50mg</i>	Prednisone 50mg  Prednisone 50mg	<i>Azathioprine 50mg</i>	Prednisone 50mg  Prednisone 50mg	<i>Azathioprine 50mg</i>	Prednisone 50mg  Prednisone 50mg
<b>Week 8</b>	<i>Azathioprine 50mg</i>	Prednisone 40mg  Prednisone 40mg	<i>Azathioprine 50mg</i>	Prednisone 40mg  Prednisone 40mg	<i>Azathioprine 50mg</i>	Prednisone 40mg  Prednisone 40mg	<i>Azathioprine 50mg</i>

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## Approach to focal/multifocal alopecia

Rosanna Marsella, DVM, DACVD

Alopecia can be primary or secondary to pruritus. In this lecture *we will address primary causes* of alopecia, which means not the self-inflicted diseases but the ones in which the hair falls out on its own. The pattern of hair loss may be very helpful in selection of the differential diagnoses. In some cases it is useful to divide the conditions of alopecia into focal or localized hair loss, as opposed to symmetrical or diffuse alopecia.

*With focal alopecia the first consideration should be demodicosis* and deep skin scrapings should assist you in making this diagnosis. Appropriately done deep skin scrapings with squeezing and obtainment of capillary bleeding should elicit a finding of demodex mites except in very rare cases. These instances include: 1) demodicosis in the feet or pododemodicosis in rare cases where fibrosis has occurred AND 2) in the SharPei where it may be difficult to find the mites without biopsy. So with focal demodicosis the first test is deep skin scraping and trichogram or examination of the hair for broken shafts or the rare instance where dermatophyte hyphae or ectothrix can be seen invading hair. A negative skin scraping should be followed by dermatophyte rule out which is assisted with the trichogram, Wood's lamp exam and most importantly a fungal culture. Thirdly one should consider the possibility of previous injection site alopecia, focal post-clipping alopecia and scars. If these can be ruled out by the history then a biopsy of the area likely is indicated.

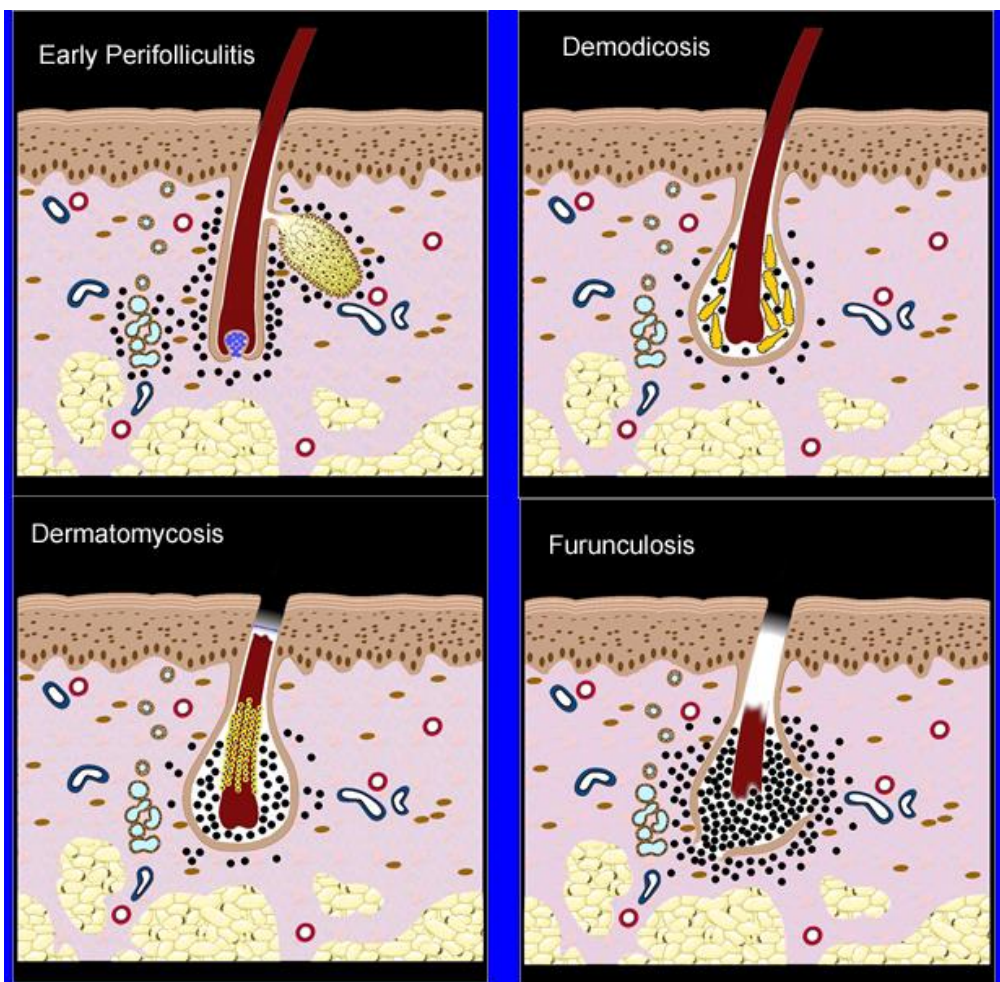
If multi-focal patches of alopecia are presenting sign again demodicosis must be the first differential diagnosis to rule out. After the deep skin scrapings and the trichogram, then if the animal is a dog, one should examine closely for primary lesions and one should consider staphylococcal infection and the "footprints" of alopecia. In the cat bacterial pyodermas do not present as multifocal alopecia. If the patient is a dog it may be necessary to rule out pyoderma by a lack of response to antimicrobial therapy. If there is no response or minimal response to antibiotics then a dermatophyte culture in conjunction with the trichogram and Wood's light examination is indicated. With negative skin scrapings, negative dermatophyte culture and a lack of response to antibiotic therapy, considerations should include sebaceous adenitis, color dilution alopecia, dermatomyositis and chronic vasculopathy. A biopsy of representative lesions should be helpful in pinpointing the diagnosis along with the history.

A diagnostic approach to symmetrical or diffuse alopecia would first include ruling out obvious causes such as congenital alopecias, testicular neoplasias, seasonal flank alopecia (symmetrical), or obvious systemic condition such as malnutrition. A history and thorough physical examination should help you with these considerations. Again the initial diagnostic tests and rule outs would be demodicosis and then dermatophytosis. If these tests are negative in the dog the next rule out would be for endocrine or systemic diseases and hemogram and chemistry profile would be initial tests. Thyroid testing and / or adrenal function testing could be done in conjunction with other blood work or at a later time. In the cat with symmetrical or diffuse

alopecia one should carefully review the history and the trichogram as most cases of this type of alopecia in the cat are self-induced. If all endocrine testing is normal (remember to also consider iatrogenic hyperadrenocorticism) then biopsies may be helpful if one is considering hair follicle dysplasia, seasonal flank alopecia, color dilution alopecia, anagen/telogen defluxion or “effluvium”, paraneoplastic alopecia (feline) or epitheliotropic lymphoma.

### Aliens that invade the Hair Follicle: Folliculitis

These would include: demodex, pyoderma, dermatophytosis and leishmaniasis (in Europe). These may produce focal, multifocal patchy or symmetrical alopecia dependent on the number and distribution of hair follicles affected.



Diagrams from Stromberg, OSU, IVIS website

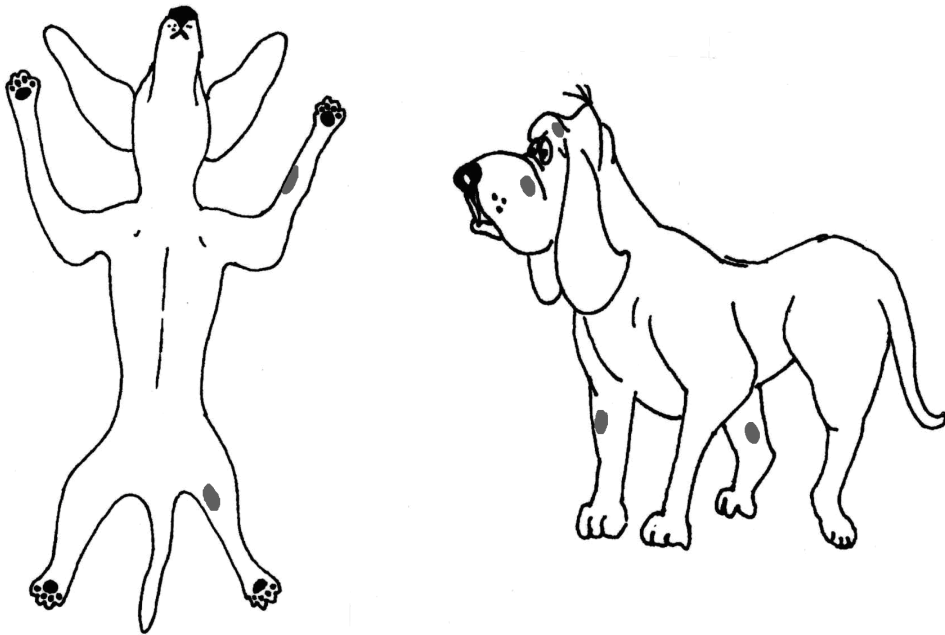
Demodicosis (Demodectic mange)

**Etiology:** Excessive proliferation of demodex mites in hair follicles. In young dogs (juvenile) this is thought to be due to some type of immune defect although it is still not clear what contribution the mites make to this immunosuppression. Adult dogs with onset of demodicosis often have it secondary to some underlying problem such as hyperadrenocorticism, hypothyroidism, internal diseases, malignancies, overzealous use of glucocorticoid therapy.

**Lesions:** Patchy alopecia, comedones (blackheads), follicular casts, erythema, scale, slate-grey hyperpigmentation of the skin. When secondary infection is present there may be papules, pustules, furuncles and rarely ulcerated draining tracts.

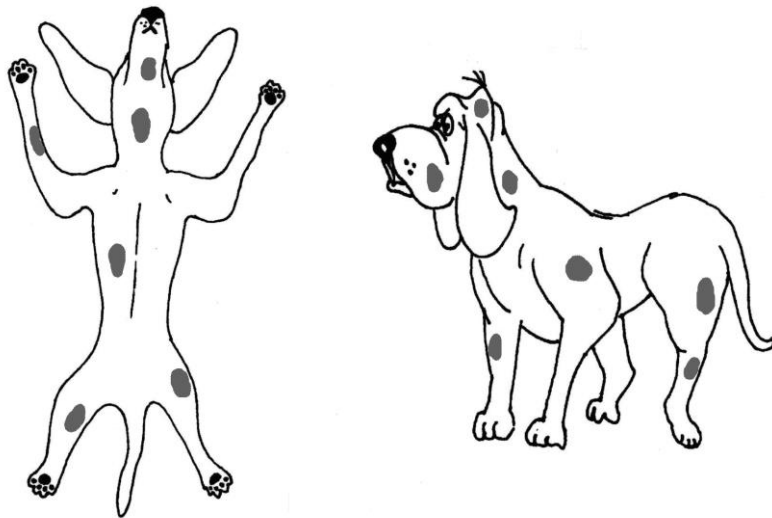
**Lesion distribution:**

Localized: focal patches on the face and/or legs

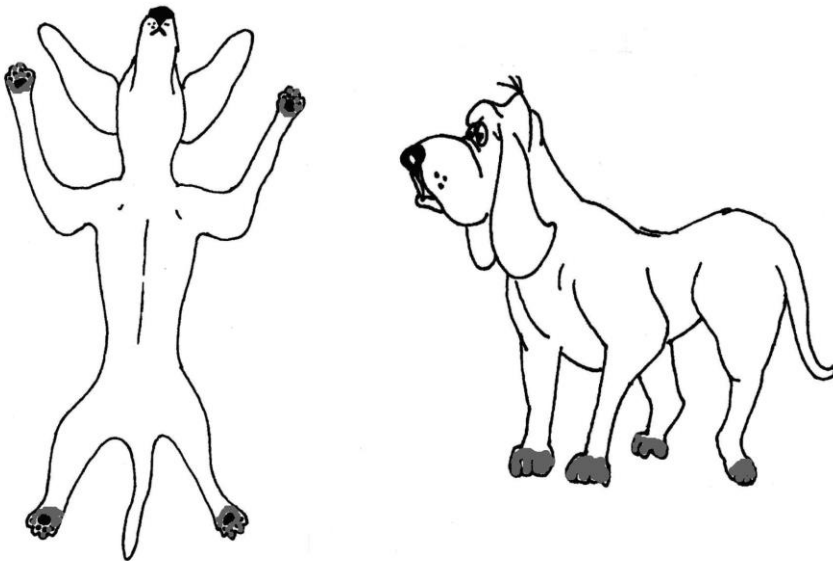


Generalized Demodicosis: multifocal or diffuse lesions over the face, legs, and trunk





Demodectic Pododermatitis: lesions on the feet.



**Tests:** Deep Skin scrapings

Hair pluckings: sometimes useful in dogs where it is difficult to obtain mites

Biopsy

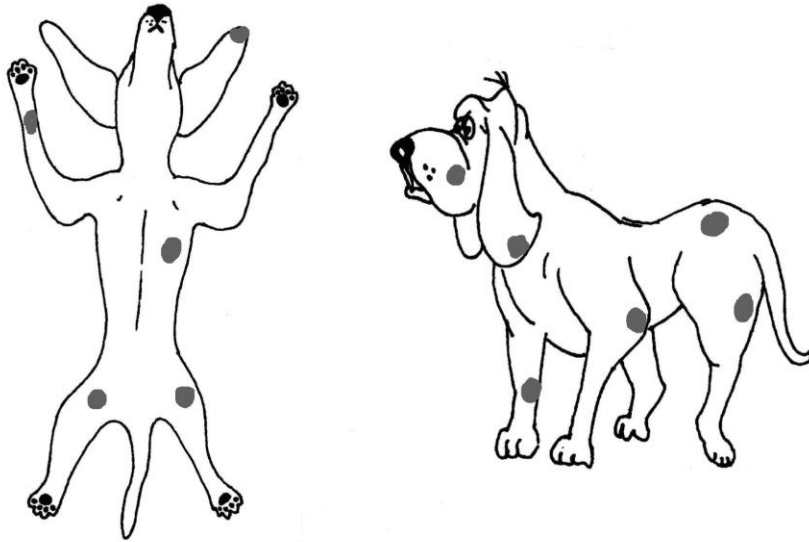
**RX:** See your sophomore notes

### **Dermatophytosis**

**Etiology:** Infection with *Microsporum* or *Trichophyton* fungi

**Predominant lesions:** Patches of alopecia and scaling with or without visible inflammation

**Lesion distribution:** Focal, multifocal, or diffuse



**Diagnostic tests:**

*Fungal culture:* the gold standard, toothbrush fungal culture technique (MacKenzie method) is ideal. This technique cannot differentiate infections from fomite carriage; however fomite carriers often have cultures that fluctuate from positive to negative and will have small numbers of colonies of fungal growth.

*Trichogram* Hair shaft direct exam of hair: tedious and time consuming, requires experience

*Wood's light exam* should warm up for 3 - 5 minutes; there is also a delay in hair fluorescence in some cases. Interestingly the same strain may not glow on all cats. The hair may fluoresce when the culture is negative. It is believed that the fluorescence is caused by tryptophan metabolites but *M. canis* has not been found to produce any tryptophan metabolites so the mechanism of fluorescence is not clear.

*Biopsy: a negative biopsy doesn't exclude the infection....sampling is important*

**RX:** Most dermatologists agree that three types of therapy are necessary. These would include:

- 1) Topical therapy to lessen the contamination from hairs and scale in the environment
- 2) Systemic treatment to shorten the time of infection in the animal and
- 3) Environmental treatment to help to prevent recurrence in the animal and to prevent transmission to other pets/people in situation.

**1) Topical Treatment**

Infective spores can be cultured as far as 10 cm from the visible lesion in man. In animals, especially cats it is almost certain that there are infective spores in non-lesional areas. Using topicals to treat focal areas of crusting or alopecia is NOT recommended. It may falsely suggest to the owner that the infection is being treated. For topical treatment, dipping (also called rinsing

but it is not washed off) is the best method. Whole body treatment should be used in all cases. Its primary purpose is for decreasing environmental contamination and exposure to others. Clipping of the Hair Coat is now considered optional and should likely depend on the severity of infection. It is indicated when large areas of the body are clearly affected. It is usually recommended in long haired cats where the haircoat is positive on Wood's light. It may be useful to decrease contamination of environment when a young kitten is heavily infected and if there are children who have not yet become infected. With most short haired or medium haired cats we no longer clip. In infected cats there may be a worsening of clinical signs after the trauma of clipping. If you do the clipping in your clinic you should have an isolated facility and all hair should be removed and burned or soaked in undiluted bleach solution. Chemical or heat sterilization is mandatory on equipment because spores are viable for long periods.

Lime Sulfur solutions ( 2-4%) are among the most effective topical products (example: LymDip®, DVM Pharmaceuticals). This chemical is very safe, but the odor is very bad. Use Elizabethan collar until solution is dry to prevent ingestion but most cats do not get ill even if they do ingest the dip.

Enilconazole (Imaverol®, Janssen Pharmaceutica) is a topical antifungal rinse sold in many countries (but not the USA) for dogs and horses. It appears to have excellent, and very rapid, action against infected hairs and spores of *Microsporium canis*. It is not labeled for use in cats. Toxicity in cats is idiosyncratic and so caution is advised. It is theorized that the toxicity is related to oral ingestion by grooming. In a study of 22 Persian cats treated with enilconazole, 6 developed elevated ALT and one developed transient muscle weakness. Monitor liver enzymes, place Elizabethan collar around the cat's neck after the dip to prevent grooming, and leave it on until he is thoroughly dry.

Chlorhexidine shampoo or solution. Not recommended. Studies suggest that chlorhexidine does not kill the fungus in infected hairs as well as other products such as lime sulfur. These solutions can irritate the eyes severely and systemic toxicity can be seen.

Miconazole (with or without chlorhexidine, as a shampoo) in one study was found to be superior to placebo or chlorhexidine shampoo alone, as an adjunct to griseofulvin treatment.

Miconazole plus chlorhexidine shampoo was recently studied in cats as an adjunct treatment to oral griseofulvin. Cats treated with shampoo+griseofulvin recovered *visually* at about the same rate as cats treated with griseofulvin alone. However, shampoo+griseofulvin cats achieved negative *fungal cultures* much more quickly than those treated with griseofulvin alone.

### **Systemic Treatment**

Griseofulvin is still a good choice systemic drug (and sometimes cheapest) for initial treatment depending on the situation. Myelotoxicity has been seen in cats and appears to be idiosyncratic and hence not predictable. It is not dose dependent. Also check for FeLV and FIV as these conditions can be cofactors in myelosuppression. Some suggest following patients with a hemogram which thus raises the cost of treatment. Most patients will be cured with griseofulvin. It should not be used in animals under six weeks of age. It should never be used in pregnant animals because of teratogenicity; however some cat breeders will use in the last trimester of queens. This drug is given orally and has enhanced absorption with a fatty meal. Treatment should be continued until negative fungal culture results are obtained and in general, this is 6-12 weeks of treatment. For cats, the usual product is the microsize of griseofulvin and it is given at

50-120 mg/kg/day (usually divided BID). If one is using the ultramicrosize in PEG base (example Gris-Peg® then 5-10mg/kg/day)

Itraconazole (Sporanox®) is very useful antifungal especially for cats. It is available in capsules or an oral liquid. The dose is 5-10mg/kg daily. Because it persists in skin and/or nails for 3-4 weeks after dosing, there is recent suggestion that we may be able to use this drug on an intermittent schedule, thus saving cost. Itraconazole has been used in a pulse treatment protocol with success. (5m/kg for 2 consecutive days per week) after an initial induction (every day for the first 2 weeks). Some dermatologists routinely uses this drug on an every-other-week schedule, thus decreasing treatment cost by 50%.

Fluconazole (Diflucan®) is likely not an alternative drug. Several recent in vitro studies have shown that MICs of fluconazole against dermatophytes are much higher than the MICs of itraconazole. This suggests that itraconazole may be the superior drug. There is no cost advantage so it is not recommended.

Terbinafine (Lamisil®) is an allylamine antifungal that is well concentrated in the skin and may be useful for treating dermatophytosis. The recommended dose for animals has been 30mg/kg. In a 2001 study, cats treated with 30-40 mg/kg/day cured significantly faster than those treated with 10-20 mg/kg/day. In a project done by a dermatology resident at UF, two normal cats of 10 had generalized erythema and pruritus developed as a drug reaction to Terbinafine. This drug is metabolized by the liver (although not through P 450) and increased liver enzymes can be seen with this drug thus liver monitoring is recommended when used for prolonged time.

Lufenuron (Program®) is a chitin synthase inhibitor for flea control and it has been reported to be useful in feline dermatophytosis. Since the initial report of success several other studies have reported treatment failure with a wide variety of higher doses. There are no controlled studies to support its use as being effective in treating dermatophytosis.

How Long To Treat is generally dependent on the conditions of the infection. Treating until clinical cure is not generally satisfactory. Most like to have two successive brush cultures to be negative at 2-3 weeks apart. The initial culture is taken at 4-6weeks after instigating treatment and the treatment should be continued until the second culture is deemed negative.

### **Environmental Control**

The importance of mechanical removal of hair and debris cannot be overemphasized. This can be a monumental task in certain situations like catteries. Hairs with infected arthrospores can reside in the “right” environment for many months-years and still be infective. A vacuum is of critical importance. The more often and more vigorous use of the vacuum the more effective. Studies have shown that many of the disinfectants labeled as effective for killing dermatophytes are not effective for this purpose. (DeBoer-) “Disinfectants are tested for antifungal actions by observing their effects on suspensions of fungal spores or fungal mycelium in a test tube. However, in a house or a veterinary hospital, the predominant contamination is not with spores or mycelium, but rather with small fragments of infected hairs. It is possible that the hair shaft protects the fungus from the actions of disinfectants. Initial studies that simulate the actual conditions of use demonstrated that, of many different disinfectants tested, only very concentrated chlorine laundry bleach (0.05 to 0.5% sodium hypochlorite = 1:10 to 1:100 dilution) and enilconazole environmental spray were very effective.

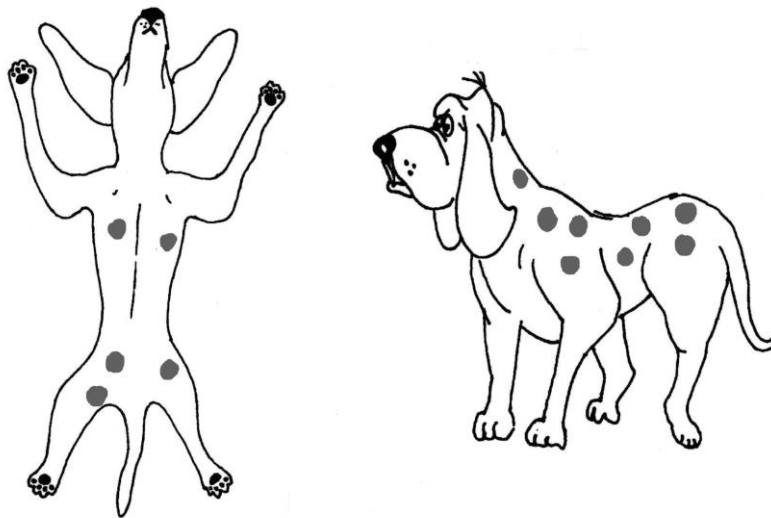
Current recommendations: Concentrated chlorine bleach solution (1:10 to 1:100) Clinafarm® (enilconazole) environmental spray – licensed for cattery use in most of Europe but not available here in the US except as an EPA regulated product for spraying in turkey farms.

**Superficial pyoderma (aka superficial folliculitis, staphylococcal pyoderma)**  
(see papular pustular diseases in earlier notes)

**Etiology:** Staphylococcus intermedius or rarely Staphylococcus schleferi schleferi)

**Predominant Lesions:** Usually staphylococcus causes a pruritic papular pustular eruption. However in some dogs especially those that are short-haired, the major lesions can be non-inflammatory circular patches of alopecia with peripheral scaling (epidermal collarettes).

**Lesions Distribution:** Multifocal over the trunk. Rarely does staphylococcal infection spread to the head and pinna and only after it has been on the trunk for an extended time.



**Appropriate diagnostic tests:**

Direct examination of the dog,

Cytology

Bacterial culture (if it doesn't respond to initial antimicrobial treatment)

**RX:** Systemic antimicrobial therapy for a minimum of 3 weeks; antimicrobial shampoos may be adjunctive

## Vasculopathy: Canine ischemic dermatopathy folliculopathy

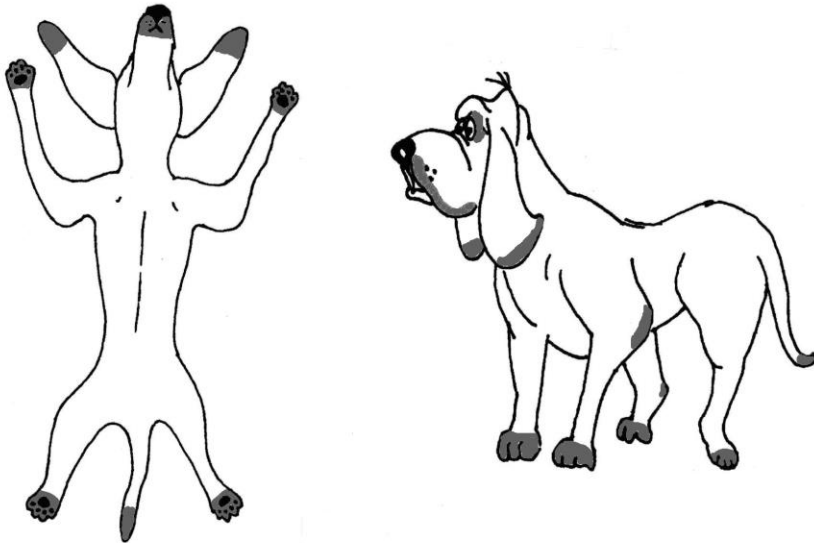
### 1. Dermatomyositis

**Etiology:** uncommon disorder of shelties and collies which seems to be due to a combination of genetic factors and possible infectious such as viral or some other antigen trigger.



**Predominant Lesions:** Patchy alopecia with some scaling and crusting. There may be muscle atrophy that affects the facial and temporal muscles. Lesions generally begin in dogs under 6 months of age. The severity and progression of the condition is not predictable but if the condition is severe it is usually progressive in the first year of life. Animals present with erythema, scaling, alopecia and crusting.

**Lesions Distribution:** Face, tips of ears, tip of tail and over distal extremities; temporal muscle atrophy



**Appropriate diagnostic tests** Biopsy : hydropic degeneration of basal cells of skin and hair follicles, follicular atrophy "faded follicles" and vasculitis. Muscle biopsies show signs of fiber necrosis and atrophy .EMG : positive sharp waves and fibrillation potentials in muscles of head and distal extremities.

**Prognosis:** guarded

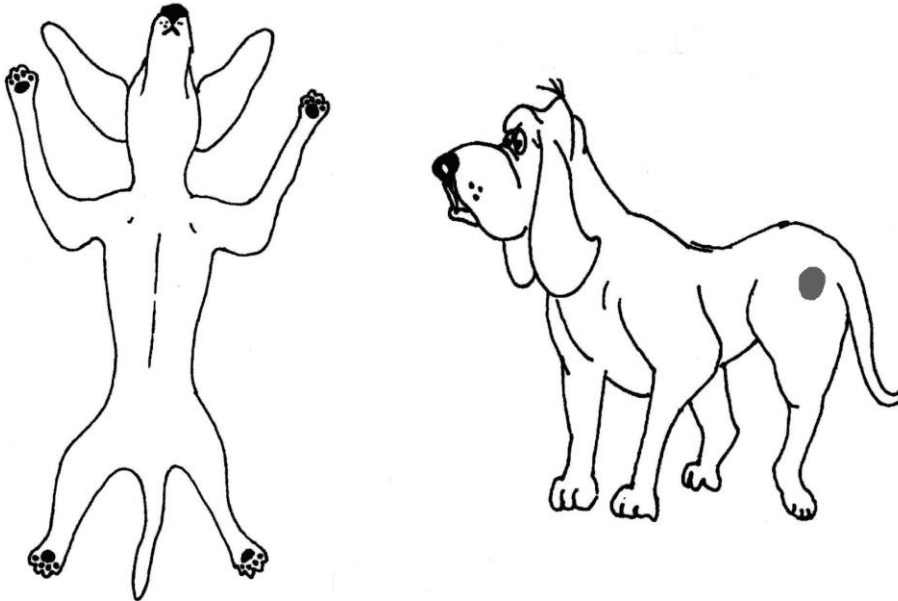
**RX:** Steroids may be helpful. Pentoxifylline @ 5-15 mg/kg TID; increases microvascular blood supply and has anti-inflammatory properties

### 2. Post-vaccine vasculitis

**Etiology:** Focal alopecia reaction to injection. This has been seen most prominently with rabies vaccine. With rabies the alopecia is associated with a vasculitis and predominance of the rabies virus in the deep muscle at site of injection. This can appear several weeks to months after injection.

**Predominant Lesions:** Focal patch of alopecia

**Lesions Distribution** On the back of the neck or over the caudal portion of the rear legs, occasionally intramuscular lumbar injection site



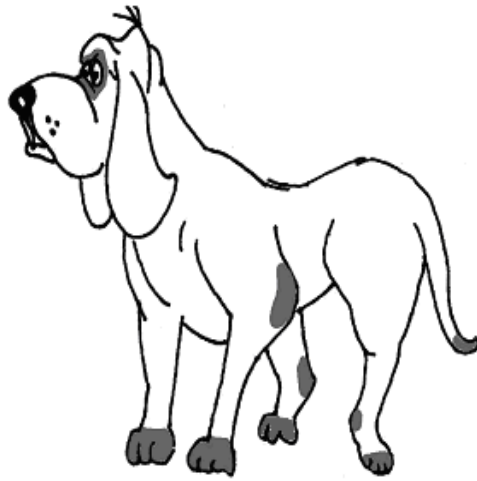
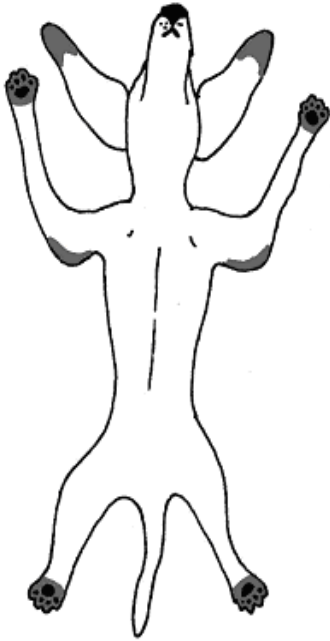
**Appropriate diagnostic tests:** biopsy: deep vasculitis

### **3. Past-vaccination dermatopathy**

**Etiology:** idiopathic ischemic dermatopathy with clinical lesions similar to dermatomyositis of collies/shelties. May be predisposition in toy breeds.

**Predominant lesions:** Lesions may be ulcerated or alopecic and have the atrophic appearance of a scar

**Distribution:** pinnal margins, bony prominences, pads, tail tip and periocular regions



**Diagnostic tests:** biopsy and rule outs of other vasculitis (infectious etc.)

**Rx:** Pentoxifylline, Fatty Acids, Tetracycline/niacinamide

### **Alopecia areata**

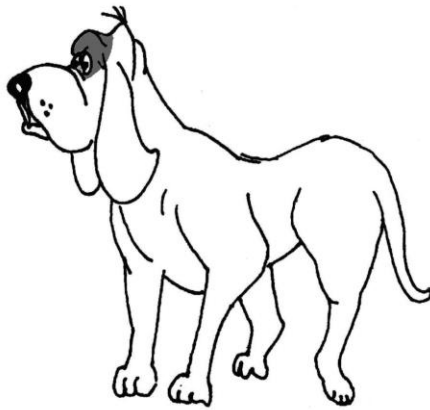
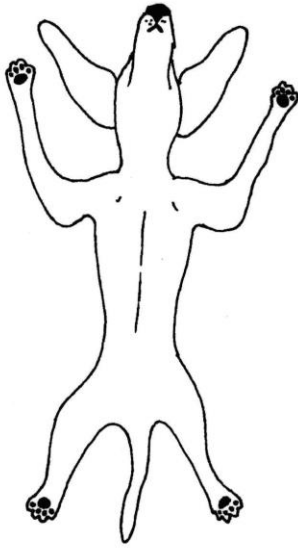
**Etiology:** Autoantibodies target the hair follicles (rare condition)

**Predominant Lesions:** focal or multi-focal patches of non-inflammatory alopecia  
hair regrowth may be white. Dachshunds may be predisposed.



**Lesions Distribution** usually on the head but may be on neck or trunk, rarely generalized





**Appropriate diagnostic tests:** biopsy and trichogram (telogen, dysplastic and exclamation point hairs) Biopsy reveals peribulbar accumulations of mononuclear cells (the classical “swarm of bees.”)

**RX:** Specific treatment which is effective not well described. Topical, intralesional or systemic steroids may be helpful and topical picrolimus or tacrolimus may be tried.

**Pattern baldness**

**Etiology:** genetically determined alopecia due to miniaturization of hair follicles, dachshunds and greyhounds

**Predominant Lesions:** Focal areas of alopecia

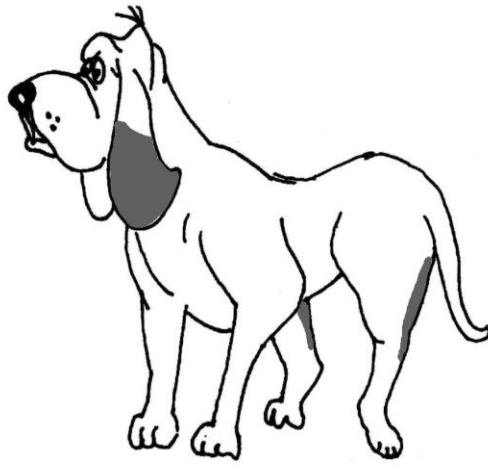
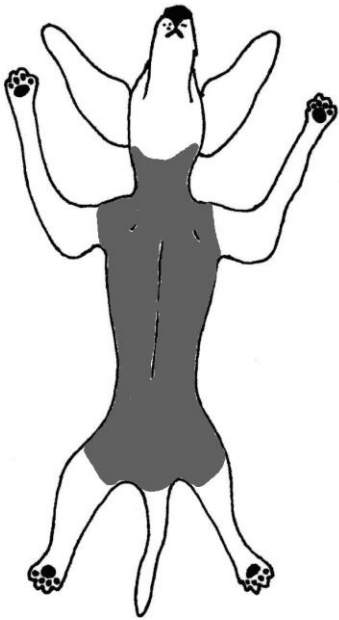
**Lesion distribution:**

- 1) Pinnal alopecia in dachshunds
- 2) American Water Spaniels and Portuguese Water Dogs: alopecia of the ventral neck, caudiomedial thighs and tail



: alopecia of the ventral neck,

- 3) Greyhounds: hair loss on caudal thighs and may evolve to ventral alopecia
- 4) Post auricular region, ventral neck, ventrum and caudomedial thighs: dachshunds, Boston terriers, Chihuahuas, whippets, Manchester terriers, greyhounds and Italian greyhounds



**Diagnosis:** Biopsy shows miniaturization of hair follicles and hair shafts, adnexa appear normal.  
**RX:** Melatonin(3-6 mg orally qid) has been used successfully in a few cases.

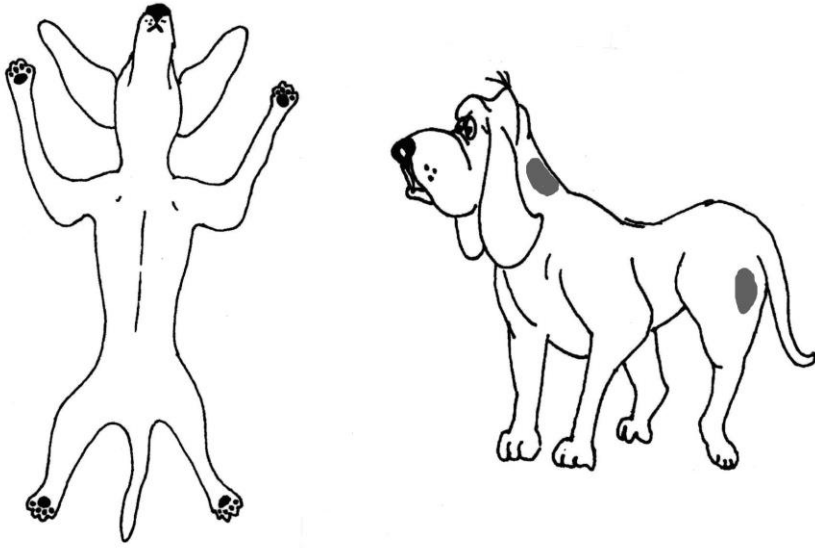


**Medication or injection site alopecia:**

**Etiology:** Reaction of topical medication (e.g. spot on insecticide) or reaction to injection (usually steroid). Poodles most often reported

**Predominant Lesions:** Focal patch of alopecia

**Lesions Distribution** On the back of the neck or over the caudal portion of the rear legs



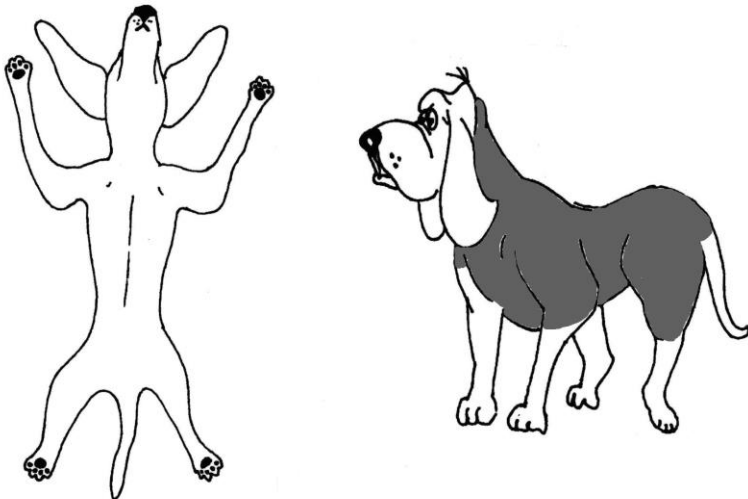
**Appropriate diagnostic tests:** biopsy

### **Post Clipping Alopecia**

**Etiology:** Lack of hair regrowth after clipping as part of grooming or for surgery, blood collection, etc Etiology is unknown and considered to possibly be related to interference with the dog's normal shedding cycle.

**Predominant Lesions:** Non-inflammatory alopecia

**Lesions Distribution:** site of prior clipping



**Appropriate diagnostic tests :** Trichogram, endocrine tests and biopsy which shows catagen arrest and the affected areas are similar histopathologically to unaffected areas

**RX:** Prognosis is good; hair regrowth usually occurs eventually ( 12-24 months); no treatment needed

**Endocrine diseases** will be covered in the symmetric alopecia lecture.

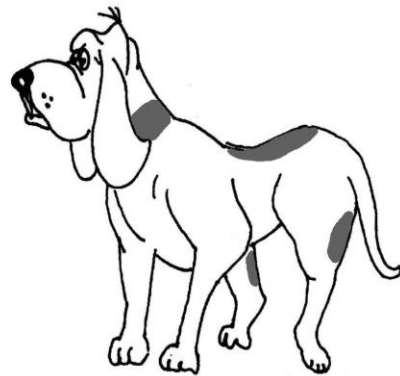
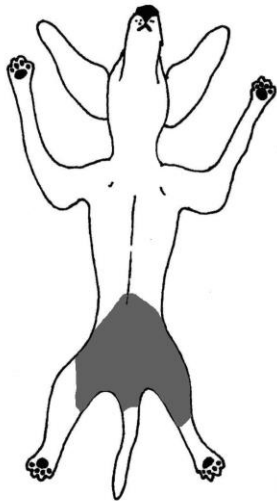
### **Follicular dysplasia**

**Etiology:** A genetically determined abnormality in hair follicle development leading to defective hair. Some breeds affected include Irish water spaniels, Portuguese water dogs, Curly coated retrievers, Siberian Huskies, other breeds

**Predominant lesions:** Alopecia

**Lesion distribution:**

Caudal dorsum, caudal thighs, perineum, neck but can affect the whole trunk



**Diagnostic tests:** Trichogram, biopsy

**Rx:** No effective treatment, antibiotics may help with secondary infection

### **Color dilution alopecia (Color mutant alopecia) or black hair follicle dysplasia**

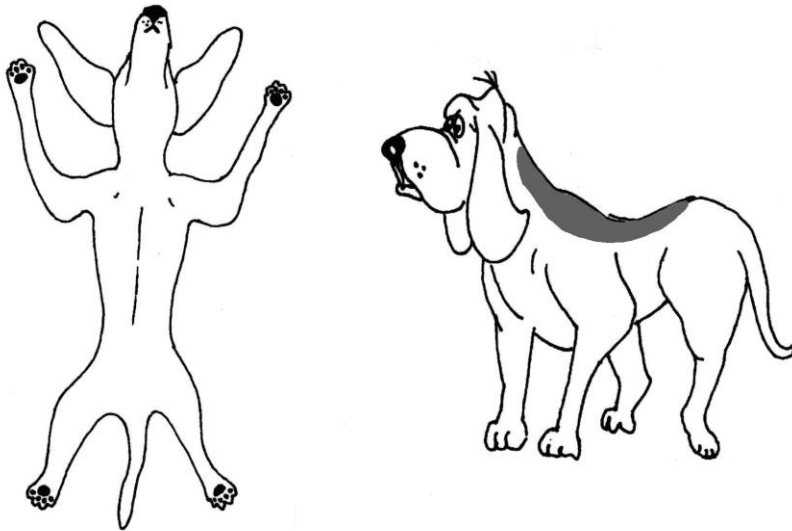


**Etiology:** Genetically determined diseases in which the alopecia results from abnormal packaging of melanin granules within the hair shaft resulting in distortion and hair breakage. Color dilution occurs in fawn (Isabella) and blue Doberman pinschers, dachshunds, whippets and

some other breeds. Black hair follicle dysplasia occurs in bi or tri-colored coats (Papillons and black and tan dachshunds) and only the black hairs are affected.

**Predominant lesions:** Alopecia & dry, stubbly hair, secondary staphylococcal pyoderma  
These conditions begin at 1-2 years of age as a patchy alopecia. It can progress to extensive or total alopecia; Not every blue dog has this condition

**Lesions distribution:** Over the dorsum but may generalize or can be restricted to the black areas



**Diagnostic tests:** Trichogram, biopsy shows irregular distortions and bulges of hair follicle walls and keratin blocking hair canals; cystic hair follicles with no hair shafts, follicular hyperkeratosis

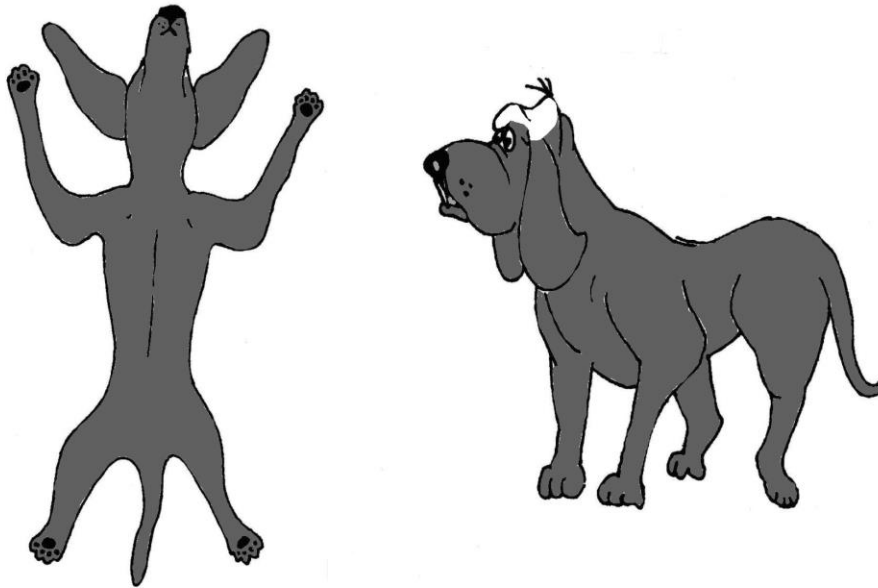
### **Congenital Alopecia**

1) Feline Alopecia Universalis: Sphinx Cat, Canadian Hairless;

Kittens are born hairless (naked cat), but there is sometimes a mixed normal/abnormal litter, genetics unknown: Skin is often greasy and smelly, necessitating frequent bathing. Histologically hair follicles are totally absent; sebaceous glands open directly onto the skin.

2) Congenital hereditary hairlessness African sand dog, Abyssinian dog, Turkish dog, Chinese Crested dog, Mexican Hairless dog, Xoloitcuintli.;

Some of these breeds have hair on head and tail; Many have abnormal dentition; Not usually seborrheic.



**Etiology:** Genetically determined alopecia present at or shortly after birth caused by malformation of the hair follicles. This is “normal” in some canine breeds.

**Predominant lesions:** alopecia, comedones, scaling and secondary infection

**Lesion distribution:** generalized, may spare head and feet or head and feet may be primary areas of alopecia

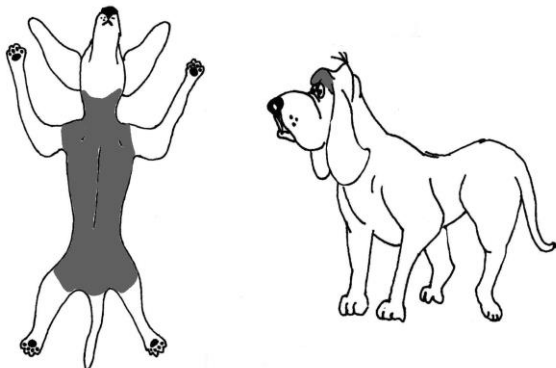
**Appropriate diagnostic tests;** trichogram, biopsy

### 3) Canine hypotrichosis

Reported in miniature poodles; begins as patches of hair loss several weeks after birth;

Progresses to large patches of baldness especially on the temporal region; then remains static; Seen in other breeds sporadically.; Some dogs with hypotrichosis have multiple ectodermal defects. Cutaneous appendages such as glands may be absent.

Dentition may be abnormal. Reported in lhasa apsa,cocker spaniel, whippet et al.



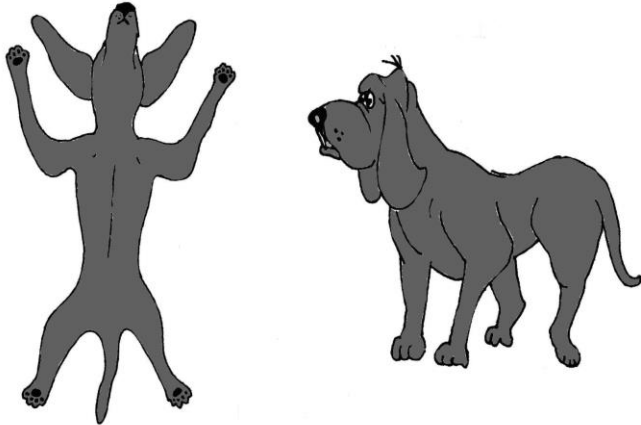


**Sebaceous adenitis**  
(see notes Crusting)

**Etiology:** Granulomatous inflammation of the sebaceous glands of unknown cause, resulting in their ultimate destruction. Commonly affected breeds include the Standard Poodle, Samoyeds, Vizslas and arctic breeds

**Predominant lesions:** Alopecia and fine silvery white scaling. Follicular casting is often present and looks like wax dripping from the haircoat.

**Lesions distribution:** Usually generalized involving the trunk, face and extremities (dogs may look like they are clipped when they have not been for many months.)



**Appropriate diagnostic tests:** Biopsy, trichogram

**Rx:** Topicals (Keratolytic shampoos 50-75% propylene glycol in water two to three times weekly, batho oil soaks

Systemics : Fatty acids , Retinoids are helpful in some cases; Cyclosporine

**Telogen/Anagen defluxion**

**Etiology:** Telogen defluxion occurs when large numbers of hair follicle are synchronized in the telogen phase. New hairs push the old hairs out resulting in a temporary but dramatic shed.

Anagen defluxion usually occurs when the growth of anagen hairs is halted by chemotherapeutic drugs. Alopecia is only seen in breeds with anagen dominated hair coats (Poodle, Bichon Frise etc)

**Predominant lesions:** Excessive shedding, alopecia

**Lesion distribution:** generalized

**Diagnostic tests:** trichogram, biopsy

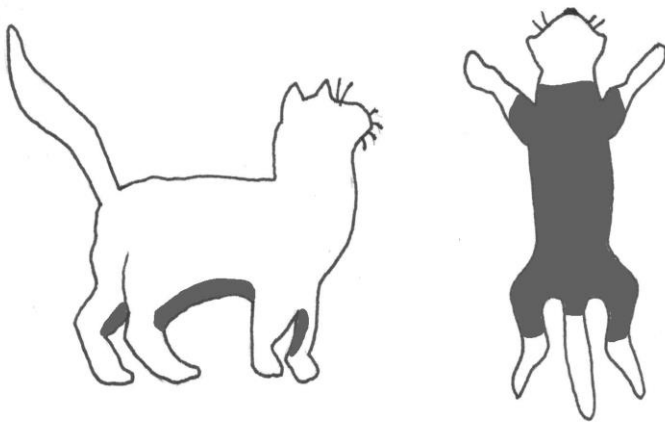
**Epitheliotropic lymphoma :** rarely presents with alopecia as the primary problem.

### *Alopecia Unique to the Cat*

#### **Feline Paraneoplastic alopecia**

Alopecia associated with smooth glistening skin.

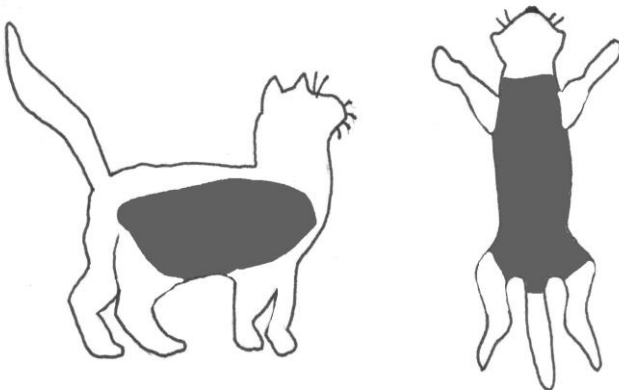
**Distribution:** ventrum and legs



**Diagnostic tests:** chemistry profile, biopsy, abdominal and thoracic ultrasound, potentially laparotomy

#### **Feline symmetrical alopecia (FSA)**

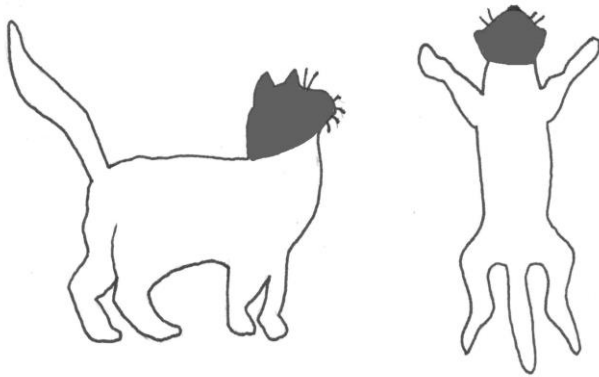
Investigate causes of pruritus first.



#### **Alopecia mucinosa**

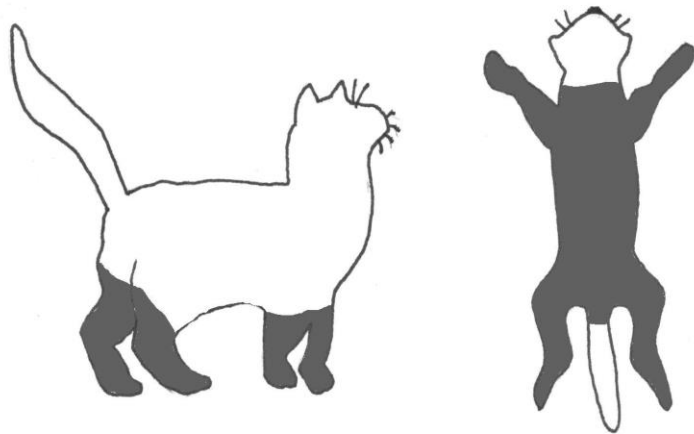
Two cats have been described with nonpruritic alopecia of the head, neck and ears. Biopsy revealed mucinosis of the hair follicles. In both cats a Tcell lymphoma was diagnosed several months later.





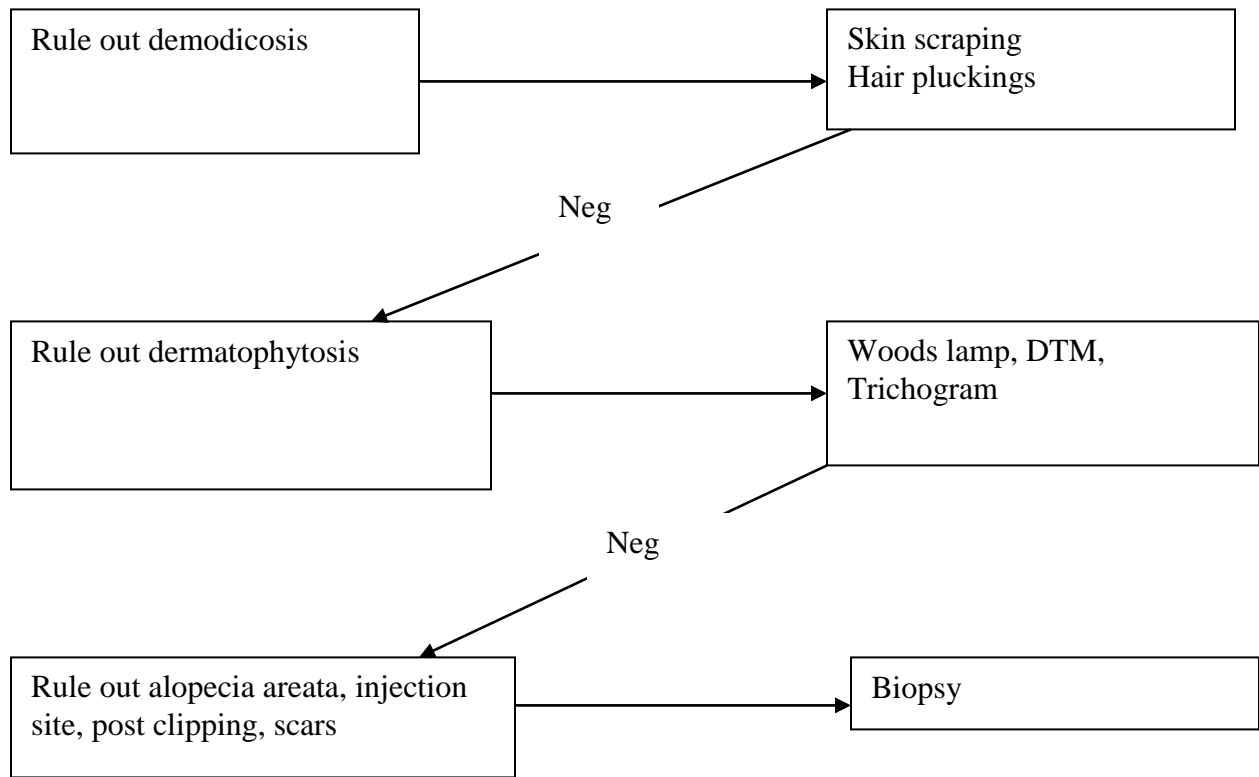
### Pseudopelade

Non-pruritic non inflammatory alopecia of ventrum and legs. Loss of claws was present. The biopsy showed early lymphocytic follicular invasion followed by follicular atrophy.



**Algorithm summarizing approach to multifocal alopecia**

Diagnostic Approach to Focal Alopecia



## Approach to nodular dermatoses

Rosanna Marsella, DVM, DACVD

There are numerous causes of nodules and draining tracts in the dog and cat. These may include infectious (bacterial, fungal, opportunistic mycobacterial, parasitic) causes, sterile / immune-mediated causes, and neoplasia. Draining tracts usually indicate the presence of an infectious agent.. Utilizing a systematic diagnostic approach should be beneficial in establishing a definitive diagnosis. Once a diagnosis is made, appropriate therapy can be recommended.

### Differentials for nodular dermatoses in the dog and cat:

Infectious	Sterile	Neoplastic
<ul style="list-style-type: none"> <li>▪ Fungal</li> <li>▪ Mycobacteria</li> <li>▪ Bacterial furunculosis</li> <li>▪ Leishmania</li> <li>▪ Pythium / Lagenidium</li> <li>▪ Acral lick dermatitis</li> <li>▪ Nocardia</li> <li>▪ Actinomyces</li> <li>▪ Actinobacillus</li> </ul>	<ul style="list-style-type: none"> <li>▪ Foreign body</li> <li>▪ Nodular panniculitis</li> <li>▪ Eosinophilic granuloma</li> <li>▪ Sterile granuloma /pyogranuloma</li> <li>▪ (Acral lick dermatitis)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Histiocytic diseases</li> <li>▪ Mast cell tumor</li> <li>▪ Basal cell tumor</li> <li>▪ Cutaneous lymphoma</li> <li>▪ Glandular tumors</li> <li>▪ Cysts</li> <li>▪ Other tumors</li> </ul>

#### Diagnostic Approach to a Nodule

History is usually critical in dermatologic diagnosis. This is true with nodular diseases, as well. How long has the nodule been present, and has it changed in character? Is it a single or multiple nodules? Have the nodules ulcerated and/or developed draining tracts? In addition, some diseases tend to occur in certain geographic regions, so a travel history may be indicated. Response (or lack of) to previous therapies can also be useful information. As a front line veterinarian, however, you may be the first one to see this case, so your history may be limited. Signalment of the patient and the presence of other clinical signs may also provide useful information before formulating a diagnostic plan. Depending on the clinical presentation, routine diagnostics such as skin scraping and culturing for dermatophytes may be indicated.

*Cytology* is typically indicated with cutaneous nodular diseases. It has the advantage of being simple, quick, and relatively inexpensive. Cytology can be obtained by fine needle aspiration, direct impression of exudates, or direct impression of biopsy samples. Special stains may be applied to these samples to

highlight some infectious organisms. The lack of organisms on a cytological preparation does not rule out an infectious etiology. Cytology may provide a definitive diagnosis (deep pyoderma, mast cell tumor, lipoma). More often, it provides direction for the next steps in the diagnostic work up.

***Biopsy for dermatohistopathology*** is indicated for most nodular dermatoses. To obtain a diagnostic sample, full-thickness biopsies are usually necessary. This requires an incisional or excisional biopsy technique. Biopsy of an intact nodule is best, and if possible, multiple samples should be provided. For best results, samples should be sent to a dermatohistopathologist. Special stains for bacteria, opportunistic mycobacterial, and fungal organisms may aid in the diagnosis. Typically, you will have to specifically request these stains. Lack of visible organisms, even with special stains, does not rule out an infectious etiology.

***Culture*** is an important diagnostic step for both infectious and some immune-mediated dermatoses. For most infectious etiologies, culture provides a definitive diagnosis, and may aid in choosing an effective therapy. Tissue samples should be obtained in a sterile manner for macerated bacterial, opportunistic mycobacterial, and fungal culture. Culture of exudates is typically unrewarding and discouraged. Some immune-mediated processes cause granulomatous / pyogranulomatous inflammation, and not all infectious organisms are detectable on histopathology, even with special stains. Therefore, infectious etiologies must be ruled out via negative culture results.

### **Abscesses**

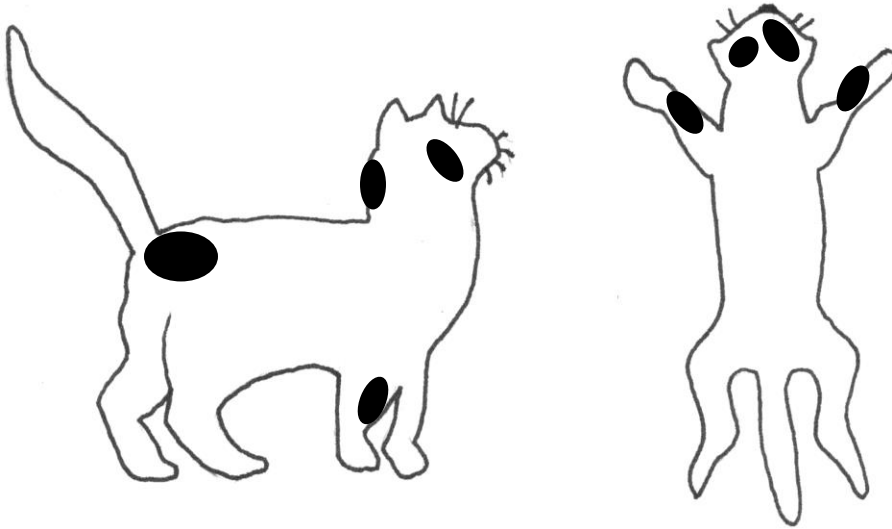
**Etiology:** A subcutaneous accumulation of pus; in the cat often caused by *Pasteurella multocida*...common due to bite wounds from other cats. When these occur in dogs they may be from fighting, tooth root infections, infected anal sacs or foreign bodies.

**Predominant Lesions:** Subcutaneous swelling which may lead to drainage.

### **Lesion distribution:**

Cats: face, tail, legs predominantly

Dogs: bite wound area, below the eye (carnassial tooth root abscess) lateral to anus (anal sac abscess etc).



**Diagnostic Tests:**

Clinical diagnosis, Lancing or draining, cytology

**Rx:** Generally broad spectrum antibiotic but establishing drainage is most important.

**Deep Pyoderma (Deep Bacterial Infection)**

**Etiology:** rupture of the hair follicle (infected with staphylococcus) which can occur at the deep level or extending outside the follicle and into the surrounding dermis. Both **localized and generalized pyoderma** can occur at the deep level. When the follicle ruptures and keratin is liberated into the surrounding dermis, the term furunculosis is used.

**Predominant Lesions:** Nodules and draining tracts

**Lesion distribution:** Varies

**Localized:** In many instances these localized conditions of deep pyoderma have little tendency to generalize. Owners may report the conditions to be pruritic but upon closer questioning, it is usually a case of increased licking by the dog; it is a natural behavior for dogs to lick their wounds or exudative areas if they can reach them. Localized pyodermas are often associated with a fair amount of scarring (fibrosis) and chronicity. The feet are often perceived by the veterinarian and / or owner to be pruritic. Demodex and dermatophytosis are among two of the differentials for localized deep pyoderma. The muzzle, the pressure areas, and the interdigital webs generally have associated keratin foreign body granulomas on histology. Which is cause and effect in these cases can be difficult to determine because the patients usually present with a long history.

1.) **Muzzle pyoderma**: This occurs most often in large breed dogs and can be chronic if the dogs do not “outgrow the condition at puberty”.

2.) **Nasal pyoderma**: This is not a common condition but when it is the only location for pyoderma, insect bites or stings should be considered and a biopsy in this case generally indicates an eosinophilic furunculosis. If insect bites are involved, corticosteroids may be beneficial in conjunction with antimicrobial therapy. Actinic changes, autoimmune conditions, and even zinc responsive dermatosis as well as foreign body (cactus, thistles et al), histiocytosis, and neoplasia should receive consideration.

3.) **Pressure point pyoderma**: Usually occurs in large dogs that prefer to lie on hard or abrasive surfaces, causing trauma to hairs and the foreign body reaction. These can be very difficult to manage because of the patient’s lifestyle.

4) **Pododermatitis**: Differentials in addition to demodex and dermatophyte would include contact allergy or irritant, foreign body such as grass awns, hookworm dermatitis, autoimmune, zinc responsive, and the hepatocutaneous syndrome. Classically this condition is seen as an interdigital swelling which later fistulates and drains hemorrhagic, purulent exudate.

5) **Mucocutaneous Pyoderma** This condition is uncommon and can occur at all mucocutaneous areas or primarily at the lips and perioral skin. There is generally scaling and crusting present. The lips may be cracked and swollen and depigmentation can occur with chronicity. This is responsive to antibiotics systemically and topically but the response is slow. Differentials include DLE, demodicosis, and nutritional responsive dermatoses (zinc and generic dog food).

**Generalized deep pyoderma**: occurs generally in dogs in which we believe there is some sort of immunocompromise and often in those with generalized demodicosis.



**German shepherd dog pyoderma**: This condition is a very frustrating one which is seen generally along the lateral thorax and abdomen and often extends down the rear limbs in middle aged to older German shepherd dogs. Owners often have no idea of the extensiveness of the infection until the

haircoat is clipped away revealing multiple ulcerated areas and draining tracts. These dogs are often described as pruritic. They often have peripheral lymphadenopathy and may have fevers of low grade. These dogs have been examined extensively for immunologic abnormalities, and nothing to date has been consistently found as abnormal in these German shepherds. These dogs generally have the condition for life once it is acquired. It can be successfully managed in most cases with topical therapy and systemic antibiotics.



**Bull Terrier deep pyoderma:** This breed, like the German shepherd, may have some immune deficient state yet to be well characterized. Some of these dogs get deep hemorrhage filled abscesses over their bodies, even including their heads. Always do your best to pursue all of the underlying causes of deep pyoderma before making this diagnosis. At one time, it was believed that there might be some connection between zinc deficiency and the immune system problem noted in the skin of these dogs. However, supplementation with zinc has been unrewarding in most cases.

**Diagnostic Tests:** Skin scrapings, cytology, cultures, biopsy. An important point of difference between superficial and deep pyoderma is seen on cytology. Typically, organisms are plentiful on cytology from pustules or crusts associated with superficial lesions. With deep pyoderma, pyogranulomatous inflammation, rich in eosinophils is seen, but organisms may be difficult to find. Deep pyoderma is often diagnosed based on clinical signs (nodular dermatitis with draining tracts), and the appearance of the discharge (hemorrhagic to purulent). Biopsy for culture and sensitivity testing should be performed in order to determine the appropriate antibiotic of choice.

\*\*A search for the underlying cause should be undertaken in order to prevent relapses.

These may include: ( CBC, Chemistry, thyroid, adrenal, allergy, immune, radiographs & ultrasound)

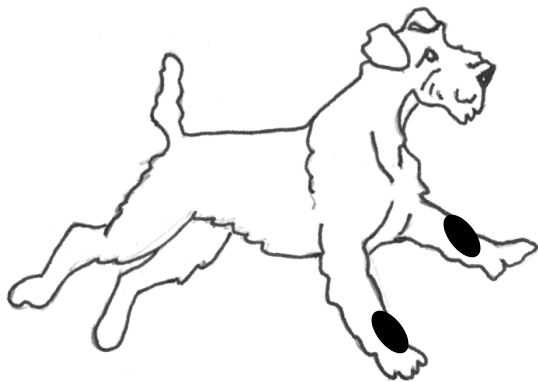
**Rx:** Six to sixteen weeks of therapy (perhaps longer) may be indicated in order to get resolution of the infection. Concurrent topical treatment of localized lesions using mupiricin may speed healing.

### **Acral lick dermatitis**

**Etiology:** Usually has a staph component

One of the most frustrating disorders in veterinary medicine. Like many dermatologic disorders, there is usually an underlying reason for this disorder. Underlying causes include hypersensitivities, previous injury, foreign body reaction, referred pain from DJD, infectious etiologies, and psychogenic disorders. A systematic approach to determining and managing the underlying cause(s) is critical to long-term management.

**Predominant lesion and distribution:** Acral lick lesions are raised, ulcerated nodules that result from chronic licking. They are often found on the anterior aspect of the carpal region, but the location can vary. Lesions may be single or multifocal. There is an increased incidence in large breed dogs, such as Dobermans, Great Danes, Golden retrievers, Labrador retrievers, and the German shepherd dog.



**Diagnostic tests:** Initial diagnostics include ruling out demodicosis and dermatophytosis. Acral lick lesions can have a similar appearance to *Pythium* / *Lagenidium* or other fungal infection. Biopsy may be indicated to rule out these more serious infections and neoplasia.

**RX:**

Acral lick lesions are almost always deeply infected with *Staphylococcus intermedius* (furunculosis). Culture and sensitivity testing and long-term antibiotics are indicated in almost all cases. Topical therapy with mupirocin ointment may also speed healing. Once the infection is treated, symptomatic treatments can be initiated. These include:

- Topical corticosteroids (betamethasone ointment or Synotic with Banamine)
- Hycodan 5 mg / 20 kg TID for 3 weeks, then taper
- Naltrexone 2.2 mg/kg qd
- Cryotherapy, laser surgery, or acupuncture
- Psychological counseling and behavioral modifying drugs (clomipramine, fluoxetine)



- Lidocaine / capsaicin topically, but only after infection is resolved. These medications need to be applied four times daily for 2 weeks, then tapering (protocol adapted from UC-Davis dermoids). Lidocaine can usually be discontinued after a few weeks. Capsaicin cream may need to be continued chronically, especially if any underlying cause cannot be determined / controlled.

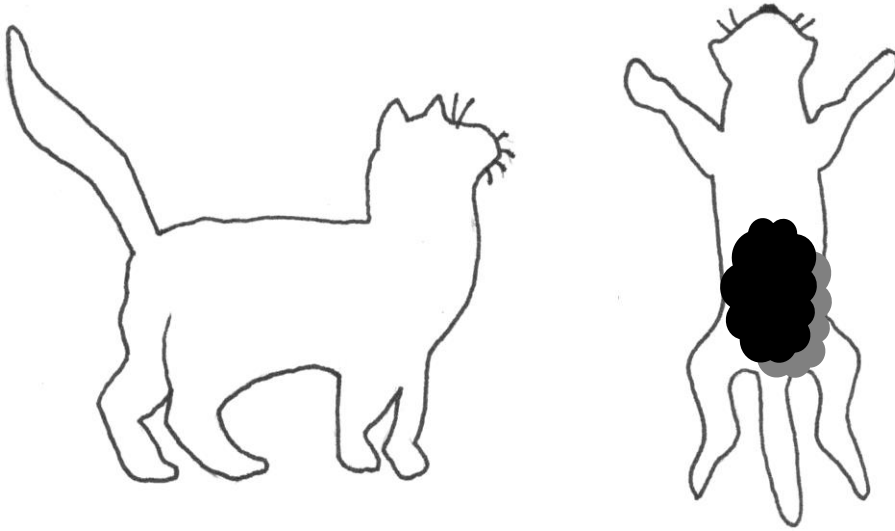
Having the dog wear an E-collar or bucket can be very beneficial in the beginning of therapy.

Bandaging can be useful in rare cases, but most affected dogs will quickly remove bandaging. Surgery is contraindicated except in rare instances.

### **Opportunistic (atypical) mycobacterial infections**

**Etiology:** uncommon cause of nodules and draining tracts. The incidence varies depending on the geographic location. This is a disease you will see if you practice in the southeastern US. *Mycobacterium fortuitum*, *M. chelonae*, *M. phlei*, and *M. smegmatis* are most commonly reported. These organisms are ubiquitous in the environment, and are generally thought to be opportunistic pathogens. Infection occurs through traumatic implantation into the skin and SQ tissues. Cats are most commonly affected, but infection in dogs and humans is also reported.

**Lesion and lesion distribution:** After introduction into the tissues, it may take weeks before a nodular lesion develops. Lesions tend to present as nonhealing wounds with a serosanguinous discharge. Affected animals may have lesions for months or years, yet show minimal systemic signs of illness. These organisms tend to be “fat-loving,” so lesions are often found on the ventral fat pad of cats or in the lumbar region in dogs. Over time, multiple nodules may coalesce, forming a focally extensive area of nodular swelling with multifocal draining tracts. In spite of extensive lesions, patients often have no signs of systemic illness.



**Diagnostics:**

Diagnosis is based on finding acid-fast organisms on cytology, histopathology, or culture of affected tissues. Full-thickness biopsy of affected tissue is necessary to obtain a diagnostic sample for histopath and culture. Cytology samples can be obtained by making impression smears from the bottom of a histopath sample.

The pathologist should be notified of concern for these organisms. Special stains (Ziehl-Neelsen or Fite-Faraco) are necessary to highlight acid-fast organisms. A careful search should be made in order to identify organisms at the center of fat vacuoles in the subcutaneous tissues. Organisms are typically few in number, making diagnosis difficult. A lack of visible organisms on histopathology does not rule out opportunistic mycobacterial infection.

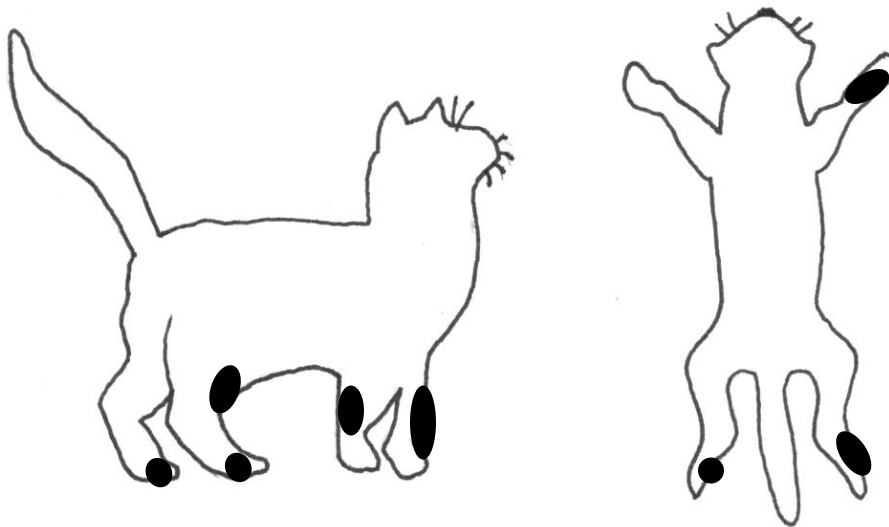
Samples for culture should be taken using aseptic technique, and must be submitted to a lab with experience growing these organisms. Special culture media (blood agar, Lowenstein-Jenson medium, or Stonebrink's medium) are required.

**RX:** Long-term antibiotic therapy is indicated once a diagnosis is confirmed. If possible sensitivity testing done at National Jewish Hospital (Denver, CO) should be done. Empirical treatment with tetracyclines, clarithromycin, or enrofloxacin may be successful. Antibiotic therapy should be continued for at least 4-6 weeks past clinical cure (no palpable lesions). This usually takes months to years. In some cases, life long therapy may be required. Surgery is generally not recommended, as wound dehiscence is common. An exception to this may be when wide surgical margins can be obtained (not common).

## **Nocardia and Actinomyces**

**Etiology:** *Nocardia* and *Actinomyces* can produce clinically similar cutaneous lesions in the dog and cat. These include cellulitis, ulcerated nodules, and draining tracts. Infection usually results from traumatic implantation of the organism into the skin.

**Lesion and distribution:** The most common locations for Nocardiosis include the limbs and feet. Regional lymphadenopathy may also occur. Cats with *Nocardia* are often systemically ill and have an underlying disease that may immunosuppress them (i.e. FIV/FeLV). Lesions of actinomycosis occur most frequently on the head or neck, thoracic, paralumbar, or abdominal regions. Tissue grains may be present, in association with a foul smelling, hemorrhagic discharge.



### **Diagnostics:**

Diagnosis is based on identification of these organisms on cytology, histopathology, and/or culture. Special stains are necessary to identify the organisms on cytology and histopath. Anaerobic culture is indicated to grow *Actinomyces*, while aerobic culture is indicated for growth of *Nocardia spp.*

### **RX:**

When possible, wide surgical excision of lesions is the treatment of choice. Empirical medical treatments for actinomycosis include high dose penicillins, clindamycin, erythromycin, cephalosporins, chloramphenicol, and tetracyclines. Multi-drug therapy may be indicated for nocardiosis, as resistance may rapidly occur. Combining potentiated sulfonamides, enrofloxacin, amoxicillin-clavulanate, erythromycin, clarithromycin, cephalosporins, and tetracyclines has been reported. Therapy should be

continued for at least a month past clinical cure. The prognosis for medical cure with both of these organisms is guarded.

### **Deep Fungal with systemic manifestations:**

**Blastomyces** is uncommon in Florida, unless the dog has a travel history. The organism is most commonly diagnosed in areas along the Mississippi and Ohio River valleys (acidic soils). Inhalation of infectious spores is the most common route of infection. When skin lesions are present, systemic infection should be suspected. These dogs may have systemic signs, including anorexia, weight loss, dyspnea, cough, and ocular disease. Diagnosis should be made via cytology, histopathology, and/or serology. Culture of the organism presents a zoonotic hazard to lab personnel.

**Histoplasmosis** is also uncommon in Florida. This organism has a similar geographic distribution, being diagnosed most often along the Ohio, Mississippi, and Missouri River valleys. Cats and dogs are both susceptible to infection. Patients are usually systemically ill, and have gastrointestinal symptoms. Dissemination of the organism is common. Cutaneous nodules are uncommon (approximately 10% cases). Diagnosis is usually confirmed via aspirate cytology or histopathology of affected tissues.

**Cryptococcosis** is the most common deep fungal organism affecting the cat. Infection in dogs also occurs. Infection most likely occurs through inhalation of the organism from the environment. The organism forms a protective capsule *in vivo*, which protects it from the host's immune system. Respiratory symptoms are the most common sign of infection, but nodular skin lesions are present in 40-50% of cats. A large, firm, subcutaneous mass may appear over the bridge of the muzzle. Spread to the CNS is possible. Skin lesions are less common in the dog, and may appear as ulcerative nodules with draining tracts. Diagnosis can be made by serologic testing, cytology, or histopathology. The organism has a characteristic capsule that differentiates it from other fungal organisms. Special stains may be required to make a diagnosis.

**Coccidioidomycosis** is a soil-borne organism. In the US, it is primarily diagnosed in the southwestern portion of the country. The most common route of infection is inhalation. Symptoms include intermittent fever, anorexia, weight loss, lameness (due to bone lesions), and ocular symptoms. Cutaneous nodules that ulcerate and drain are not uncommon. In the dog, skin lesions may often be associated with osteomyelitis of underlying bone. Skin lesions are common in cats infected with coccidioidomycosis, but

osteomyelitis is less common. Diagnosis can be confirmed via cytology, histopathology, or serologic testing. Culture is not recommended due to zoonotic potential.

### **Subcutaneous fungal organisms:**

**Sporotrichosis** is a fungal organism with worldwide distribution. It is found primarily in soils rich in decaying organic matter. Dogs and cats are both susceptible to infection. Infection usually occurs through traumatic implantation of the organism through the skin. Dogs most commonly develop the cutaneous or cutaneolymphatic forms of this disease. Dissemination is uncommon in the dog. Cats often have cutaneous lesions, but multifocal or regionalized infection may occur, presumably due to the cat's grooming behavior. Dissemination appears to be more common in the cat.

**Diagnosics:** Diagnosis in the dog often requires histopathology (with fungal stains), culture, or immunofluorescence testing. Organisms are rare in affected tissues in the dog, making visualization on cytology or histopathology difficult. Organisms are plentiful in feline lesions, so diagnosis is often possible via cytology in the cat. Sporotrichosis is considered to be a zoonotic organism. Great care should be taken when handling affected cats, due to the large number of organisms in exudates. Zoonosis is less likely in canine cases.

**Rx:** Systemic antifungal therapy is indicated in all cases of sporotrichosis. Options include supersaturated potassium iodide (SSKI), itraconazole, and ketoconazole (dog).

**Eumycotic mycetomas** result from infection with any number of ubiquitous, saprophytic organisms. By definition, lesions include nodule formation, draining tracts, and tissue grains within the discharge. Eumycotic mycetomas are rare in the US. Diagnosis is based on the clinical appearance of the lesions, cytology, and histopathology. Organisms are usually easy to demonstrate on biopsy. Wide surgical excision is the treatment of choice. Medical management is unreliable.

### **Phaeohyphomycosis**

**Etiology** is also caused by a number of different saprophytic fungal organisms.

Pigmented (dematiaceous) hyphal structures are seen within the lesions, but tissue grains are not present.

**Diagnosis** may be confirmed with cytology and histopathology.

**RX:** Wide surgical excision is the treatment of choice. If that is not possible, systemic treatment should be based on fungal culture and sensitivity testing.

**Zygomycosis:**

**Etiology:** The zygomycetes are true fungal organisms that include the genera *Basidiobolus* and *Conidiobolus*. Although other species within this order may cause progressive disease in immunocompromised patients, infection by *Basidiobolus ranarum* and *Conidiobolus coronatus* are the most commonly described pathogens in the dog. Both of these organisms cause granulomatous to pyogranulomatous dermatitis in the dog, although well-described cases are rare. *Conidiobolus sp.* has been reported to cause ulcerative lesions in the hard palate of two dogs and multifocal, subcutaneous nodules with draining tracts in a third dog. Regional lymphadenopathy was a feature in the dog with subcutaneous lesions. *Basidiobolus* has been reported to cause cutaneous nodules with draining tracts, as well as disseminated disease in dogs.

**Diagnosis** is discussed below with the oomycetes. *Conidiobolus sp.* and *Basidiobolus sp.* should be more responsive to medical therapies, since they are true fungi.

**RX:** Few cases have been described in the literature, so specific treatment recommendations are hard to make. Surgical excision should be attempted if possible. If medical therapy is necessary, treatment with liposomal amphotericin B and/or itraconazole is recommended.

## Oomycetes

are plant pathogens that are ubiquitous in the environment. They are not true fungi, but they are often discussed with fungal organisms, as they appear as hyphal structures within the dermis and subcutaneous tissues. Nodular dermatitis due to *Pythium insidiosum* has been recognized in animals and people for many years. *Lagenidium* species have only recently been described as pathogens in the dog. The clinical signs, cytological, and histologic findings of these organisms, as well as the zygomycetes (above) are similar, making them difficult to distinguish. Reaching a definitive diagnosis is important because the prognosis for these organisms may be different.

## Pythiosis

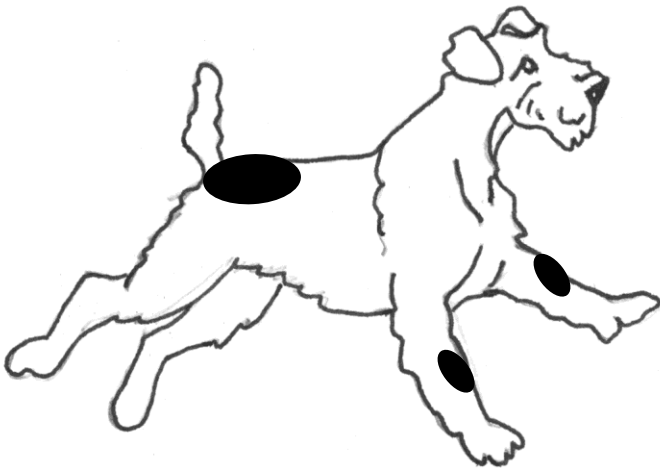
**Etiology:** Pythiosis is an invasive, pyogranulomatous disease caused by the organism *Pythium insidiosum*. This organism has been reported to cause cutaneous and subcutaneous lesions in several species, including humans. It also causes gastrointestinal disease in the dog. *P. insidiosum* has a worldwide distribution in tropical and subtropical areas, including the southeastern US. While most US

cases have been reported to originate from states bordering the Gulf of Mexico, a few cases have been reported as far north as Indiana.

Because of the difficulty in distinguishing *P. insidiosum* from the zygomycetes, these organisms were grouped together in early literature, referred to as “phycomycosis.” This term is obsolete. Separation of pythium from the zygomycetes is important because the zygomycetes are true fungi, and should be more responsive to medical therapy.

Pythiosis commonly affects young, large-breed dogs. German shepherd dogs may be over-represented. Most dogs have a history of swimming or exposure to wet, swampy environments.

**Lesions and Lesion distribution:** Cutaneous pythiosis often occurs as solitary or multiple lesions on distal extremities, the tailhead, perineum, and face. Initial lesions are raised and ulcerated, and may be mistaken for acral lick dermatitis. However, pythiosis lesions enlarge rapidly into large, boggy masses with ulceration and draining tracts. A hemorrhagic to purulent discharge is usually seen, and these lesions may be extremely pruritic.



**Diagnostics:** See below for *Lagenidium*

## **Lagenidiosis**

**Etiology:** Until recently, *P. insidiosum* was considered the only oomycete to be a mammalian pathogen. In 1999, however, an oomycete in the genus *Lagenidium* was isolated from a dog at Louisiana State University. Since then, many other dogs with subcutaneous nodular dermatitis have been determined to be infected with this *Lagenidium sp.*

**Lesions and distribution:** The clinical signs of lagenidiosis are similar to those of pythiosis. Most are young to middle-aged dogs from the southeastern US. Many had a history of swimming in freshwater. Lesions are typically progressive, cutaneous and/or subcutaneous nodules with ulceration and multifocal draining tracts. Discharge is usually hemorrhagic mucopurulent. Regional lymphadenopathy is common, and may occur prior to the onset of skin lesions. Most dogs with lagenidiosis have also been found to have lesions elsewhere, including the great vessels, lungs, urethra, and mediastinum.

**Diagnostics for both pythium and lagenidium:** The principles of diagnosis are the same as with other nodular disorders in the dog and cat.

**Cytological** findings (via FNA or impression smears) with the zygomycetes and oomycetes are non-specific. Eosinophilic pyogranulomatous inflammation is seen, but hyphal structures are difficult to find. Rarely, hyphal ghosts may be visualized on samples. Hyphae can be seen with GMS-stained cytological samples. Cytology is suggestive of an infectious etiology, but is unreliable for establishing a diagnosis.

**Histologically,**

Cutaneous pythiosis causes a nodular to diffuse granulomatous to pyogranulomatous dermatitis and panniculitis. Foci of necrosis and large numbers of eosinophils are often present. Organisms are difficult to see on H&E and PAS stained samples. With GMS stain, hyphal structures are readily seen as wide, occasionally septate, and irregularly branching. These structures are often found at the center of the granulomatous inflammation. The histologic lesions of the zygomycetes are essentially identical to pythiosis. Immunohistochemistry on paraffin-embedded tissues may be helpful in distinguishing the oomycetes from the zygomycetes. However, some cross-reaction has been reported with *Conidiobolus* and *Basidiobolus* species, so even this technique is not perfected.

The histologic lesions of lagenidiosis are similar to pythiosis, with some exceptions. An eosinophilic granulomatous to pyogranulomatous nodular dermatitis and panniculitis is typical. Hyphal structures of *Lagenidium* are usually visible with H&E stained sections, unlike with pythiosis. In addition, the hyphal structures are usually larger than those of *P. insidiosum*, and vary in size within the same section.

**Culture** has traditionally been used to distinguish pythiosis from the zygomycetes. However, culture of these organisms may be difficult, and a lab familiar with the characteristics of these infections should be utilized. Using growth media that discourage bacterial overgrowth significantly improves the recovery rate with these organisms. Unfortunately, even successful culture does not always provide a definitive diagnosis, as it is not always possible to distinguish the organisms by their gross morphology.

**Serology** may hold the most promising results for distinguishing pythiosis, lagenidiosis, and zygomycosis. Agar gel immunodiffusion is effective in detecting precipitating antibody in most equine



and human patients with pythiosis. However, it has been less useful in the diagnosis of canine pythiosis. A soluble mycelial antigen-based ELISA assay for detection of anti-*P. insidiosum* antibodies in dogs has been developed at LSU. This assay appears to be highly sensitive and specific. This ELISA also appears to be useful in monitoring success of therapy. In dogs and cats with surgically excised disease, significant decreases in antibody levels have been seen 2-3 months post-operatively. ELISA-based assays for *Lagenidium sp.* and the zygomycetes have also been developed at LSU, but may not be as specific as the pythium ELISA.

PCR-based assays for detection of *P. insidiosum* and *Lagenidium sp.* have also been developed. These assays can be performed on DNA extracted from either cultured isolates or from infected tissue samples. Tissue samples need to be either frozen or stored in 95% ethanol to preserve DNA. Diagnostic testing for pythiosis and lagenidiosis can be performed at LSU's School of Veterinary Medicine. Contact Dr. Amy Grooters (225-578-9600) prior to submission of any samples.

Again, pythiosis, lagenidiosis, and zygomycosis have very similar clinical and histologic findings. Each of these organisms carries a poor-guarded prognosis for cure, but the zygomycetes should be more responsive to medical therapy. For that reason, establishing a definitive diagnosis should be attempted.

**Rx:** Wide surgical excision (including amputation) of infected tissue is the treatment of choice in cases of pythiosis and lagenidiosis. Neither of these organisms is particularly responsive to medical therapy (they lack significant ergosterol within their cell walls), so the best chance for cure is aggressive surgery. Because *Lagenidium* appears to commonly spread to distant locations, thoracic radiographs and abdominal ultrasound are indicated prior to surgery. When medical therapy is necessary, a combination of antifungal drugs may offer the best chance for success. Likely less than 15-25% of cases of pythiosis may respond to liposomal amphotericin B, in combination with itraconazole and terbinafine. Treatment should continue at least two months past clinical cure. In addition, medical therapy has occasionally been used to "shrink" lesions to a point where surgical excision is possible. Successful treatment of cutaneous pythiosis has been reported in a single case using pythium immunotherapy (vaccine). Pythium immunotherapy has been successful in equine cases in the past, but typically only in cases with lesions less than 2-3 months duration. Further studies are indicated before immunotherapy can be advocated as sole therapy for canine pythiosis. Pythium immunotherapy is available through PanAmerican Veterinary Labs ([www.pavl.com](http://www.pavl.com)).

## **Foreign Bodies**

**Etiology:** Foreign Bodies

**Predominant Lesions: Draining tracts**

**Lesion distribution:** Can be grass awns-interdigital skin but may migrate

Wood splinters: ventral neck after pharyngeal penetration

Porcupine quills...migrate everywhere

**Diagnostic Tests:** Exploration of tracts

cytology

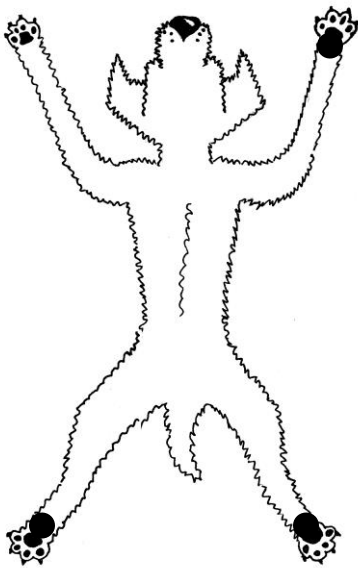
**Rx:** Surgical exploration and debridement may be indicated to remove traumatically implanted foreign materials

**Focal metatarsal fistulation**

**Etiology:** Uncommon, occurs in German shepherds

**Predominant Lesions:** Solitary draining lesions usually above the central pad and distal to the upper pad

**Lesion distribution:** May occur on any one or many feet, usually hind limbs are affected



**Diagnostic Tests:** Biopsy, exploration surgically, cytology

**Rx:** Antibiotics and steroids; sometimes topicals are effective

**Immune-mediated Causes of Nodules:**

**Sterile nodular panniculitis** is an autoimmune disease, causing inflammation of the subcutaneous tissues.

**Lesions and distribution:**

Lesions may be solitary (cats) or multifocal (dogs). Dachshunds may be more commonly affected. Lesions may initially develop as subcutaneous nodules, but often they will break open and drain an oily, blood-tinged fluid. Affected animals may have constitutional symptoms prior to the onset of new lesions. Differential diagnoses include all of the infectious etiologies that cause nodules and draining tracts.

**Diagnosics:** Full thickness biopsies, including the subcutaneous tissues are indicated for histopathology and culture (aerobic and anaerobic bacterial, fungal, opportunistic mycobacterial). A thorough search of biopsy specimens, including the use of special stains, should be undertaken by the pathologist. Because many of the infectious organisms are difficult to identify on histopath, negative cultures must be obtained before initiating treatment for sterile, nodular panniculitis.

**RX:** Treatment with immunosuppressive doses of corticosteroids is indicated once a diagnosis is confirmed. Treatment should be tapered slowly over weeks to months. Long-term remissions may occur. Life-long therapy is sometimes necessary.

### **Sterile granuloma / pyogranuloma syndrome**

**Etiology:** is an idiopathic disorder, thought to be due to immune dysregulation.

**Lesions and distribution:**

Firm, painless papules, plaques, and nodules may occur. Ulceration and draining tracts are uncommon. Lesions are usually multifocal, and may occur on the head, pinnae, and paws. Trunkal lesions are also seen. Differentials include infectious etiologies, sterile panniculitis, and neoplasia.

**Diagnosics:** Biopsy specimens are usually compatible with an infectious etiology, but organisms are not found. Biopsy for culture is negative.

**RX:** Patients may respond to immunosuppressive doses of corticosteroids, tetracycline / niacinamide, or azathioprine (dog only, rarely necessary). Once remission is obtained, medications can be tapered. Long remissions may or may not be possible. Lesions in the cat may undergo spontaneous remissions.

**The Histiocytic Diseases** are a complex set of cutaneous (and occasionally systemic) disorders.

Although these syndromes have previously been discussed as immune-mediated in nature, recent research indicates they are more likely neoplastic.

There are 5 types of histiocytic diseases that can affect dogs; 1) Benign histiocytoma; 2) Cutaneous (reactive) histiocytosis; 3) Systemic (reactive) histiocytosis; 4) Localized histiocytic sarcoma and; 5) Disseminated histiocytic sarcoma. Distinguishing them from other granulomatous inflammations or

round cell tumors such as lymphoma can be difficult. This disorder is due to a reactive or neoplastic proliferation of either dendritic antigen presenting cell (including the langerhan cell) or macrophages.

**Cutaneous histiocytoma** is a benign tumor that often affects young dogs (<3 years of age) and is a solitary, non-pruritic, button-like (dome-shaped) nodule. They are usually less than 2.5 cm in diameter. The predilection sites are on the head, neck, ears and extremities. Diagnosis may be made with cytology or biopsy. The most important differential to rule out is mast cell tumor. Treatment includes benign neglect, because these tumors often spontaneously regress, or surgical excision. Prognosis is very good for a solitary histiocytoma. Cases of multiple histiocytomas at different sites are uncommon. Shar Pei dogs or their crosses are over represented in this group. A few cases of multiple histiocytomas with malignant behavior have been observed in young dogs.

**Reactive histiocytosis** includes both cutaneous and systemic histiocytosis. Cutaneous histiocytosis (CH) is a rare, benign, histiocytic proliferative disease in dogs that involves cutaneous structures only. This disorder is seen in dogs between 3-13 years, and there is no sex or breed predilection. CH primarily targets the skin and subcutaneous tissue and is characterized by solitary, or more often multiple, nonpruritic and non-painful, haired or alopecic cutaneous plaques or nodules, predominately on the head, neck, perineum, scrotum, and extremities. Diagnosis is made by biopsy. Often to confirm a diagnosis of histiocytosis, immunophenotyping is recommended to differentiate from other round cell disorders. This is available at UC-Davis by pathologists, Dr. Verena Affolter and Dr. Peter Moore. Spontaneous regression may occur, predominately in the early stages of the disease. Surgical excision may be successful in solitary lesions but does not prevent the development of new lesions elsewhere. Treatment success with immunosuppressive doses of steroids has been variable. Cyclosporine has also been used to control this disease with some success.

**Systemic histiocytosis (SH)** involves not only cutaneous lesions, but other organ systems such as lymph nodes, nasal cavity, eyelids, sclera, lung, spleen, and bone marrow. Lesions may also occur in retro-orbital and testicular tissue. Bernese Mountain Dogs, Rottweilers, Golden and Labrador Retrievers are predisposed, but SH has been diagnosed in other breeds. Ages range from 4-7 years. The majority of these cases exhibit a slowly progressive behavior.

**Diagnosis:** biopsy. Often to confirm a diagnosis of histiocytosis, immunophenotyping is recommended to differentiate from other round cell disorders. This is available at UC-Davis, by Dr. Verena Affolter and Dr. Peter Moore. It is also important to perform chest and abdominal radiographs, and abdominal

ultrasound to assess for systemic involvement. Biopsies of affected organs and lymph nodes may be required.

**RX:** Treatment success with immunosuppressive doses of steroids has been variable. Cyclosporine and Leflunomide have also been used to control this disease with some success. Prognosis is guarded.

**Localized histocytic sarcoma** presents as a rapidly growing solitary, locally aggressive soft tissue mass. Flat Coated Retrievers, Golden Retrievers, Labrador Retrievers and Rottweilers are predisposed, but other breeds may be affected. There is no sex predilection and ages range from 6-11 years of age. They have been diagnosed in dogs as young as 2 years old.

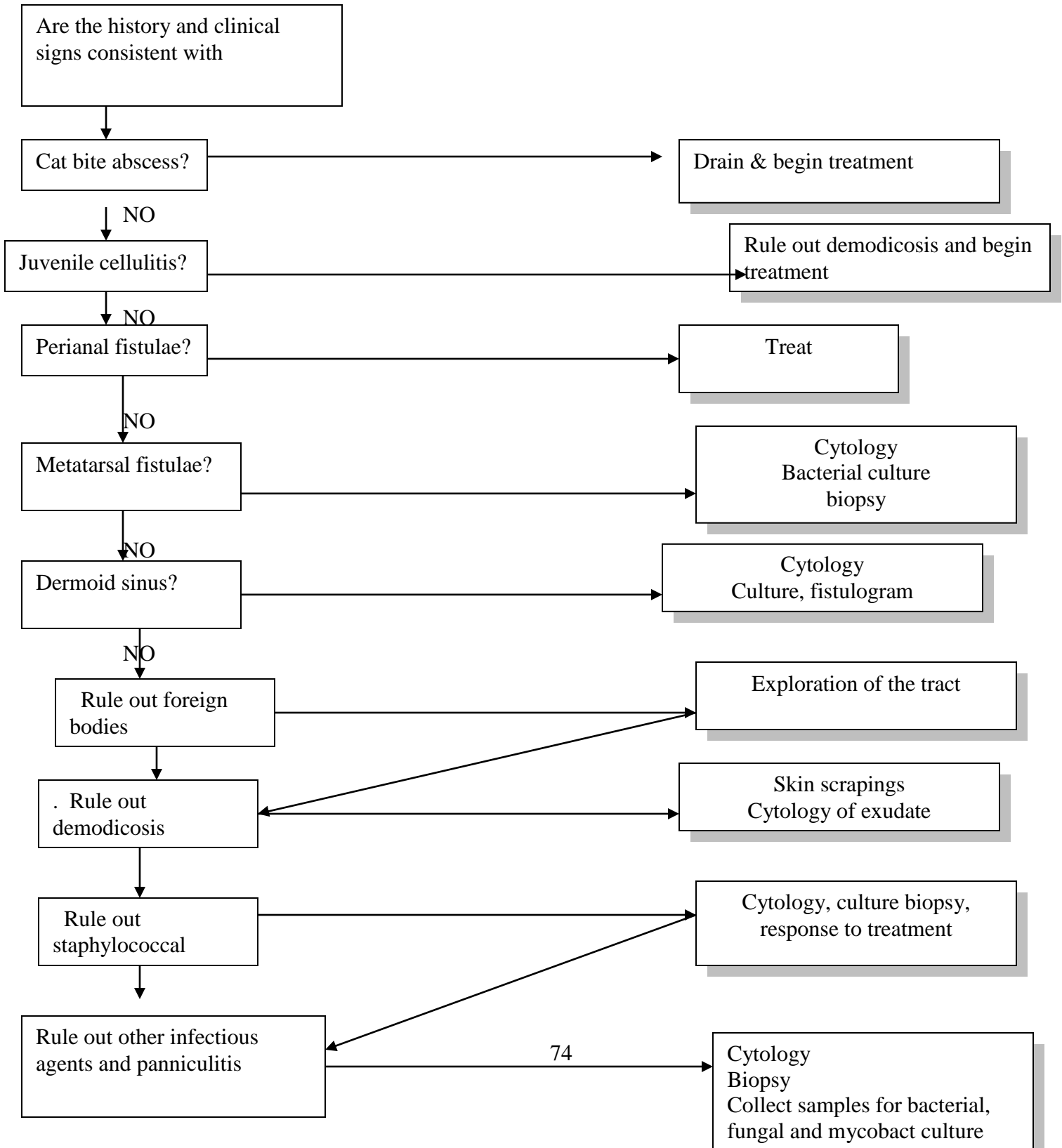
**Lesion distribution:** Predilection sites are skin, subcutis, and underlying tissues on extremities. The lesions are often located in close proximity to a joint and encircle it, involving the joint capsule, tendons and skeletal muscles. Histocytic sarcomas can develop in other locations such as lymph nodes, spleen, liver, gastric wall, CNS and tongue.

**Diagnosis** is made by biopsy. Often to confirm a diagnosis of histocytosis, immunophenotyping is recommended to differentiate from other round cell disorders. This is available at UC-Davis, by Dr. Verena Affolter and Dr. Peter Moore.

**RX** Complete surgical excision or amputation is recommended. Prognosis is poor if unable to completely excise or if systemic disease is present.

**Disseminated histocytic sarcoma** (previously known as malignant histocytosis), is very aggressive multi-systemic disease. This disease is recognized in Bernese Mountain Dogs, Golden Retrievers, Labrador Retrievers and Rottweilers. This disease is poorly understood, and it is not known whether the lesions represent a localized histocytic sarcoma with metastasis. This disease primarily affects the spleen, lymph nodes, lungs and bone marrow. Dogs often present systemically ill, and are between 3-11 years old. Diagnosis is made by skin biopsy. Biopsies of affected organs and lymph nodes may be required. Often to confirm a diagnosis of histocytosis, immunophenotyping is recommended to differentiate from other round cell disorders. This is available at UC-Davis, by Dr. Verena Affolter and Dr. Peter Moore. This type of histocytic disease has a very poor prognosis due to the multicentric distribution. In addition, this disease shows a very poor response to immunosuppressive or chemotherapeutic drugs.

### Algorithm summarizing approach to nodules and draining tracts



# PruritUs

Dunbar Gram, DVM, DACVD

Pruritus is NOT a disease  
Pruritus is a symptom  
PruritUS affects “all of US”

Acute: treat the symptom, while working up the disease  
Chronic: cure the disease. If not possible, safely control

## Pruritus

Clients may not equate itching and pruritus with the following. You may have to ask about  
Scratch, Chew, Bite, Rub, Lick, Scoot, Alopecia w/o obvious itch (especially cats)

## Pondering Pruritus

What causes it?  
Short Term treatment?  
Long Term treatment?  
Is treatment worse than the disease?  
Can meds help or hinder the diagnosis?

Pruritus: Is response to therapy part of a work up?

Yes and No!  
It depends on the rest of the work up.  
Should not be the only work up...for chronic cases  
Acute: Many options and steroids are one of them

Pruritus: What causes it? the diseases that cause the symptom

It is atopy/fleas 80-90% of the time.  
The real questions: If true, is it significant enough to warrant the use of medications?  
Does effective medical therapy hinder proper work up and worsen long term prognosis?

In the long term, many pets need more than

Antihistamines  
Apoquel  
Cyclosporin  
Steroids

Short term: Which diseases to consider  
Short term: Which medications to consider  
Short term Habit: Client Education!  
Short term medical therapy

Long term plan: If not resolved within 3 months... refer (educate client at first visit)

Habit forming medications

Is there anything wrong with judicious and prudent use of short term medications? Not in my opinion.

However,....

Coexisting/complicating conditions/drugs

Masks symptoms/ignoring the underlying causes/allows atopy to progress long term

Depends on the patient and frequency of use

Client education

Pruritus: Repeat Visit

What Causes it?

If the first assumption (Atopy or Fleas) was correct, Pruritus will likely return.

Repeat Visit Question for clients: Did the meds help last time?

Yes 100%- It was likely atopy or fleas.

Duration of effect?

How often can the meds be repeated?

No... Or Maybe...

Give more meds, consider other causes

Uh Oh, I have missed something, "Damn It." Consider other causes. What a "PAIN for ME"

What causes Pruritus

"DAMNIT" acronym what are the other causes besides allergies & fleas

"PAIN ME" acronym to remember differentials

Will the response to meds help identify the cause?

PAIN ME

Parasitic: Fleas, Scabies, Demodex, Otodectes

Allergic: Flea, Environmental, Contact, Food

Immune mediated/Idiopathic/Idunno

Neoplastic

Microbial: bacteria and yeast (& dermatophyte)

Endocrine: endogenous and iatrogenic (infxn)

PAIN ME: Clinical Approach

Questions we ask ourselves about diagnoses

Confirmable

Embarrassing to miss



Curable                      Embarrassing to miss

Controllable                Art of Medicine

Crazy (frustrating)        My passion

### PAIN ME

confirmable, curable, controllable, or crazy

Parasitic: Confirm or ~100% "Cure/control" (?fleas?)

Allergic: Can NOT confirm, cure or 100% control=crazy

Imun/Idio: Variable

Neoplastic: Confirm

Microbial: Confirm and temporarily cure (secondary)

Endocrine: Confirm and hopefully totally control

Classic Allergic: Environmental, Flea, Food, Contact

Classic Parasitic: Fleas, Scabies, Demodex

Parasitic Causes: Fleas: the "F" word

Parasite alone causes symptoms, but allergy is far worse and insidious.

Up to 40% of normal dogs may have positive allergy test. Up to 80% of atopics are positive

Positive reaction may correlate better with exposure than clinical allergic disease.

15% of clinical FAD patients lack any flea evidence: Especially true statement in a flea scarce environment

Causes: Scabies

Non seasonal, severe pruritus, steroids do improve 30%, ear margins, elbows and ventrum.

Can occur coincidentally w common diseases such as atopy or fleas. Otherwise acute onset

Positive pinnal-pedal reflex (75-90%). Hx of contagion???

Skin scrape positive 20% of the time. Serum test option

Empirical therapy may be only way to rule out

Lym Dyp (also antipruritic), Moxidectin and Selamectin are the only approved therapies

Parasitic : Demodex

#1 presenting parasite in many practices (besides invisible fleas)

Just remember to skin scrape (and pluck: can miss)

Variably pruritic: Some do, Most do NOT

Localized vs generalized: treatment options

Demodex Therapy: Amatrax, Moxidectin, ivermectin (not collies, white feet and more, but genetic test for sensitivity)

Parasitic: Feline Demodicosis

D. cati: symptoms similar to D. canis: typical & ears. Slender appearance/Minimal pruritus

D. gatoi: symptoms similar to scabies & potentially contagious.

.....Careful skin scrapes. Stubby. Pruritus

Treatment: Lym Dyp (only approved therapy) & amatraz (off label) and weekly moxidectin (off label)

Parasitic diagnosis summary: Relatively straightforward

Confirmable with exam (most, but not all): fleas, lice, canine demodex, otodectes, ?SCABIES?

Confirmable with definitive therapy (often): feline demodex, otodectes, scabies

Curable: all except fleas (make me CRAZY)

“Cur/trol” w meds and parasite control: Fleas (and lice, otodectes, scabies) depending on attributes of specific products

Parasitic: Diagnosis Highlights

Perform good gross and microscopic exam

Consider definitive therapy while tx symptoms

Remember that other diseases may also be present (atopy or food allergy)

CE: Within 2 months, You can either see them, cure them or control them (for flea allergic pets, the infestation and symptoms may require a little bit of steroids-which can be confused with atopic pets)

<u>Parasite</u>	Outcome	Defin Diag	Steroid result	
	<u>Curable</u>	<u>Exm, DefTx</u>	acute	chronic
Fleas	?	+/-, +/-	+	+
Scabies	+	+/-, +	+/-	-
Otodectes	+	+/-, +	+/-	-
Demodex	+?	+ , ?	+/-	-

Parasites may be identified on exam, cured or controlled within 1-2 months. Atopy complicates assessment. Steroids can complicate diagnosis

Chronic medications (steroids, Apoquel, Cyclosporin) may cause side effects and delay appropriate therapy

Summary: steroid response is NOT straightforward

You can miss parasites on exam and still have an initially positive response to steroids, especially with acute infestations or if pet is hypersensitive to parasite (fleas, Scabies, Otodectes)

Chronic use does not treat the underlying problem

Chronic use may facilitate diagnosis of mites (Scabies, Otodectes, Demodex) or directly cause Demodicosis. This is not a “good idea”

Parasite Summary

-EMBARASSING to miss them

- If you can't find them, you can "curtroll" them
- Just remember gross and micro exam, therapeutic trial for scabies (otodectes, feline demodex) and possible steroids or Apoquel for flea allergic pets: Steroids w flea/mite control
- May be present concurrently with allergies
- Rule out parasites first or concurrently with allergy workup

#### "Standard protocol"

- Examine the patient (and communicate with the client). Use meds/flea control if appropriate
- Skin scrape and parasite control
- Embarrassing to miss scabies and/or cause Demodex with repeat visits. True for both the primary and secondary veterinarian.
- If not improving, reevaluate/reeducate/refer
- Reconsider scabies and concurrent allergies

#### Allergy: Highlights

- Atopy: Seasonal to progressive, initially steroid responsive disease starting age 2-5 years (3 Months to 12 years)
- Food: Consistent/constant pruritus at any age (Threshold), but not always classic. May not respond to meds
- Contact: Mostly Florida with and body distribution hints
- Flea: Extremely important. Can have flea allergy without ever seeing fleas.
- Parasite (other than fleas) hypersensitivity: Scabies, Otodectes, internal parasites
- Microbial: Malassezia and bacteria: hypersensitivity
- Malassezia and bacterial proteins can directly exacerbate atopic dermatitis lesions without Hypersensitivity

Atopy and Flea factor = Fear factor ("The F Word")when it comes to itch

Common causes

Similar appearance

Respond to steroids.

Thus the flea control & steroid mantra

FAD = "rumpitis:" often but NOT always

No doubt that many pets are undertreated. Once a month tx is not enough in FAD.

#### Allergy History

Supportive evidence that is circumstantial. It helps build a case for a particular diagnosis.

Many complicating factors and diseases.

Pets and People move geographically

Concurrent diseases in addition to allergic diseases

People Lie; knowingly and unknowingly.

Steroids not help: I can't remember or it came back.

Steroids help: itch, but not paws or helped 3 years ago

Allergy Sound Bites (that may come back to bite you)

Bulldogs and others may not itch/can not itch

Rumpitis: 39% of atopics that were not flea allergic. 40% eventually became generalized.

OTITIS may be the ONLY symptom of allergies

Food: 33-50% < 1 year old. "Best allergy to have."

Beef-60%, soy-32%, chicken-28 %, milk-28%, corn-25%, wheat-24%, eggs-20%

another study showed Fish-50%. Rice-9%.

Concurrent Atopy/Flea: 75%

Allergy diagnosis dilemma: Confirmation

Atopy: Common coexisting diagnosis. Expensive & time consuming test.

Positive test does not prove as the only factor or even a significant factor=Frustrating/crazy

Food: Strict 8-10 weeks elimination diet is only method. Complicated by atopy & fleas

Contact: avoidance and in some cases biopsy (use a dermatopathologist)

Malassezia & Bacteria: Only treat infections without antipruritics

Flea & Mite: Only treat infestations without antipruritics

Allergy diagnosis summary highlights

History & examination: Most important but suggestive findings do not mean the only dx

Ancillary test: Not confirmatory for any of the allergies as the/or only etiology. Biopsy?

Definitive therapy:

For atopy is uncertain (Immunotherapy: 1 year)

Food (2 months)

Flea (Indoors: 3-6 months. Indoor/Outdoors: difficult)

Prednisone, Antihistamines, Cyclosporin, Apoquel

History, Exam and Steroid Response: are helpful with atopy and flea allergy

Allergy: steroid response without coexisting or complicating factors

	Acute	Chronic
Atopy	+	+ side effects
Flea	+	+ side effects
Contact	+/-	+ side effects
Food	+/-	V side effects
Malassezia, bacteria & other: variable		

Parasite	Outcome w Steroids	
	<u>Acute</u>	<u>Chronic</u>

Fleas	+	+	side effects
Scabies	+/-	-	
Otodectes	+/-	-	
Demodex	+/-	-	death

### Parasites, Allergies and Steroids

Steroids will make ALMOST any parasitic or allergic diseases better in the short term.

As long as the secondary infections are controlled.

Food allergy and demodex may be exceptions.

If blindly follow this path, you will be burned by scabies, demodex, bacteria, yeast et al

Topical therapy is important to reduce infections

### Pruritus: Allergy Summary

If history and gross exam suggest allergies and microexam is negative (parasites, bacteria and yeast), pursue a short course of steroids and fleas/scabies control. Add antimicrobials if necessary.

CE: Failure = repeat microexam (microbial steroid opportunist), food trial & scabicial therapy. If failure continues, consider referral

### Success: Many options

#### Medical Therapy: \$ Monthly Costs For 50# dog & Side Effects

Prednisone	13	Many issues
Immunotherapy	20-40	I like it
Antihistaminics:	25-175	Twice daily
Topicals	20 +/-	Few
Pentoxifylline:	25-100	GI issues
Apoquel:	75-100	Infxn, mange, neoplasia
Cyclosporin:	150-200	GI, Immune, gingival hyperplasia and oral papiloma, contraindicated if hx of malignancy. Cost reduced with ketoconazole but hepatopathy.

#### Medical Therapy: \$ Monthly Costs For 50# dog & Evidence Based

Prednisone	13	Yes, Yes, Yes
Immunotherapy	20-40	Yes, Yes
Topicals	20 +/-	Variable
Pentoxifylline:	25	Yes
Misoprostol:	75	Yes
Antihistaminics:	25-175	Variable
Cyclosporine:	150-200	Yes, Yes
Apoquel:	75-100	Yes, Yes

The American College of Veterinary Dermatology Task force on Canine Atopic Dermatitis  
Veterinary Immunology and Immunopathology: Vol. 81. Thierry Olivry (NCSU); Doug DeBoer  
(University of Wisconsin); Craig Griffin (San Diego); Richard Halliwell and Peter Hill  
(Edinburgh); Andrew Hillier (OSU); Rosanna Marsella (UF), Candice Sousa (Sacramento)

The treatment of canine atopic dermatitis is multifaceted and consists of a combination of actions that include the use of allergen avoidance, anti-inflammatory agents, allergen specific immunotherapy and antimicrobial drugs

The importance and order of these treatment steps vary from patient to patient.

Microbial proteins can either exacerbate AD lesions directly or can serve as allergens

#### Anti-allergic Pharmacotherapy

Inhibitors of allergic immediate-phase-reaction

Prevent mast cell degranulation: Cromoglycate, cyclosporin A, Glucocorticoids (GC)  
Prevent vasoactive and pruritogenic effects of histamine: antiH1 receptor antihistamins, GC

Inhibitors of allergic late-phase-reaction

Prevent the activation and release of mediators with Chemo attractive effects (Misoprostol, pentoxifylline, cyclosporine, GC)

#### Anti-allergic Pharmacotherapy

Inhibit both immediate & late phase reactions following IgE mediate mast cell activation  
Glucocorticoids (GC), Cyclosporine A

#### Anti-allergic therapy

Glucocorticoids: High quality, strong evidence to support the use of oral low dose

Misoprostol and Pentoxifylline: Fair evidence to support their use.

Allergen Specific Immunotherapy (ASIT): Well documented for humans with respiratory atopic disease and stinging insect allergy. Large body of clinical observations suggest

ASIT is effective in controlling the clinical signs of dogs with Atopy.

Cyclosporine: Good evidence

Apoquel: Good evidence

#### Anti-allergic therapy

Antihistamine therapy: Insufficient evidence to conclude for or against the efficacy.

However, “clinical impressions” suggest... worth a try

Serotonin-reuptake antagonist, Leukotriene inhibitors, tacrolimus, capsaicin: Insufficient evidence for or against

Fatty Acids: Insufficient evidence to recommend for or against the use of EFAs.

However... “clinical impressions” suggest...

Most Allergies may be controlled with steroids or other meds and diet change within 1-2 months (food=2) if complicating factors are eliminated and strict dietary trial is pursued.

Allergies definitive diagnosis can be elusive when compared to Parasites

Parasites may be identified on exam, cured or controlled within 1-3 months (Scabies 3 weeks, fleas 3-6 months). Atopy complicates many patients with parasites. Unlike Allergies definitive diagnosis is NOT elusive for parasites if you treat for them

Allergy Review: Similar appearance and not exclusive diagnoses

Atopy is a clinical diagnosis, difficult to absolutely confirm as primary/only cause of pruritus. Usually steroid responsive. Skin Test is best & Gold standard. Serum test have improved

Flea allergy coexist/complicates all and may be overlooked in a flea scarce environment. It is steroid responsive.

Food allergy is impossible to confirm without a 8-10 week STRICT DIETARY TRIAL. Variably steroid responsive. NO GOOD BLOOD TEST. NO GOOD SKIN TEST.

Allergies, Parasites and Steroids: The use of steroids

Can help control pruritus in many patients

Is not of diagnostic value unless other diagnostics (exam, microscreen and food trial are performed)

May mask symptoms until atopy becomes resistant

Can lead to EMBARRASSMENT: (demodicosis, scabies, dermatophytosis, pyoderma and yeast)

Other problems (Death)

Practical Pruritus: Realistic 1-3 month Plan

Gross & microscopic exam for Neoplasia, Immune/Idiopathic and Microbes

Parasites may be identified on exam or cured/controlled within 1-3 months  
(if use Selamectin, Moxidectin etc and steroids)

Allergies may be controlled with steroids/Apoquel for 1-3 months if no complicating/microbial factors (strict dietary trial pursued: wait till winter)

After 2 months, (expose to original diet: OK low maintenance steroids for atopy/ flea allergy), Then taper meds if not already discontinued

Practical Pruritus: Realistic 3 or more month Plan  
Refer

Causes: Immune Mediated & Idiopathic

Variably pruritic: foot licking and face rubbing with pemphigus or lupus  
Dermatomyositis: face and feet  
Concurrent diseases can be pruritic

Causes: Neoplastic

Variable presentation  
Chronic allergic patient may demonstrate subtle changes in symptoms/location  
Typically only mild response to steroids

Summary: beware of any older patient with symptom change, oral depigmentation, or focal thickening. R/O other ddx. BIOPSY

Causes: Microbial

Bacteria: inflammation and potential hypersensitivity  
Malassezia: inflammation and potential hyper-sensitivity. YOU SHOULD LOOK FOR THIS, especially if fails abt therapy  
Dermatophyte: inflammation and potential hypersensitivity  
Steroids and Allergies predispose

Microbial: Highlights

Predisposing factors: Endocrine, Parasites, Allergy. Incompletely controlled atopy and food may be relatively non pruritic,  
Diagnosis: gross and microscopic exam  
Treatment: systemic and topical (especially if using steroids concurrently)

Microbial: Malassezia

It is a relief to diagnose 3<sup>rd</sup> most common dx  
Itchy, Odor, Erythema, Lichenification: Greasy or dry, Skin fold (face, ankles, feet), Nail-bed, ventral paws, dorsal web, Anywhere  
Consider Malassezia Hypersensitivity

Microbial: Malassezia diagnosis

Tape impression, swab, direct impression smear, dry skin scrape  
Diff-Quick or other  
Microexam: >1 yeast per oil power field with cells or keratin debris  
Response to therapy



Microbial: Malassezia therapy

Topical or Systemic or Combination

Topical: My first choice due to potential side effects of systemic therapy. Works best with truncal/non fold involvement.

Shampoos/Rinses/Spray/Pledgets/Wipes

Microbial: Malassezia therapy (systemic)

Systemic: Ketoconazole or Fluconazole (2.5-5mg/#/Day) or Itraconazole (2.5 mg/#/Day)

Keto side effects include: nausea, liver. Worse in cats=25%. Decreases metabolism of cyclosporine and anticonvulsants

Itraconazole side effects: COST, generally fewer side effects except at high doses in cats

Terbinafine: Cheap but potentially less effective.

Pulse therapy?

Microbial: Malassezia

Symptoms: odor, pruritus, nail, neck, more

Predisposing factors: Parasites, Allergy, Endocrine, previous antibiotic use.

Diagnosis: gross, microscopic exam, response to therapy

Treatment: systemic and topical

Microbial: Diagnostic Dilemmas & Steroid Response

Bacterial: Remember cytology. Secondary problem with variable steroid response

Malassezia: Remember cytology. Secondary problem with variable steroid response

Dermatophyte: False positive woods lamp & DTM. Variable steroid response

Steroids may predispose to microbial infections and may blunt symptoms/inflammation

Causes: Endocrine

Seldom pruritic if not secondarily infected or have concurrent other diseases:  
such as Parasites/Allergy

Cushing's

Hypothyroidism

Testicular neoplasia

Sertoli cell tumor and estrogen hypersensitivity

Mimic flea allergy yet respond to castration

PAIN ME

<u>P</u> arasitic	Confirmable/Curable/Controllable
<u>A</u> llergic	Chronic control....Crazy
<u>I</u> mm/ <u>I</u> di	Varies
<u>N</u> eoplastic	Varies
<u>M</u> icrobial	Curable but recurrent
<u>E</u> ndocrine	Control or cure hormonal hypersens

### Practical Pruritus (Short duration)

Most pruritus cases have a history and exam compatible with fleas and atopy.

Impossible (virtually) to make a definitive diagnosis or utilize a definitive treatment for atopy/fleas as the sole cause

The standard mantra of flea control and short-term medication is appropriate in most cases.

Consider Scabies, Demodex, Microbial causes

### What about long term or recurrences?

A) Repeat medications until they do not work or side effects become intolerable

B) Alternate safer medical therapy such as antihistamines while tapering pred, Apoquel

C) Food trial in the winter (esp if "B" fails)

D) Monitor for microorganisms and side effects

E) Refer for allergy test if >3 months duration

F) Consider Scabies, Demodex, Microbial at any time

### Practical Pruritus: Chronic pruritus

Atopy may be controlled with alternatives to steroids for years, but only palliative. Often cost more and allows disease to progress. Judgment call: breed, family history, location

Allergy test before persist/recurs for more than 3 months out of the year

### Allergy Testing Indications

After clinical diagnosis has been made

Ruled out other disease and treated infections without adequate long term resolution

### Medical therapy

Side effects

Expensive

More than 3 months out of the year

### Chance to "Cure" with immunotherapy

### Allergy Testing: Options

Intradermal Allergy Test

Considered "gold standard"

Patch of normal skin, drug withdrawal times, sedation, technically complex, test in target organ

### Serum Allergy Test: IgE is result, not cause

Improved reliability over the years.

Dogs, cats, horses

Send serum to laboratory

"Fine tuning" of injection protocol improves success

Better choice than long term medication

### Positive allergy test does not confirm the diagnosis

Correlate with history (allergen selection)

Early Spring: Trees

Spring/Summer: Grasses

Summer/Fall: Weeds

Year round: Dust, Dust Mite, Molds

Immunotherapy Protocols: Can vary considerably

Flares During Immunotherapy

Treat as would without immunotherapy

Remember the differentials for pruritus

PAIN ME

Fleas

Scabies

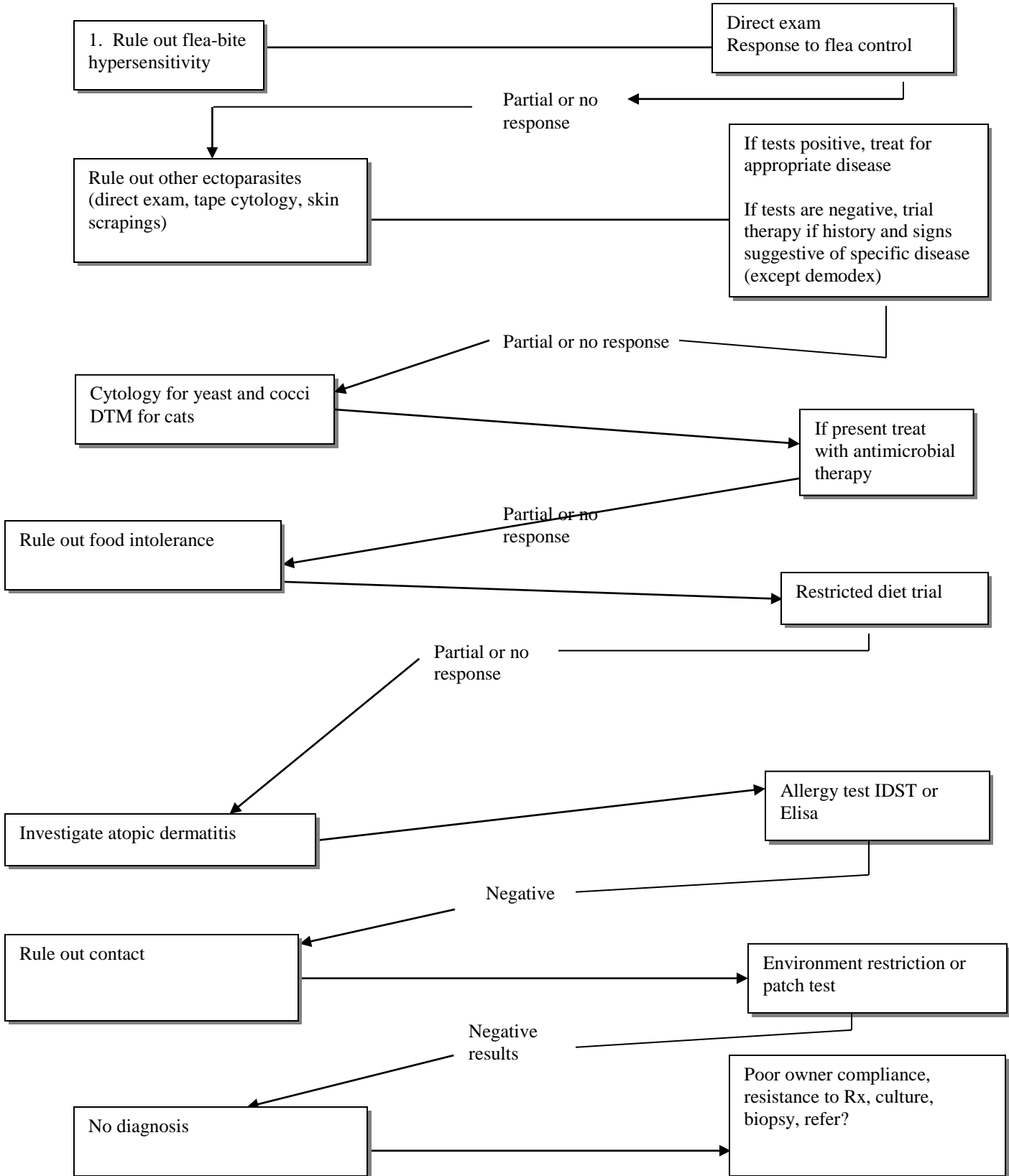
Bacteria

Yeast

DEMODEX (especially if steroids are being used)

Food

# PRURITUS



## Management of pruritus

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### Introduction

- *Pruritus (or itch) is one of the most common clinical signs in both dogs and cats. Pruritus is defined as unpleasant sensation inducing the desire to scratch, to bite, to lick or to rub. Pruritic diseases may include to parasitic, allergic, infectious, metabolic and neoplastic conditions.*
- *In cats, sometimes pruritus is difficult to recognize being misinterpreted as normal grooming.*
- *Dogs and cats manifest pruritus in different ways (e.g. location, clinical appearance, modalities of scratching). Moreover, non-pruritic dermatoses in dogs may be pruritic in cats.*
- *A good history and physical examination are essential to differentiate between secondary pruritus (bacterial or yeast infection) and a primary one.*
- *In case of an impossibility to perform a good diagnostic work-up, some treatments will help to reach a more definitive diagnosis.*
- *This lecture is mainly focused on the management of pruritic dermatoses common in dogs and cats analysing the different options available:*
  - Systemic
    - Glucocorticoids (GC)
      - These will be discussed in the following lecture
    - Cyclosporine A (CsA)
    - Oclacitinib
    - Antihistamines
    - Pentoxifylline
  - Topical
    - Glucocorticoids
    - Tacrolimus
    - Capsaicin

### Cyclosporine A

- Fungal metabolite with immune-modulatory properties
- Used in dogs and cats for more than 30 years
- Mechanism of action: inhibition of calcineurin and suppression of inflammatory cytokines production. Cyclosporine (CsA) also inhibit antigen presenting cells, mast cells, and eosinophils. In people CsA has been shown to decrease the number of T

regulatory lymphocytes when administered in high doses, but it increases them when administered in low doses. CsA also inhibits the release of allergen-induced histamine in basophils

- **Indications:** skin allergies (D, C), sebaceous adenitis (D, C), autoimmune diseases (D, C), and perianal and metatarsal fistulae (D)
  - The efficacy of CsA for atopic dermatitis in dogs is around 75% and comparable with glucocorticoids and oclacitinib
- **Dose:** CsA is administered orally at the dose of 5 mg/kg every 24 hours with a possibility of reduction of the dosage to every other day after achieving 75% improvement (generally after 4-6 weeks). Generally dogs can be maintained on a minimum dose of 5 mg/kg q48 and less commonly on 5 mg/kg q72. This latter maintenance dose is more commonly achievable in cats
  - Topical applications are not effective for reduced transepidermal absorption
- **Significant clinical differences between brand name, generic, emulsified and microemulsified formulations**
  - Generic: bioequivalent to the brand name, not identical; increased clinical variability due to lower absorption and tissue distribution
  - Emulsified: variable bioavailability leading to a lower clinical efficacy.
  - Microemulsified: reduced daily variations, better correlation between blood concentration and drug exposure, increased and steadier intestinal absorption
- **Pharmacokinetic:** after intestinal absorption CsA is rapidly (~30%) metabolized in by the cytochrome P450. CsA accumulates in the skin, liver, kidney, and adipose tissue. It achieves a peak blood concentration 1.5 (D) to 2 (C) hours after oral administration (in empty stomach). CsA has a half-life of 8-12 hours in dogs and up to 19 hours in cats
  - ***Please consider drug interactions***
    - Metabolized by cytochrome P450
    - CsA is a substrate for P-glycoprotein
- **Monitoring:** not necessary – lack of correlation between blood concentration and clinical efficacy, and lack of alteration on CBC and chemistry panel although a slight increase in glucose can be observed
- **Adverse effects:**
  - Vomiting (27%)
  - Diarrhea/soft stools (14%)
  - Lethargy (9%)
  - Anorexia (7%)
  - Gingival hyperplasia (2%)
  - Hypotrichosis (hirsutism) (<1%)
  - Non-viral induced papillomatosis (1%)
  - Urinary tract infections (1%)
  - Superficial skin infections (high doses)
- **Cost:** can be high in large breeds

### **Oclacitinib**

- Immune-modulatory drug with mainly antipruritic properties

- *Not recommended in combination with other immune-modulatory drugs*
- Registered only for use in dogs for the past 2 years
- Mechanism of action: inhibition of Janus Kinase (JAK)/STAT pathway leading to the suppression of pruritic and inflammatory signal
  - JAK/STAT complex is associated with many cytokine receptors and it is fundamental in the transmission of the stimulus in the nucleus and activation of the gene machinery
- Indications: pruritic diseases and atopic dermatitis in particular
  - The efficacy of oclacitinib for atopic dermatitis in dogs is around 50-67% (up to 80% - anecdotic) and comparable with CsA and glucocorticoids.
  - The speed of action is anywhere between 10 minutes and 4 hours
- Dose: Oclacitinib is administered orally at the dose of 0.4-0.6 mg/kg every 12 hours for 14 days and then every 24 hours
  - A further reduction of the dosage to q48 or on as needed basis is recommended if possible
- Pharmacokinetic: after intestinal absorption oclacitinib reaches a blood peak in <1hour with an absolute bioavailability of 89%. Food administration does not affect the kinetic of the drug. It has a half-life of 4-6 hours
- Monitoring: not necessary – lack of alteration on CBC and chemistry panel have been published
- Adverse effects:
  - Pyoderma (12%)
  - Non-specified dermal nodules (12%)
  - Urinary tract infection (11%)
  - Otitis (9%)
  - Vomiting (9%)
  - Pyoderma (9%)
  - Diarrhea (6%)
  - Lethargy (3%)
  - Superficial yeast infections (2.5%)
  - Demodicosis in young dogs
  - Viral papilloma (anecdotic)
  - Weight gain (anecdotic)
  - Leukopenia, elevated ALT, proteinuria (anecdotic)
- Cost: can be moderately high in large breeds

### **Antihistamines**

- Preventative treatments and not useful as acute phase treatment
  - Low efficacy used as symptomatic (~30%)
- Mechanism of action: competitive blockage of histamine receptors type 1 (H<sub>1</sub>) leading to lack of inflammatory cascade histamine induced
  - First, second and third generation antihistamines
    - **1<sup>st</sup> generation:** The oldest H<sub>1</sub>-antihistamines. They also behave as muscarinic acetylcholine receptor (anticholinergic) antagonists. They also

act on  $\alpha$ -adrenergic and 5-HT receptors. Due to poor selectivity and high lipophilia, these drugs can cross the blood brain barrier causing sedation in most individuals. Examples are: hydroxyzine, diphenidramine, clemastine, chlorpheniramine, cyproheptadine, etc.

- **2<sup>nd</sup> generation:** They are newer drugs with a higher selectivity for peripheral H1 receptors compared to the central H1 receptors and cholinergic receptors. This selectivity and a lower lipophilia (polar compounds at physiological pH) significantly reduce the occurrence of sedation. Examples are: cetirizine, loratidine, ebastine, terfenadine, etc.
  - **3<sup>rd</sup> generation:** They are the active enantiomer or metabolite derivatives of second-generation antihistamines. They are intended to have higher efficacy and fewer side effects. Examples are: levocetirizine, desloratadine, fexofenadine
- Indications: type I hypersensitivity reactions including atopic dermatitis
  - Dose: it depends from the compound
  - Pharmacokinetic: it is known only for few antihistamines in dogs such as hydroxyzine that gets rapidly converted in cetirizine
  - Monitoring: not necessary – lack of alteration on CBC and chemistry panel although a slight increase in glucose can be observed
  - Adverse effects: minimal. Mainly sedation when using 1<sup>st</sup> generation antihistamines
  - Cost: reasonable

### Pentoxifylline

- Immune-modulatory drug with mainly anti-inflammatory properties
- Mechanism of action: Pentoxifylline is a methyl-xanthine derivate and as such act as competitive nonselective phosphodiesterase inhibitor increasing intracellular cAMP concentration. This leads to activation of protein kinase A and inhibition of proinflammatory cytokines (e.g. TNF- $\alpha$ , IL-1, IL6) and leukotrienes synthesis. It also stabilizes mast cell membranes. Pentoxifylline also increase red blood cell deformability, reduces blood viscosity, and decreases platelets aggregation and thrombus formation
- Indications: Atopic dermatitis, contact allergy, vasculitis, etc.
  - It is moderately effective as adjunctive therapy for canine AD administered for at least 60 days (lesions and pruritus)
  - Best results when associated to antihistamines or polyunsaturated fatty acids (linoleic acid, linolenic acid, oleic acid, eicosapentaenoic acid, docosahexanoic acid, and  $\gamma$ linoleic acid)
- Dose: it is given at 10-20 mg/kg q8-12
- Monitoring: not necessary – lack of alteration on CBC and chemistry panel
- Adverse effects: minimal. Mainly GI upsetting and anorexia
- Cost: reasonable

### Topical glucocorticoids

- Many GC are available with different power, efficacy, and severity of side effects
  - Hydrocortisone 1%



- Triamcinolone acetonide 0.1%
- Budesonide 0.025%
- Hydrocortisone aceponate 0.058%
- Mometasone 0.1%
- Prednicarbate 0.1%
- Useful to decrease severity of canine AD, excoriation and pruritus. Possibility of intermittent therapy
- Possible systemic absorption and increased side effects based on the individual GC. Less side effects with the new generation of GC (mometasone, hydrocortisone aceponate, and prednicarbate)
- Side effects: skin atrophy, comedones, and calcinosis cutis (cutaneous signs of Cushing's)

### **Tacrolimus**

- Same class of drugs that CsA. It is a calcineurin inhibitor, but 50 times more powerful than CsA. Available in oral form, but mainly used as topical. Very large molecule thus transdermal absorption is very little on intact skin and for this reason rarely associated to side effects
- Formulations: available as 0.1% and 0.03% ointment; the former is more effective
- Useful for localized canine AD
- Side effects: minimal. No skin atrophy or decreases local/systemic immunity have been reported. Mild erythema, burning sensation and pruritus have been reported

### **Capsaicin**

- Capsaicin is an alkaloid from chilli pepper able to decrease pain and pruritus locally inducing neurogenic inflammation. The mechanism of action is unknown, but a depletion of substance P from sensory nerve endings and desensitization of the C fibres is hypothesized. An initial worsening of the pruritus can be observed
- Formulation: 0.025 ointment

# **Corticosteroid Therapy Revisited: Promulgating Prudent Prednisone Policy**

Dunbar Gram, DVM, DACVD, MRCVS

## **INTRODUCTION:**

Judicious corticosteroid administration can be an extremely useful therapeutic modality for the treatment of inflammatory dermatological conditions. Unlike many other pharmacological options, the response to therapy is often quickly noticed by the client and rapidly beneficial to the patient. The dose is also easily altered. It is important to note that there is a difference between short term therapy and long term therapy. Twenty years ago, I found myself spending a great deal of time educating clients about avoiding steroid abuse. In recent years, I have found myself educating clients about the benefits of prudent steroid administration (promulgating prudent prednisone policy). I would like to thank Dr. Candice Sousa for publicizing the potential careful benefits of steroids as well as providing the permission to utilize parts of her written notes. Most of you already know, or were once taught, the basics of what I am about to review. You may not remember all the specifics of the pharmacology, but while working for veterinarians you have witnessed the benefits of proper prednisone utilization and seen some of the side effects. I ask that you keep these in mind when comparing other therapeutic options. At the conclusion, we will review the doses of corticosteroids that I use in clinical practice.

## **WHAT ARE THEY**

**Steroids** are compounds that are manufactured from and resemble cholesterol. Steroids are primarily produced in the cortex of the adrenal gland but other organs, such as the testicles and ovaries, also contribute to their production. Some of the metabolically active substances included in this group are the sex hormones, bile acids, and cortisone.

**Corticosteroids** (or **corticoids**) (**CS**) are 21 carbon steroid hormones that are primarily produced by the adrenal cortex. The major stimulus for the adrenal cortex to synthesize and secrete steroids is adrenocorticotropic hormone (**ACTH**), which in turn is synthesized in and released from the pituitary gland. **ACTH** release is stimulated by corticotrophin-releasing factor (**CRF**), produced by the hypothalamus.

**Mineralocorticoids** (**MC**) are a **CS** produced primarily in the zona glomerulosa of the adrenal cortex. They exert their greatest effect on electrolyte metabolism – sodium, potassium and chloride in particular.

**Glucocorticoids** (**CG**) increase gluconeogenesis (i.e. cause an increase in blood sugars and liver glycogen). More than 95% of the secreted corticosteroids are considered **GC**. These are products of the inner zones of the adrenal cortex, the *zonas fasciculata* and *reticularis*. The primary physiologic corticoid is **cortisol**, also termed **hydrocortisone**. **Cortisone** is the inactive form of the hormone. The active form, **hydrocortisone (cortisol)**, is formed by dehydroxylation in the liver. In man, cortisol production is estimated to be produced at a rate of 10 mg/day. The daily production rate of cortisol can rise 10-fold in response to severe stress. In dogs, daily cortisol production is 0.2 to 1 mg/kg/day. No information is available for cats.

If an additional double bond is added to hydrocortisone, this results in increased glucocorticoid activity and a decreased rate of degradation. The product of this first synthetic change is **prednisone**, which is also an inactive form. Activation requires hydroxylation in the liver at the C-11 position converting **prednisone** to **prednisolone**, the biologically active form. There is good evidence that **horses**, and anecdotal evidence that **cats**, may not convert prednisone to prednisolone in the liver possibly due to a lack of 11 $\beta$ -hydroxydehydrogenase, making the latter a more appropriate therapeutic choice in these species.

**Methyl-prednisolone** is formed by the addition of a methyl group to **prednisolone** at C-6. When a fluorine molecule is added to **hydrocortisone** at the C-9 position, this results in increased glucocorticoid but also marked mineralocorticoid activity (**fludrocortisone, Florinef**.) Further modification of this molecule by methylation at C-16 results in **triamcinolone, dexamethasone, or betamethasone**. These molecules have high GC but low MC effects.

Pharmacologically, the duration of action of synthetic GC is determined by the structure of the drug molecule. This in turn determines potency and the dosage given. Generally, the larger the dose and the more potent the glucocorticoid, the longer the drug will have an effect. (Table 1). Clinically, the route of administration and the water solubility of the carrier substance are usually more important factors affecting the duration of action. Oral GC are generally formulated as a free base or an ester that is digested to the free base and subsequently absorbed. Parenteral GC (i.e. injectable) are usually esters of acetate, diacetate, sodium phosphate or sodium succinate. The sodium phosphate and succinate esters are very water-soluble and rapidly attain serum levels even when given intramuscularly. In contrast, the acetate or diacetate esters are poorly water-soluble and are slowly absorbed at a continuous low level of glucocorticoid for several days to weeks. This slow absorption may greatly prolong the adrenal suppressive effects. Concern regarding adrenal suppression is the basis for the recommendation of alternate day dosing of short acting oral GC when long-term treatment is needed.

## HOW DO THEY WORK?

Glucocorticoids influence a variety of body functions because they affect most cells in the body. They exert most of their actions by binding to **intracytoplasmic** steroid receptors which are then transported to the **nucleus** where they bind to cellular DNA and **alter gene expression**.

In general, GC alter carbohydrate, fat, and protein metabolism; fibroblast proliferation (important for wound healing); the inflammatory response; electrolyte and water balance; synthesis of red blood cells; central nervous system function; gastric acid production; muscle strength and function; the immune system; and a variety of other metabolic processes. As stated earlier, they seem to have some effect on every metabolic process.

One of the most important medical uses of corticosteroids is for their **anti-inflammatory** effects. Inflammation comprises the changes in the tissue in response to injury. There are 4 classical signs of inflammation: pain (dolor), heat (color), redness (rubor), and swelling (tumor). When tissue injury occurs, whether it be by bacteria, trauma, chemicals, or any other phenomenon, histamine and other humoral substances are liberated by the damaged cells into the surrounding fluids. This causes an increase in local blood flow and also increases the permeability of the capillaries, allowing large quantities of fluid and cells to leak into the tissue.

Glucocorticoids: 1) Stabilize the membranes of lysosomes so that they rupture with difficulty. This helps prevent the usual tissue damage and destruction that occurs when lysosomal enzymes are released. 2) GC also decrease the production of bradykinin, which is a potent vasodilating substance. This decreases the permeability of the capillary membrane, which then prevents protein leakage into inflamed tissues. 3) GC minimize the inflammatory response through the action of lipomodulin, which inhibits phospholipase A<sub>2</sub> which normally converts membrane phospholipids into arachidonic acid (AA), a pro-inflammatory product. The decrease in AA limits available precursor molecules for lipoxygenase and cyclo-oxygenase to produce the AA-derived mediators of inflammation. 4) Lastly GCs inhibit the expression of adhesion molecules on the endothelial cells (particularly ELAM-1 and ICAM-1) and thereby interfere with the movement of leukocytes from the vasculature into inflamed tissues. This is the cause of the commonly noted leukocytosis seen with GC administration.

Glucocorticoids block the inflammatory response to an allergic reaction exactly the same way that they block other types of inflammation. The basic allergic reaction between an antigen and antibody is not affected and even some of the secondary effects of the allergic reaction, such as the release of histamine, still occur. However, the subsequent inflammatory response is responsible for many of the serious and the sometimes fatal effects of the allergic reaction, administration of GC can be lifesaving.

A complete understanding of immunosuppression induced by CS is not known. The effect is more pronounced on the cellular arm than the humoral arm of the immune system. Whereas allergen specific immunotherapy (ASIT or "allergy shots" seem to affect the humoral arm). However, the two arms are interrelated. GCs have minimal effects on plasma immunoglobulin concentrations but can modulate immunoglobulin function. For example, opsonization of bacteria is inhibited.

At immunosuppressive doses (the exact dose has not been scientifically determined) GC can induce decreased production of intracellular signaling cytokines such as IL-1, IL-6, TNF- $\alpha$ , IFN- $\gamma$  and granulocyte colony-stimulating factor (GM-CSF). These are the signals that T and B lymphocytes use to communicate and will result in an alteration of the immune system at multiple stages. In general, there is a decline in the number of leukocytes at the site of infection or inflammation and an interference with their function.

Glucocorticoids cause marked changes in leukocyte numbers and distribution. A mature neutrophilia is a characteristic component of a physiologic stress response and to exogenous GC treatment. This occurs from a combination of an increased release of mature neutrophils from the bone marrow, decreased margination and decreased migration of neutrophils out of the blood vessels, resulting in a prolonged circulatory half-life.

In contrast, the administration of GC leads to a decreased number of circulating lymphocytes, eosinophils, monocytes and basophils. Lymphopenia results from a redistribution of circulating lymphocytes to nonvascular lymphatic compartments such as the lymph nodes. As lymphopenia is not a marked or consistent component of the feline stress leukogram, this species is considered relatively steroid resistant.

Systemic glucocorticoids are probably the most commonly used drugs in veterinary medicine and are undoubtedly the most commonly used and abused drugs in veterinary dermatology. Their intended and appropriate use in veterinary dermatology is for their anti-pruritic, anti-inflammatory, and immunomodulatory properties. A beneficial response is seen in

animals with allergic disorders, inflammatory skin diseases, and autoimmune or immune-mediated dermatoses.

The specific GC effects that will occur with their therapeutic use are summarized below and need be considered particularly if ongoing therapy will be needed.

1. suppress the release of ACTH by the pituitary gland and therefore suppress the release of corticosteroids by the adrenal cortex
2. reduce the number of circulating lymphocytes through redistribution and suppress T lymphocyte function
3. reduce the number of circulating eosinophils
4. help maintain cell membrane activity
5. inhibit macrophage function
6. suppress antibody production
7. inhibit the release of endogenous pyrogen (IL-1)
8. depress prostaglandin and leukotriene synthesis
9. alter the complement and kinin cascades
10. interfere with leukocyte migration and adhesion
11. suppress lysosomal release from neutrophils by stabilizing lysosomal membranes
12. suppress phagocytosis
13. reduce fibroblast activity resulting in delayed healing and thinning of the skin
14. effect enzyme actions and other cellular functions

## **SIDE EFFECTS**

As with any other class of drugs, corticosteroids have clear value when used to treat a disorder for which they have proven therapeutic benefit and when administered at the appropriate dose, frequency, and duration of administration. Their recognized anti-inflammatory and immunosuppressive effects make them a valuable addition to veterinary medicine. There is no question that side effects do occur with GC therapy. However, excessive concern for these may prevent the appropriate use of this class of drugs when they are indeed indicated. Yet CS tend to be shunned by some practitioners who worry about iatrogenic suppression of the hypothalamic-pituitary-adrenal (HPA) axis, immune suppression and other side effects.

The benefits of any therapy must always be weighed against the possible and / or probable side effects. It is well-recognized that the excessive use of GC can be associated with many adverse effects. The anti-inflammatory and immunosuppressive actions of GC, though desired for their therapeutic effects, may facilitate the establishment or spread of other infectious or parasitic diseases. As a result, dogs treated with GC have a tendency to develop secondary bacterial infections of the skin, urinary tract or respiratory tract. Urinary tract infections have been documented in 18 to 39% of dogs who are treated with 0.28 to 0.8 mg/kg of GC for more than 6 months.

The most serious side effects of CS are related to prolonged use of large doses which may suppress the HPA axis. The effects of chronic elevations in glucocorticoid levels are readily seen with naturally occurring hyperadrenocorticism (Cushing's disease). Unfortunately those same problems can be created by overuse of GC by the veterinarian and / or client, even when

administered on an alternate-day basis. These high levels of exogenous steroids can result in hyperglycemia, fat redistribution, decreased skin elasticity, atrophy of the skin, poor wound healing, a pendulous abdomen secondary to a redistribution of body fat, poor quality coarse hair, alopecia (e.g. hair loss from breakage and failure to regrow), comedones (e.g. follicular plugs or blackheads), a variety of bacterial infections (especially of the bladder and skin) and even calcinosis cutis (e.g. mineral deposits in the skin). Localized dermal and adnexal atrophy following subcutaneous and occasional intramuscular repositol GC have also been reported. If the glucocorticoid used also has mineralocorticoid effects then polyuria (e.g. production of an increased amount of urine) and polydipsia (e.g. drinking an excessive amount) may also be present.

Iatrogenic secondary adrenocortical insufficiency is a side effect that can be seen after withdrawal of the glucocorticoid therapy. When an animal is treated with a glucocorticoid, the adrenal gland, in natural response to the effect of the exogenous GC on the HPA, will stop producing steroid hormones for some period of time. The duration of this suppressive effect is known to be dependent on the type of steroid and duration of treatment. However, the precise degree and length of suppression in any individual dog can not be predicted. Generally speaking the longer the therapy and the higher the dosage, the longer the time before natural production of steroid hormones resumes by the adrenal gland. This resultant lack of endogenous (physiological) GC is the cause of weakness and possible circulatory collapse that can occur with cessation of exogenous glucocorticoid therapy.

One intravenous injection of dexamethasone at 0.1 mg/kg, which equals approximately 3 mg of hydrocortisone (cortisol) or 3X the highest daily natural production can suppress the HPA for 32 hours in a healthy dog.

## **USE OF CORTICOSTEROIDS IN VETERINARY DERMATOLOGY**

Cortisone and ACTH were first used to treat a variety of inflammatory dermatoses in humans in the 1950s. The major indications for their use in veterinary dermatology include treatment of allergic or pruritic dermatoses, autoimmune dermatoses and feline eosinophilic granulomas.

The use of glucocorticoids is an art that requires the clinician to skillfully integrate the many details about the patient, the owner, and the disease so that an appropriate type and dose of glucocorticoid can be used. Changes and adjustment in dosages and even the type of corticosteroid used must be made depending on the response of the disease and the side effects that develop. Physiologic doses of GC are those that approximate the daily cortisol production by normal individuals. In dogs, daily cortisol production has been reported to be 0.2 to 1 mg/kg/day. A pharmacologic dose of GC exceeds physiologic requirements. There is no optimal dosage established in the veterinary literature and each case should be treated individually. There are guidelines, however, which serve as a good starting point. Using oral prednisone or prednisolone (or methylprednisolone) in dogs as the drug of choice the recommendations are:

Antipruritic doses: 0.5 mg/kg/day for 7 to 10 days then decreased to lowest effective dose

Anti-inflammatory doses: 1.0 - 1.5 mg/kg/day for 7 to 10 days then decreased to the lowest effective dose

Immunosuppressive doses: 2.0 – 6.0 mg/kg/day for induction then decreased

as possible to maintain control of the disease  
Compared with dogs, cats seem to require about twice the dose of oral GC to achieve the same effects.

## **LONG TERM USAGE OF GLUCOCORTICOIDS**

This section now presents **Dr. Sousa's personal beliefs** regarding a safe dose of GC used long term as there is no true evidence-based formula. Every animal and every disease condition differs.

The following is her formula for dogs. Starting with the fact that dogs manufacture 0.2 to 1 mg/kg/day of cortisol and need this to survive, and using a 40 kg (88#) dog as an example:

40 kg X 0.4 mg X 365 days = 5840 mg of cortisol produced / year (I chose 0.4 mg as it's on the lower side of the mid range for production)

Since prednisone is considered to be about 4 times as potent as hydrocortisone (cortisol), dividing 5840 by 4 is 1460mg of prednisone. Thus, this 40kg dog would "see" in a normal physiologic state approximately 1460 mg of prednisone (or prednisolone) / year

From these calculations I have I have developed what I called my "safe annual steroid dose" formula:

$$\text{BW (kg) X 30} = \text{mg prednisone / year}$$

or

$$\text{BW (lb) X 15} = \text{mg prednisone / year}$$

This number (30) is based on a combination of several publications reporting the side effects of GC as related to dose and on over 10 years of using this in my own practice and seeing the safe use.

Again considering the 40kg dog I would calculate

40 X 30 = 1200mg of prednisone to be the "safe annual steroid dose". This value is less than the range of what is considered physiologic for that dog.

If this dog required more than what I believed to be the "safe annual dose" of prednisone or prednisolone to control its dermatologic disease (i.e. pruritus from allergies or atopic dermatitis) then I would either add a second medication in an effort to decrease the amount of GC needed or change medications (e.g. to cyclosporine.) Steroid treatment protocols generally begin with higher doses and then are tapered but again looking at these calculations in this way can be helpful guides.

If the dog needed more than the "safe annual steroid dose" and the owner declined further diagnostic work up or other therapy then I recommend monitoring for weight gain and urinary tract infection as these are the most prevalent side effects with ongoing GC therapy. First, I would discuss in detail my recommendations for feeding and have the dog weighed to make sure that it wasn't gaining weight. I would also perform a cystocentesis for urinalysis and urine culture and sensitivity test. It is critical that the urine be cultured as in dogs receiving

steroid therapy due to the dilution of the urine and the anti-inflammatory effects of the steroids, actual bacteriuria or the suggestive urinalysis findings of infection may not be detected. Although it would be expected that the urine specific gravity to be low (about 1.012) if there was protein or glucose in the dilute urine a serum chemistry to assess for any early renal disease or diabetes would be indicated. I would expect the alkaline phosphatase and alanine aminotransferase (ALT) to be elevated as well as for the CBC to reveal a stress leukogram.

In **summary**, the rational use of glucocorticoids in veterinary dermatology requires the clinician to be familiar with the pharmacological and physiological effects and side effects of steroids as a class and the individual formulations used in their practice. Glucocorticoid use should be limited and kept to a minimum by using adjunctive therapies (such as antibiotics, antihistamines, topical therapies, etc.) whenever possible. A diagnosis should be made prior to determining the therapeutic regimen. And long-term therapy should be monitored with frequent examinations and laboratory testing as indicated.

Table 1  
Comparison of Water-Soluble Glucocorticoids Used in Dogs and Cats

Generic Drug	Relative Mineralocorticoid Potency	Relative Glucocorticoid Potency (Anti-inflammatory Potency)	Equivalent Dose (mg)	Plasma Half-life (Hours)	Biologic Half-life in Humans (Hours)
Hydrocortisone	1	1	20	1	8-12
Prednisone / prednisolone	0.8	4	5	(?) 1	12-36
Methylprednisolone	0.5	5	4	1.5	12-36
Triamcinolone <sup>a</sup>	0	3 - 5	4	(?) 4	24-48
Flumethasone		15	1.5		
Dexamethasone	0	29	0.75	2	35-54
Betamethasone	0	30	0.6	(?) 5	>48

<sup>a</sup> Triamcinolone acetonide has a greater potency (approaching that of dexamethasone)

“**A Dunny’s Guide to Dermatitis**” has been derived from Dunbar Gram’s many years of practice and thought, but only a relatively few days of hard science and math. When faced with a pruritic patient, a few important questions arise. If I am running behind in my busy practice, the staff is trained, to give me a “one liner” history (duration, historical seasonality and steroid responsiveness). Naturally the physical exam, a more in-depth history and ancillary tests are also important, but the “one liner” is like a “pick up” line when I walk in the exam room.

If a pruritic and inflamed patient is not steroid responsive, I will evaluate the dose of steroids that had been used and compare to anti-inflammatory doses discussed in Dr. Sousa’s notes. Like Dr. Sousa, I find many newer veterinarians do not seem to have the training or the desire to use steroids appropriately. If the dose has simply not been high enough, I will consider a higher dose for short term therapy for the benefit of the patient. The long term management is a different lecture. If the dose has been adequate, but the pruritus has not subsided, I worry that



the patient may have a pruritic dermatitis that is not steroid responsive or that perhaps the symptoms have become refractory to the once beneficial particular steroid.

In the latter situation as well as “routine allergic patients”, I often use Dexamethasone Sodium Phosphate (DexSP): 4mg/mL injection for horses which is equivalent to 3mg Dexamethasone/ml. Based on the above chart, 0.75 mg of Dexamethasone (Dex) is equivalent to 5mg of pred. My standard **DexSP dose is 1 mg/10 pounds SQ or IV** or 0.75mg Dex/10 pounds, (0.75mg Dex/4.54 kg X 5mg pred/0.75mg dex = 1.1mg Pred/kg). As stated earlier, the anti-inflammatory dose of pred is 1.0-1.5mg/kg/day, for 7-10 days. The anti-inflammatory dose is approximately 2-3 times the antipruritic dose. However, most of my pruritic patients are also inflamed. In these cases, I **simply** give one injection of Dex SQ to “break the inflammatory cycle” and often do not need any more steroids while utilizing other medications. If more steroids are needed, I will then start oral prednisone 1-2 days later, at a standard antipruritic dose of 0.5mg/kg every 2-3 days. If the inflammation is severe, I will use a higher dose. For **convenience** sake, I often simply have the clients start the pred pills the day after the injection. For practical reasons, I typically administer the dex subcutaneously, but will consider intravenously (IV) if necessary. I use the IV route if the client and patient need the quickest response possible (a dinner party that evening or their therapist has cancelled) or if the client is uncertain regarding the response to steroids in the past. In the latter case, we call the client 24 hours later to document the response. Clinically, this technique works well in patients who have been well controlled with immunotherapy and/or other forms of medical therapy, but have suffered an exacerbation.

I emphasize the words **simply** and **convenience** because the patient’s primary care giver (the client) is often burdened with many other tasks. I feel this approach is both medically appropriate and helps prevent care giver burnout as well as many financial concerns. I use the term emotionally and financially exhausted when I write my referral letters to describe clients that are overburdened with caring for an allergic pet. The doses were arrived at by comparing it to what would be necessary if prednisone was utilized, but trying to avoid the mineralocorticoid side effects. I justify its use by comparing the dose used in a high dose dexamethasone suppression test. My naïve thought is that if I had been taught to use the same drug at a similar dose for a diagnostic test in a diabetic ketoacidotic cushings suspect (high dose dexamethasone suppression test), without worrying about the side effects, then why not consider it for therapeutic reasons.

For example, a 40 pound (18kg) dog receiving a high dose dex test, based on the 0.1mg/kg or 1mg/kg IV or IM, would receive 1.8-18mg dexamethasone or 0.6-6.0ml of DexSP. The same size dog that was itching would receive 1.0ml of DexSP. One of my associates actually commonly utilizes ½ of my dose and has good results. A “Dunny’s Guide” to mathematical estimation implies that this dose of dexamethasone should not be repeated more than every 22 days (based on dogs normally manufacturing cortisol at the low end of 0.2mg/kg/day. In my practice, before I had “done the math” I typically had been telling my clients to do this as seldom as possible, but if one injection a month works for them, then it is likely to be safe. Using Dr. Sousa calculations for a safe dose of glucocorticoids used long term (based on cortisol production of 0.4mg/kg/day), it would be every 33 days. I do realize that the patient is also producing cortisol. Adding the different numbers together is complex, considering the patient’s own production varies from day to day. However, if we utilize conservative

endogenous cortisol production numbers, the figures proposed by Dr. Sousa seem quite reasonable. If we use the “high end of endogenous cortisol production then this dex dose is equivalent to 4-5 days of endogenous cortisol.

Dr. Sousa and I studied dermatology at two totally different universities, practiced on two different coasts for many years and seem to have reached a similar conclusion. I call it “convergent evolution.” Corticosteroids can be used safely for the benefit of our patients and clients. You intuitively know this. As with any drug, the potential for side effects exist and should be considered when comparing therapeutic options. Oral and short acting injectable corticosteroids quickly exert their beneficial effects thus enable rapid dose alteration or re-initiation. They should not be overlooked as a therapeutic option for both acute and chronic therapy. In my opinion, they are the treatment of choice to gain control of an itchy and inflamed allergic patient.

### **References**

Sousa, C. Kirk’s Current Veterinary Therapy XIV, Elsevier: 2009: PAGE 400

## **Approach to symmetric alopecia**

Dr. Dunbar Gram

### **LEARNING OBJECTIVES**

1. For both hypothyroidism and hyperadrenocorticism in the dog please be able to describe the:
  - A. Cutaneous signs
  - B. Clinical signs; common, and uncommon
  - C. Laboratory abnormalities
  - D. Most commonly used diagnostic tests (pros and cons)
2. Be able to list non-thyroidal factors (drugs or diseases) that may affect tests used for hypothyroidism.
3. Know the treatment of choice for canine hypothyroidism, frequency of administration and why, as well as appropriate patient monitoring.
4. You should also be able to list the dermatologic manifestations associated with hyperadrenocorticism disease in the cat.
5. You should be able to list the 2 diseases that must be ruled out in a suspected case of growth hormone/adrenal sex hormone disease.

## I. CANINE HYPOTHYROIDISM

### A. Thyroid physiology

#### 1. Control of production

- a. Pituitary TSH activates thyroid gland follicle cells via cyclic AMP production. Plasma  $T_4$  levels rise for 8-12 hours after TSH administration (Max @ 4-6 hrs).
  - b. TSH release is stimulated via TRH (thyrotropin-releasing hormone) from the hypothalamus.
  - c. Negative feedback control by effect of  $T_3$  on TSH and TRH secretion.
  - d. Glucocorticoids (either endogenous or exogenous) suppress TSH release as well.
2. Although the most common clinical laboratory test for thyroid function in dogs is basal  $T_4$ , the most important metabolically active form is  $T_3$ .
- a.  $T_4:T_3$  excretion ratio is 4:1.  $T_4$  is preferentially secreted from the thyroid gland along with smaller amounts of  $T_3$ .  $T_4$  is converted to  $T_3$  in the peripheral tissues.  $T_3$  is the more metabolically active hormone but is primarily intracellular.
  - b.  $T_4:T_3$  plasma ratio is 25:1 because  $T_3$  enters cells more readily
  - c. Additional  $T_3$  is produced by deiodination of  $T_4$  inside the target cells.
  - d.  $T_3$  is more metabolically active ( $T_4$  is sometimes referred to as a prohormone, although it is also active).
3.  $T_4$  is bound to thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA), albumin and other globulins in the plasma.
4. There is a high turnover rate in the dog (115% daily). Most excretion is biliary. This is why dogs receiving thyroid replacement therapy require a much higher dose/kg compared to humans.
5. There are specific  $T_3$  binding sites on cell nuclei. The hormones have extremely diverse effects, probably by affecting DNA function.
6. Physiological effects of thyroid hormones:
- a. Promote growth and maturation

- b. Support the basal metabolic rate
- c. Regulate the production and turnover rate of many enzymes and other cellular products
- d. Support normal skin structure and function, synthesis of proteins, hematopoiesis, reproductive function, gluconeogenesis and normal lipid metabolism

## B. Etiologies of hypothyroidism

### 1. Primary hypothyroidism- most common

- a. Lymphocytic thyroiditis - immune-mediated destruction of the thyroid gland, can be familial.

Lymphocytes, plasma cells and macrophages infiltrate the thyroid gland leading to progressive destruction of follicles and secondary fibrosis. End stage mimics thyroid atrophy. Clinical signs develop when more than 75% of the gland is destroyed. Circulating antibodies to thyroglobulin and thyroid microsomal antigen can be detected before end stage thyroid disease.

- b. Idiopathic atrophy- Most commonly diagnosed. Thyroid parenchyma replaced by adipose tissue, cause unknown, probably this represents end stage lymphocytic thyroiditis.
- c. Neoplastic destruction- destruction of greater than 75% of normal thyroid tissue by an expanding tumor (rare).
- d. Iatrogenic (surgical)

### 2. Secondary hypothyroidism - rare

- a. Deficiency of TSH (thyroid stimulating hormone) from the pituitary gland leads to thyroid gland follicular atrophy. May be due to either:
  - i. Pituitary malformations (congenital)
  - ii. Pituitary destruction (neoplasia)

### 3. Tertiary hypothyroidism - rare

- a. Decreased production of TRH from the hypothalamus. This leads to decreased TSH production and subsequently to thyroid gland atrophy.

4. Iodine deficiency- rare in domestic animals. Not when fed commercial foods.
5. Miscellaneous
  - a. Conversion defects- not documented in veterinary medicine.  $T_4$  is normally converted to  $T_3$  in the peripheral tissues but not in affected patients. "Refer to Thyroid Physiology."
  - b. "Sick euthyroid"- transient decrease in serum  $T_3$  and  $T_4$  concentrations in sick animals or those receiving specific medications. There are several mechanisms of drug induced decreases in  $T_3$  and  $T_4$ :
    - i. Decreased TSH secretion
    - ii. Decreased  $T_4/T_3$  synthesis or secretion from thyroid gland.
    - iii. Inhibition of the enzyme which converts  $T_4$  to  $T_3$  leads to increased  $rT_3$  which is the inactive metabolite ("decreased peripheral conversion").
    - iv. Decreased Thyroxine Binding Globulin (TBG) mediated serum transport.
    - v. Increased hepatic metabolism +/- biliary clearance.

Table 1. Mechanisms of drug induced depressions in serum T4

	↓ TSH secretion	↓ T4/T3 synthesis	↓ peripheral conversion	↓ TGB binding	↑ metabolism/clearance
Glucocorticoids	X		X	X	
Sulfonamides (> 6 weeks of Rx)		X (inhibits Thyroid peroxidase)			
Phenobarbital (> 6 wks of Rx)					X
Carprofen				X	

Table 2. Effects of drugs on blood thyroid levels: ↓, ↑, = indicate that the measurements can be respectively decreased, increased or unchanged.

	Total T4	Free T4	TSH
Glucocorticoids	↓	↓	= or ↓
Sulfonamides (30 mg/kg q 12 hrs)	↓	↓	↑
Phenobarbital	= or ↓	= or ↓	= or ↑
Carprofen	↓	↓	↓

### C. Clinical Signs of hypothyroidism

1. Many body systems can be affected. Signs are variable (see table 3).  
In some patients the onset of hypothyroidism is insidious and may mimic the aging process.
2. Dermatologic- alterations in the skin and hair coat are the most commonly observed abnormalities.
  - a. Alopecia (truncal, bilaterally symmetric), telogen hairs
  - b. Coat- dryness, scaling, coarseness, dullness, puppy coat" - loss of guard hairs
  - c. "rat tail"
  - d. Slow hair regrowth - cessation of anagen
  - e. Myxedema – due to fibroblast proliferation
  - f. Secondary pyodermas and chronic
  - g. Seborrhea - sicca usually or oleosa
  - h. Hypothyroidism is not typically a pruritic disease unless secondary Infections or concurrent infestations are present.  
Remember... Fleas are EVERYWHERE.

### D. Signalment - young and old dogs

1. Breed predisposition:

**Golden Retriever**  
**Doberman Pinscher**  
Dachshund  
Irish Setter  
Miniature Schnauzer  
Great Dane  
Poodle  
Boxer

Shetland Sheepdog  
Pomeranian  
Cocker Spaniel  
Airedale  
Malamute  
Chow Chow  
Irish Wolfhound  
Bulldog  
Afghan Hound  
Newfoundland  
Beagle  
Basenji



**TABLE 3- SYSTEMIC SIGNS ASSOCIATED WITH HYPOTHYROIDISM**

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**ALTERATIONS IN CELLULAR METABOLISM**

**Lethargy**

Mental dullness  
Exercise intolerance

**Weight gain (or loss)**

Aggression  
Cold intolerance

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**REPRODUCTIVE**

**Female**

Infertility  
Prolonged interestrus interval  
Failure to cycle  
Weak, silent cycles  
Prolonged estrous bleeding  
Weak, dying, stillborn pups  
Inappropriate gynecomastia  
Inappropriate galactorrhea

**Male**

Lack of libido  
Testicular atrophy  
Hypo-/azoospermia  
Infertility

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**NEUROMUSCULAR**

**Weakness**

Laryngeal paralysis  
Megaesophagus  
Para/tetraparesis  
Pseudomyotonia  
Stiffness  
Knuckling, dragging feet  
Muscle wasting  
Cranial nerve neuropathy (7&8 peripheral)

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**DERMATOLOGIC**

Coarse, dull hair coat  
**Bilaterally symmetrical alopecia**  
"Rat tail"  
Puppy coat  
Hyperpigmentation  
**Seborrhea oleosa, sicca**  
Myxedema (puffy skin)  
**Pyoderma**

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**CARDIAC**

**Bradycardia**

Cardiac arrhythmias  
Thrombosis  
von Willebrand exacerbation  
Atherosclerosis

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**OCULAR**

Keratoconjunctivitis sicca

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**GASTROINTESTINAL**

Constipation  
Diarrhea  
Vomiting

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Modified from: Canine and Feline Endocrinology and Reproduction. Feldman EC, Nelson RW. WB Saunders Co., 1987. p.60.

## E. Diagnosis

1. Minimum data base (CBC, chemistry panel, urinalysis)
  - a. Elevated cholesterol (> 500 mg/dl)
  - b. Normocytic, normochromic, mild, non-regenerative anemia
2. Must be sure to rule out other diseases/ drugs which falsely lower your blood thyroid level such as hyperadrenocorticism, medications that cause falsely low blood thyroid levels and concurrent illness.
3. Measurement of basal hormone levels (TT4, FT4 and TSH).
  - a. Total T<sub>4</sub>- (TT4) is the sum of the protein bound fraction and free (unbound) fraction in the serum. Greater than 99% T<sub>4</sub> is bound to plasma proteins, while slightly less T<sub>3</sub> is bound. T<sub>3</sub> adds little information over T<sub>4</sub> alone. Normal serum concentrations vary with each laboratory, and should be established for each lab. If a pet has a low TT4 **AND** symptoms compatible with hypothyroidism, some clinicians consider a trial course of therapy; Treatment for 6 weeks and re-evaluate 6 hr post-pill T<sub>4</sub> blood levels and the **clinical response**. Keep in mind that 60% of normal dogs may have low T<sub>4</sub> during the day due to natural diurnal fluctuations in blood levels.
  - b. Total T<sub>4</sub> is a more accurate indicator of thyroid function than T<sub>3</sub>. T<sub>3</sub> is commonly low in non-thyroid illnesses "euthyroid sick."
  - c. There are a number of factors that can affect basal hormone concentrations, (usually lowering serum concentrations), giving a clinician a false impression of hypothyroidism (see Table 4). For example, an animal that is receiving or has recently received glucocorticoids (or a patient with hyperadrenocorticism) may have markedly decreased measured basal hormone concentrations, and this should be taken into account when they are evaluated.

**TABLE 4**

<b>Condition</b>	<b>Effect on Thyroid Hormone Values</b>
<b>Age</b>	
Neonates	Serum T <sub>4</sub> is increased 2-5 times normal adult concentrations.
Adult dogs	Serum T <sub>4</sub> concentrations decrease significantly with age.
<b>Anti-thyroid hormone antibodies</b>	Antibodies to T <sub>3</sub> or T <sub>4</sub> interfere with assays for measuring thyroid hormone concentrations producing very elevated apparent T <sub>3</sub> or T <sub>4</sub> values respectively, when using solid phase RIA and some double antibody RIAs. However, other double antibody procedures and charcoal-precipitated RIAs may produce falsely low results when anti-thyroid hormone antibodies are present.
<b>Breed</b>	T <sub>3</sub> and T <sub>4</sub> tend to be higher in small breed dogs and lower in large breed dogs. Serum T <sub>4</sub> concentrations are higher and serum T <sub>3</sub> concentrations are lower in Grey-hounds than in mix-breed dogs.
<b>Drugs</b>	Plasma T <sub>4</sub> can be depressed by the following <u>drugs</u> : glucocorticoids, diphenylhydantoin, phenobarbital, phenylbutazone, o,p'DDD, trimethoprim-sulfonamides, androgens, diazepam, furosemide, salicylates, imidazoles, phenothiazines, progesterone (diestrus)
Diseases "Euthyroid sick syndrome"	Serum T <sub>3</sub> and T <sub>4</sub> are decreased, rT <sub>3</sub> is increased, i.e. deep pyoderma, fasting, liver and renal disease, Addison's, Cushings, diabetes mellitus
Hypoproteinemia	May see decreased basal T <sub>3</sub> and T <sub>4</sub> concentrations due to decreased plasma protein binding.
Obesity	Serum T <sub>3</sub> and T <sub>4</sub> are increased in obese dogs.

From Current Diagnostic techniques for evaluating thyroid function in the dog. Beale, KM, Vet Clinics N Am, November 1990.

- d. In some cases of lymphocytic thyroiditis autoantibodies may form against T<sub>3</sub> and T<sub>4</sub>. These antibodies can interfere with this assay, and depending upon the methodology used, may result in either a measured serum concentration of zero, or markedly elevated values.
- e. Free T<sub>4</sub>- (FT<sub>4</sub>) is the measurement of free or unbound thyroid hormone in the circulation (this is the form that is available for tissue uptake.) Utilizing basal T<sub>4</sub> and free T<sub>4</sub> decreases the likelihood of having a false positive diagnosis of hypothyroidism by 15%. The normal range of fT<sub>4</sub> varies with the lab, but should be approximately 0.28-1.70 ng/dl. It is important to request that the fT<sub>4</sub> is measured using equilibrium dialysis method.
- f. TSH blood levels – An assay is available for canine TSH. We recommend assessing T<sub>4</sub> and cTSH (canine TSH) together. TSH should be elevated in patients with primary hypothyroidism and decreased in animals with secondary or tertiary hypothyroidism. However several studies have demonstrated that dogs with proven hypothyroidism may have a normal TSH (13-38% of cases) thus normal results do not always rule out the possibility of hypothyroidism.
- g Biopsy for histopathology
  1. Thyroid biopsy: excellent, however, it is an invasive procedure.
  2. Skin biopsy may be helpful; not diagnostic. Common findings are hyperkeratosis and follicular hyperkeratosis and increase in the percentage of telogen phase hair follicles
- h. Stimulation tests
  - 1 TSH stimulation test; Bovine TSH and human-use drug are no longer available.
  2. TRH stimulation test- TRH is available for canine use. The protocol is similar to that for TSH stimulation; however, 250-750 mcg TRH is administered/dog. T<sub>4</sub> should increase by 1.0 mcg/dl. (Some normal dogs,

however will not increase significantly). Differentiates secondary hypothyroidism from tertiary hypothyroidism.

- i Response to therapy - examine long-term effects (resolution of recurrent pyoderma), not immediate (hair regrowth). Not recommended as a diagnostic test.

#### F. Treatment:

1. Synthetic T<sub>4</sub> (sodium levothyroxine, Soloxine) is the initial treatment of choice. 0.01 mg/lb twice daily (BID), best to give BID in most dogs, and based on estimated normal weight. Use a lower dose in old dogs and dogs with diabetes, Addison's disease or heart disease **0.005 mg/kg BID**.
2. Synthetic T<sub>3</sub> (sodium liothyronine) is almost never indicated. Other products which are rarely used include combination products and desiccated thyroid which is not always effective. Some dogs may not respond well to generic preparations.
4. Levothyroxine sodium is available for IV use. This is indicated for use in life threatening myxedema coma.
5. An alternative dosing regime is to correlate metabolic rate with body weight i.e. a small dog has a greater metabolic rate than a large dog. Based on body surface area the dosage of levothyroxine is **0.5 mg/m<sup>2</sup> BID**.

#### G. Therapeutic monitoring:

1. Follow-up levels should be assessed 6 weeks after initiating supplementation, yearly and after dosage change. Dosages should be adjusted accordingly. To evaluate the thyroid hormone blood level during supplementation, take blood prior to administration of thyroid supplementation medication and 6 hours after the pill is given.
2. If administering T<sub>4</sub>, The peak, "post pill "serum concentrations should be in the upper end of the normal range.
  - Thyroid Toxicity → polyuria, polydipsia, polyphagia, panting, fever, weight loss, nervousness

3. Clinical improvement for non-dermatologic symptoms (i.e. activity) may be noted as early as 1-2 weeks after initiating therapy, while dermatologic conditions may take up to 4-6 weeks to improve, other signs 2 months.

\*\* Many dogs are treated indefinitely based on clinical signs with or without a low T<sub>4</sub> test. Before you do this, consider the catabolic effects of T<sub>4</sub> and the cost and inconvenience of lifelong L-thyroxine supplementation.

#### H. Other species

1. Cat - very rare; confirm with TSH stimulation test (TSH assay not available for cats)
2. Foals - rare

## II. HYPERADRENOCORTICISM (CUSHING'S SYNDROME)

### A. Etiology:

1. Iatrogenic (excessive or prolonged glucocorticoid administration)
2. Endogenous
  - a. Functional adrenal adenoma or adenocarcinoma
  - b. Functional pituitary adenoma- excessive ACTH production

### B. Canine hyperadrenocorticism:

1. 95% of cases are associated with pituitary dysfunction
2. No sex predilection
3. Majority of dogs > 8 yrs
4. Breeds: Poodles, Boston Terriers, dachshunds
5. Dermatologic manifestations in the dog:
  - a. Bilateral symmetrical alopecia
  - b. \*Pyoderma, recurrent
  - c. Thin skin
  - d. Comedones
  - e. \*Calcinosis cutis - topical DMSO gel may help resolve lesions

- f. Hyperpigmentation
- g. Demodicosis (common in iatrogenic disease)
- h. Hypercortisolism is not typically a pruritic disease unless secondary Infections or concurrent infestations are present.  
Remember... Fleas are EVERYWHERE.

3. Systemic abnormalities and clinicopathologic changes have been discussed in detail in your endocrinology course.

#### 4. Diagnostic tests

##### A. Hematology

- Polycythemia (HCT: 45-55%)
- Stress leukogram: Lymphopenia, eosinopenia, neutrophilia
- Thrombocytosis

##### B. Biochemistry – elevated →

- Alkaline phosphatase
- Alanine transferase (ALT)
- Cholesterol
- Blood glucose (DM present in 5-10%)
- +/- low BUN

##### C. Urinalysis

- USG 1.015- 1.025
- Proteinuria

##### D. Blood pressure

- a. 50-80% are hypertensive

##### E. Abdominal radiographs

- a. 50% adrenal tumors mineralize (may correlate with malignancy)
- b. Hepatomegaly
- c. Osteopenia

F. Abdominal ultrasound

- a. Adrenomegaly- bilateral → PDH
- b. Adrenal nodules → ADH
- c. 50% of adrenal tumors → benign (the other 50% → malignant)

G. Screening tests:

- i. Urine cortisol: creatinine ratio. 99% sensitive, poor specificity
- ii. Abdominal radiographs- poor sensitivity/ specificity
- iii. Abdominal ultrasound- bilateral adrenomegaly seen in PDH, adrenal nodule (s) seen in ADH.

H. Diagnostic tests

- i. ACTH stimulation → diagnostic in 65-70% of PDH, 80% of ADH
- ii. Low dose dexamethasone suppression test → diagnostic in 95% of PDH, 100% of ADH
- iii. High dose dexamethasone suppression test → improves the specificity of LDDS
- iv. Endogenous ACTH: excellent screening method to detect PDH (normal to high in PDH, low in ADH).
- v. Resting cortisol: **USELESS**

5. Treatment

1. Ketoconazole

- a. Reversibly inhibits adrenal enzymes required for cortisol synthesis



- b. Side effects: vomiting, anorexia, increased liver enzymes, lightening of the haircoat
  - c. Dosage: 10-15 mg/kg BID
  - d. Reportedly effective in 50% of cases (clinical experience suggests much lower)
- 2. L-Deprenyl (Anipryl)
  - a. Monamine oxidase-B inhibitor causes dopamine depletion
  - b. Not effective for canine Cushing's syndrome
- 3. Trilostane (NOT FDA approved in USA)
  - a. Reversibly inhibits adrenal enzymes required for cortisol synthesis
  - b. Shown to be as effective and safe as Lysodren
- 4. Lysodren (o,p'-DDD)
  - a. Once, the most commonly used drug for treatment of canine Cushing's syndrome
  - b. Causes selective necrosis of zona fasciculata & reticularis)
  - c. Zona glomerulosa is usually spared-aldosterone is maintained
  - d. 35-40% of cases will experience adverse side effects: vomiting, anorexia, lethargy, diarrhea, neurological signs, Addison's disease (<5%)
  - e. Goals of Rx: eliminate clinical signs, avoid toxicity

\*\*Additional recommended reading for full details of Lysodren induction and maintenance therapy:

Canine and Feline Endocrinology and Reproduction. Feldman EC and Nelson RW. 1996 WB Saunders company. p. 219-237.

5. Adrenalectomy – for solitary adrenal tumors

C. Feline hyperadrenocorticism

1. 93% have concurrent diabetes mellitus
2. Dermatologic abnormalities:
  - a. Flank and/or ventral alopecia (87%)
  - b. Cutaneous atrophy (70%)
  - c. \*\*Extremely fragile skin that tears with routine handling (45%)
  - d. Bruising (40%)
  - e. Recurrent abscess (30%)
  - f. Comedones (14%)
  - g. Hyperpigmentation (12%)
  - h. Folded pinnae (10%)
3. Diagnosis
  - i. ACTH stimulation test - pre and 1 hour post IM synthetic ACTH (0.25 mg Cortrosyn). IN general, this test is less sensitive and less specific than it is in the dog
  - ii. High dose dexamethasone suppression test- has better specificity than low dose dexamethasone suppression test.
  - iii. Skin biopsy:
    - Dermal tissue minimal to absent (like Ehlers-Danlos syndrome)
    - Sparse collagen bundles with fine, fragmented fibers
    - Increase in the percentage of telogen hairs
    - Subcutaneous tissue minimal to absent

4. Treatment

A. The only consistently effective treatment includes bilateral adrenalectomy in cases of PDH and unilateral adrenalectomy in cases of ADH.

--- FYI ---

D. Equine Hyperadrenocorticism

1. Clinical signs - PU, PD, hirsutism (excessive hair growth), hyperglycemia
2. Diagnosis: overnight dexamethasone suppression test - 0.4 mg/kg dex IM at 5 PM; collect blood at 0, 15, 19 hours.

E. Hyperadrenocorticism in the Ferret

1. Most often due to adrenocortical neoplasia
2. Clinical signs - vulvar swelling in females, alopecia, pruritus
3. Diagnosis - clinical signs, abdominal ultrasound, exploratory laparotomy
  - a. +/- ACTH stimulation test 0.01 mg/kg ACTH (Cortrosyn) IV or IM pre and 1 hr post sample

## OTHER ENDOCRINE DISORDERS

III. **ADRENAL SEX HORMONE IMBALANCE** (AKA Growth Hormone-Responsive Dermatitis, Pseudo-Cushing's in Pomeranians, Alopecia X of plush coated breeds, unknown pathogenesis)

1. This is an acquired disease. Patients are health otherwise.
2. Breed predilections include "Plush Coated breeds": Pomeranians, miniature Poodles, Chow Chows, Keeshounds, Siberian Huskeys, Malamutes, Samoyeds and American Eskimos  
→ Average age of onset: 4 yrs, range 1-13 yrs.
3. The disease is characterized by a bilateral symmetrical alopecia of trunk, neck, pinnae, tail and caudo-medial thighs (sparing extremities), and hyperpigmentation. There are no systemic abnormalities.

4. This is considered to be due to abnormal adrenal steroidogenesis however these cases do not progress into Cushing's syndrome. This is not a life-threatening dermatosis or one with systemic manifestations.
5. Diagnosis:
  - a. Rule out hypothyroidism and Cushing's syndrome.
  - b. Biopsy: Classic endocrine changes and perhaps some traits typical of follicular dysplasia.
  - c. In the past, clinicians were taught to measure sex hormone levels (Veterinary Endocrinology Laboratory, Univ. of Tennessee) before and after an ACTH stimulation test. Most cases have elevated progesterone levels. The cost of the test and inconsistent findings have resulted in this test seldom being used.

\*Most common abnormality is elevated baseline and/or post ACTH stimulation progesterone
6. Treatment:
  - a. Usually **none**. Dog is not ill.
  - b. If intact, castrate.
  - c. If castrated, try methyltestosterone (0.5 mg/kg QOD- not to exceed 20 mg) due to its anti-progestininc properties. Side effects: behavioral changes, hepatitis.
  - d. Melatonin: Inexpensive, minimal side effects (except in diabetics). Helpful 40% of cases.
  - e. Lysodren (lower doses than the ones used for Cushing's syndrome) has been used successfully in a few cases. Careful! Use if other clinical signs are obvious and owner is well-informed of risks. Rationale of this therapy is to induce adrenal atrophy.
  - f. Trilostane is another drug used for this disease but it is not approved in the US
  - g. Don't make the therapy worse than the disease!

#### IV. ABNORMALITIES IN FEMALE AND MALE HORMONES LEADING TO DERMATOLOGIC DISEASE:

##### **SERTOLI CELL TUMOR AND HYPERESTROGENISM.**

1. Only 10% of the tumors are malignant.
2. Dermatologic signs include:
  - a. bilateral, symmetrical alopecia,
  - b. hyperpigmentation
  - c. seborrhea
  - d. ceruminous otitis externa
  - e. linear preputial dermatosis (cutaneous marker for testicular neoplasia)
  - f. gynecomastia, pendulous prepuce
3. Responds to castration, unless severe bone marrow suppression.
4. There are a number of other non-specific and poorly documented conditions that respond clinically to sex hormone therapy or neutering.
5. Results of serum hormone level testing are variable from lab to lab and, in general, have not been considered to be accurate by many investigators.

##### **Suggested reading:**

Muller & Kirk's text Small Animal Dermatology, chapter 10 (Endocrine and metabolic diseases).

**Regional dermatoses  
(perineal, pinnae, claws)**

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**Introduction**

- The involvement of pinnae and claws is fairly common in dogs and cats. Whereas diseases that affect the perineal regions are mostly reported in dogs.
- Local vs generalized vs systemic involvement as manifestation of benign or severe to life-threatening conditions.
- It is very important defining the skin lesions present on pinnae and perineal regions (e.g. pustules, crusts, and lichenification).
- A good history focusing on age of onset, signalment, presence of systemic signs, progression of the lesions (one foot vs multiple feet), and husbandry, is fundamental to reach an appropriate diagnosis.
- A good physical and a dermatological examination followed by skin cytology and skin scrapings are essential to confirm the diagnosis.
- Many diseases affect the pinnae and/or the claws or the perineum a short list would include, but not limited to:
  - Pinnae
    - Scabies
      - This condition will be discussed in another lecture
    - Otitis externa
      - This condition will be discussed in another lecture
    - Fungal dermatitis
      - Malassezia dermatitis
        - This condition will be discussed in another lecture
      - Dermatophytosis
        - This condition will be discussed in another lecture
    - Pemphigus foliaceus
      - This condition will be discussed in the following lecture
    - Vasculitis
  - Claws
    - Trauma
      - This condition will not be discussed
    - Bacterial onychitis
    - Fungal infection
      - Malassezia onychitis/paronychia

- Dermatophytosis
    - This condition will be discussed in another lecture
  - Lupoid onychitis (a.k.a. symmetric lupoid onychodystrophy)
  - Pemphigus foliaceus
    - This condition will be discussed in another lecture
  - Neoplasia
    - Metastatic pulmonary adenocarcinoma (C)
    - Squamous cell carcinoma (D)
    - Melanoma
- Perineum
  - Allergies
    - This condition will be discussed in another lecture
  - Intestinal parasites
    - This condition will not be discussed
  - Perianal fistulae
  - Anal sac impaction
  - Anal sac neoplasia
    - This condition will not be discussed

### **Vasculitis**

- Pathogenesis: the term refers to inflammation of the blood vessel walls resulting in reduced blood supply, nutrients and oxygen to the overlying tissues leading to necrotic changes. The etiopathogenesis is multifactorial and includes infectious agents, exogenous antigens, autoimmune and neoplastic diseases. Pinnal and caudal vasculitis can be secondary to trauma (e.g. shaking head).
- Predisposition: Greyhounds, Jack Russell Terriers, Saint Bernard, Collies, German Shepherd dogs and their crossbreeds.
- Clinical presentation: the clinical lesions depend on the size and depth of the affected vessels, the acuteness of the stimulus and the body region affected. The initial signs include an urticarial reaction followed by haemorrhage, ecchymoses and petechiae. These are followed by well demarcated crusts on the top of deep ulcerations and necrosis more evident on the extremities.
- Diagnosis: based on suggestive clinical signs, history and signalment. The diagnosis can be confirmed by biochemistry, haematology and urinalysis, diascopy, screen for infectious diseases (especially vector-borne diseases). A skin biopsy can also be very useful to confirm the diagnosis if characteristic microscopic abnormalities are present (e.g. alterations of the blood vessels wall and accumulation of neutrophils or lymphocytes).
- Treatment: the treatment depends on the inciting cause. In immune-mediated vasculitis the use of topical and systemic GC and/or CsA and/or tacrolimus is required. Other treatments include pentoxifylline as well as specific antibiotics.

### **Bacterial onychitis**

- Pathogenesis: associated with bacterial infection (e.g. *Staphylococcus spp.* or *Pseudomonas spp.*) secondary to trauma or underlying allergy or endocrinopathy.
- Predisposition: none.
- Clinical presentation: the most common clinical signs include pain/lameness and the presence of purulent discharge at the nail fold. Brown discoloration of the hair at the nail fold is also present due to constant licking of the paws.
- Diagnosis: based on suggestive clinical signs, history and signalment. The diagnosis can be confirmed by skin cytology and bacterial culture. Biochemistry, haematology and urinalysis can also be performed to rule out systemic diseases (e.g. endocrinopathies). Radiographs or CT scan can also be indicated to rule out bone involvement and neoplastic diseases.
- Treatment: topical and systemic antibiotics, empirically or based on culture, for at least 3-4 weeks (or until 1 week after clinical resolution).

### **Malassezia onychitis/paronychia**

- Pathogenesis: associated with yeast infection (*Malassezia spp.*) secondary to trauma or an underlying allergy.
- Predisposition: none.
- Clinical presentation: the most common clinical signs include constant licking and chewing of the paws. Most dogs present with a dry, brown to brownish red exudate around the claw fold and claws. Brown discoloration of the hair at the nail fold is also present due to constant licking of the paws.
- Diagnosis: based on suggestive clinical signs, history and signalment. The diagnosis can be confirmed by skin cytology and the evidence of *Malassezia spp.*
- Treatment: topical and systemic antifungals for at least 4-8 weeks. The treatment should be continued until new nail growth is evident.

### **Lupoid onychitis (a.k.a. symmetric lupoid onychodystrophy)**

- Pathogenesis: currently unknown.
- Predisposition: German shepherd dogs, Rottweilers, Labrador retrievers, Greyhounds and their crossbreeds.
- Clinical presentation: the most common clinical signs include pain/lameness associated with onychomadesis and subungual haemorrhage and onychodystrophy. When bacterial infections are present, purulent discharge and paronychia are also present.
- Diagnosis: based on suggestive clinical signs, history and signalment. The diagnosis can be confirmed by nail biopsy (most of the time removing the P3).
- Treatment: available treatments include essential fatty acids, tetracycline/doxycycline and niacinamide combination, systemic GC and vitamin E. The treatment should be continued until new nail growth is evident.

### **Neoplasia**

- Pathogenesis: digital metastases of a primary pulmonary adenocarcinoma (C) or unknown for squamous cell carcinoma and melanoma (D).



- Predisposition: none.
- Clinical presentation: slow onset of swelling, pain and lameness. Due to neoplastic growth, the claws get deformed. In dogs generally only one claw/paw is affected, whereas in the metastatic pulmonary adenocarcinoma multiple claws are affected at the initial presentation. In the adenocarcinoma, there is primary pulmonary mass and the digital lesions represent its metastases, while in dogs the primary tumour is at the nail fold/claw and it can metastasize to lymph node (squamous cell carcinoma) or internal organs (melanoma).
- Diagnosis: based on suggestive clinical signs, history and signalment. The diagnosis can be confirmed by skin cytology and nail biopsy (most of the time removing the P3). In cats it is important to perform a thoracic radiograph to evidentiate the primary tumour.
- Treatment: generally amputation and chemotherapy are recommended, but please refer to oncology notes for further treatment options.

### **Perianal fistulae**

- Pathogenesis: currently unknown, although an immune-mediated pathogenesis is strongly hypothesized.
- Predisposition: German shepherd dogs (although other breeds can be affected) and their crossbreeds.
- Clinical presentation: the lesions start as microabscesses that evolve in ulcers and fistulae affecting the skin, the anal sacs, the mucocutaneous junctions and rectal mucosa. Mucopurulent discharge can be drained by the fistulae. Pain during defecation is also present along with dyschezia, constipation and contact licking of the area. Chronic changes include rectal scars and fibrosis.
- Diagnosis: based on suggestive clinical signs, history and signalment.
- Treatment: available treatments include CsA and tacrolimus. Systemic GC have also been used with success. Systemic antimicrobials are necessary in case of infections. The treatment should be continued until complete healing of the lesions is evident. Surgical removal of the anal sacs is indicated only the condition is reoccurring and not manageable medically.

### **Anal sac impaction**

- Pathogenesis: currently unknown, although in some cases a neurological disorder has been hypothesized.
- Predisposition: obese and small breed dogs.
- Clinical presentation: localized pruritus (licking, rubbing and scooting). History of soft stools and diarrhoea is also common.
- Diagnosis: based on suggestive clinical signs, history and signalment.
- Treatment: manual expression of the anal sacs. Regular flushing of the anal sacs under sedation is also recommended. Surgical removal is only indicated if the condition is reoccurring and not manageable medically.

## **Regional dermatoses (nose and footpads)**

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### **Introduction**

- Fairly common affected areas in dermatological conditions in dogs and cats.
- Local vs generalized vs systemic involvement as manifestation of benign or severe to life-threatening conditions.
- It is very important defining the skin lesions present on nose and footpads (e.g. skin atrophy, pustules, crusts, hyperkeratosis, and depigmentation).
- A good history focusing on age of onset, signalment, systemic signs, progression of the lesions, and husbandry, is fundamental to reach an appropriate diagnosis.
- A good physical and a dermatological examination followed by skin cytology are essential to confirm the diagnosis.
- In many cases, the basic diagnostics (e.g. skin cytology) are not sufficient and a skin biopsy is required to confirm the diagnosis.
- Many diseases affect the nasal planum and/or the footpads a short list would include, but not limited to:
  - Mucocutaneous pyoderma
  - Nasal hyperkeratosis of the Labrador retriever
  - Feline herpesvirus
  - Plasma cell pododermatitis
  - Hookworm dermatitis
  - Cutaneous lupus erythematosus
    - This condition will be discussed in another lecture
  - Pemphigus foliaceus
    - This condition will be discussed in another lecture
  - Cutaneous lymphoma
    - This condition will be discussed in another lecture

### **Mucocutaneous pyoderma**

- Pathogenesis: currently unknown.
- Predisposition: German shepherd dogs and their crossbreeds.
- Clinical presentation: erythema, swelling, crusting and fissuring of the nasal planum, lips, nares, and eyelids. Involvement of vulva, prepuce, and anal area has also been reported.
- Diagnosis: based on suggestive clinical signs and confirmed by the cytological evidence of a suppurative inflammation with intracellular bacteria. The response to treatment confirms the diagnosis. The histopathological abnormalities (e.g. lichenoid band with

multiple plasma cells) may be useful to confirm the diagnosis and rule out other diseases. A bacterial culture is also indicated in cases of reoccurrence of the disease or lack of response to treatment or in case of rod-shaped bacteria are visualized on the cytology.

- **Treatment:** topical and systemic antibiotics for at least 3-4 weeks (or until 1 week after clinical resolution).

### **Nasal hyperkeratosis of the Labrador retriever**

- **Pathogenesis:** currently unknown, but suspected to be a genodermatosis with an autosomal recessive inheritance.
- **Predisposition:** Labrador retrievers and their crossbreeds.
- **Clinical presentation:** crusting and hyperkeratosis of the nasal planum in young dogs (<1 year of age). Depigmentation, ulceration/erosions, and fissuring have also been reported.
- **Diagnosis:** based on suggestive clinical signs and confirmed by histopathological abnormalities (e.g. parakeratotic hyperkeratosis and presence of serum lakes in the stratum corneum).
- **Treatment:** this condition is not curable, but manageable. The use of topical and systemic GC along with tetracycline (doxycycline)/niacinamide combination have been reported to be effective. The use of topical tacrolimus, vitamin E, phytosphingosine, and propylene glycol have been used with success.

### **Feline herpesvirus**

- **Pathogenesis:** feline herpesvirus 1. Many cats harbour this virus in the trigeminal ganglia without any clinical signs.
- **Predisposition:** none.
- **Clinical presentation:** erythema, swelling, ulceration/erosions, and crusting mainly localized on the nasal planum and face following the path of the trigeminal nerve. Respiratory signs, conjunctivitis, stomatitis, and corneal ulceration can also be seen.
- **Diagnosis:** based on suggestive clinical signs and confirmed by histopathological abnormalities (e.g. necrotizing eosinophilic dermatosis with flame figures). Basophilic intranuclear inclusion bodies can also be seen in the epidermis and hair follicles. The diagnosis can also be confirmed by PCR and immunohistochemistry.
- **Treatment:** this condition is not curable, but manageable. Several antiviral treatments have been used with some success. These include: L-lysine, interferon- $\alpha$ , imiquimod, and famciclovir.

### **Plasma cell pododermatitis**

- **Pathogenesis:** currently unknown.
- **Predisposition:** none.
- **Clinical presentation:** erythema, swelling (“puffy feet”), ulceration/erosions, and scaling/crusting of the footpads. Pain and lameness can also be seen.
- **Diagnosis:** based on suggestive clinical signs and confirmed by histopathological abnormalities (e.g. large number of plasma cells and Russell bodies in Mott cells).

- Treatment: many treatments options are available; however doxycycline seems to be the best option. Systemic or topical GC and topical tacrolimus have also been reported.

### **Hookworm dermatitis**

- Pathogenesis: hypersensitivity reaction to percutaneous penetration of hookworms (*Ancylostoma spp.* or *Uncinaria spp.*) into the footpads.
- Predisposition: none.
- Clinical presentation: hyperkeratosis and erythema of the footpads is common. Pruritus and pain has also been described. Other areas of the body (sternum, groin, and interdigital spaces) in contact with infected soil can be affected as well.
- Diagnosis: based on suggestive clinical signs, positive faecal floatation and confirmed by histopathological abnormalities (e.g. eosinophilic, neutrophilic, perivascular dermatitis).
- Treatment: appropriate anti-helminthic treatments. Environmental decontamination is essential.

## Approach to otitis

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### Introduction

- Otitis is one of the most common reason for which a pet goes to a veterinary clinic.
- Otitis is extremely common in dogs and less in cats
- Based on the anatomy of the ear there are three different types of otitis:
  - Otitis externa
    - Inflammatory condition affecting the external auditory canal from the pinna to the tympanic membrane
  - Otitis media
    - Inflammatory condition involving the middle ear
  - Otitis interna
    - Inflammatory condition affecting the inner ear (refer to neurology notes)
- The most common among these is the otitis externa, which can be divided in acute (<7 days), subacute (7-30 days), and chronic (>30 days). This latter is the most common type seen in the dermatology service. This type of otitis will be discussed in this lecture.

### Pathogenesis

- Predisposing factors: by themselves are not able to cause otitis, but they are able to modify the microclimate of the ear canal increasing the likelihood of otitis.
  - Ear canal conformation (stenosis), swimming, excessive hair, masses, trauma, etc.
- Primary factors: direct responsible for the inflammation, thus direct cause of the otitis.
  - Foreign bodies, allergies, autoimmune diseases, endocrinopathies, parasitic diseases, etc.
- Secondary factors: infections secondary to the inflammatory process.
  - Bacterial and yeasts
- Perpetuating factors: modifications of the anatomic-physiological status of the ear leading to the chronicity of the inflammatory condition.
  - Otitis media, mineralization or hyperplasia of the ear canal, etc.

### Acute otitis externa

- Clinical approach: a **very good history** should be taken to better identify if the patient has pruritus or pain, if the problem is unilateral or bilateral, if the patient swims, the patient habits (e.g. running unleashed in the fields), previous medical and pharmacological history. A **complete physical and dermatological examination** should be performed to evidenciate systemic (or cutaneous) alterations. These should be followed by an **otoscopic examination** of *both* ears starting with the less painful/affected. During the otoscopic examination a particular attention should be paid to assess the presence of

foreign bodies or masses, presence of discharge/debris (colour and consistency), presence of stenosis (anatomical vs inflammatory), presence of ulcerations, and status of the tympanic membrane if possible.

- **Diagnosics:** **direct observation of the parasites** done during the otoscopic examination of by collection of a small amount of debris and observed under the microscope at low magnification (10x objective). Another important tool is the **cytology**. This is achieved using a cotton swab and collecting some debris from the vertical canal and smeared on a slide. \*\*\*Remember to heat fix the specimen before staining it\*\*\*. This technique is extremely useful to identify bacteria and/or yeast present in the ear canal and prescribe the best treatment option for that particular patient.
- **Treatment:** the treatment of an acute otitis externa aims to the resolution of the primary cause, treat any secondary infections and remove the inflammation/pain. Most of the time using a cleaning agent is enough to achieve relive of the inflammation. There are many **cleaning agents** available on the market. During an acute inflammation, due to a foreign body or a flare of the allergic condition, a cleaning with soothing agents with an antimicrobial properties. The use of anti-inflammatory compounds can also be indicated to quickly decrease the inflammation and the pain. In case of a secondary infection, a **topical antimicrobial** solution is indicated. Finally, in case of severe pruritus/inflammation/pain a short treatment with **systemic GC** is highly recommended to give a rapid relief to the patient.

### Chronic otitis externa

- **Clinical approach:** as in the acute otitis a **very good history** should be taken to better identify if the patient has pruritus or pain, if the problem is unilateral or bilateral (*to be confirmed by otoscopic examination*), previous medical and pharmacological history, history or presence of systemic diseases, history of otitis, seasonality of the otitis and/or skin lesions. A **complete physical and dermatological examination** should be performed to evidenciate systemic (or cutaneous) alterations. These should be followed by an **otoscopic examination** of *both* ears starting with the less painful/affected. In case of proliferating chronic otitis externa a complete otoscopic examination could be possible due to the pain, severe stenosis of the ear canal or presence of discharge filling the ear canal. As in the acute otitis, when the otoscopic examination is possible, a particular attention should be paid to assess the presence of masses, presence of discharge/debris (colour and consistency), presence of stenosis (anatomical vs inflammatory), presence of ulcerations, and status of the tympanic membrane if possible.
- **Diagnosics:** for chronic otitis, the **cytology** is one of the most important tools available to the clinician. This technique is extremely useful to identify bacteria and/or yeast present in the ear canal and prescribe the best treatment option for that particular patient. **Bacterial culture** is generally not useful in the treatment of the majority of the otitis externa cases, due to the fact that the treatment of choice in these cases is the use of topical medications. In fact, the culture and sensitivity is indicated in severe cases in which the use of systemic antibiotic, along to the topical therapy, is recommended (extremely severe cases of otitis externa or presence of otitis media). In fact, no correlation between the sensitivity panel and resolution of the ear infection has been

proven. More important is the use of **diagnostic imaging**. Imaging, radiographs, CT scan and MRI, can be used to identify mineralization of the ear canals and evaluate the middle ear (increase density of the bulla(ae), alteration of the walls of the bulla(ae)). The most sensitive and informative technique is the CT scan followed by the MRI. This latter the best tool to identify the presence of masses in the ear canal or in the bulla (ae).

- **Treatment:** the treatment of a chronic otitis externa aims to bring the ear microenvironment to a normal status. This is achieved through regular cleaning, the use of topical and/or systemic antimicrobials and GC, treatment of otitis media (systemic and topical antimicrobials). *\*\*\*Most of the times, due to severe inflammation/pain of the ear few days of systemic GC are necessary before using the topical solutions\*\*\**. The treatments should be aimed to address the secondary infections, but more importantly to address the underlying (primary) cause of the otitis. The antimicrobial treatments should be continued until cytological resolution of the infection is achieved. The anti-inflammatory medications should be continued until there is resolution of the clinical signs and restoration of the normal environmental of the ear canal and resolution of the perpetuating factors. To help in the resolve the perpetuating factors, a **deep ear flushing**, performed under general anaesthesia with an endotracheal tube, may be necessary. The deep ear flushing is important also in the collection of middle ear fluid for culture and sensitivity (through myringotomy), collecting samples for histopathology and mechanically remove ceruminoliths from the ear canal.

### **Otitis media**

- Often a consequence of a chronic otitis externa. Infection ascending through the Eustachian tubes and the haematogenous spread of the infection is also reported.
- The diagnosis is made by history, clinical signs (neurological and behavioural) and the appearance of the tympanic membrane. This is confirmed by diagnostic imaging. The otitis media could be due to infections or presence of masses.
- The treatment of choice for infectious otitis media is a deep ear flushing to collect the fluid present in the middle ear and submit for culture and sensitivity. This is followed by a treatment with systemic and topical antimicrobials for at least 8 weeks. In case of a mass in the middle ear, this can be removed through the external ear (polyp) or through a surgical procedure (VBO or TECA-BO).

## Antimicrobial therapy and resistant pyoderma

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### Introduction

- Antimicrobial resistance is increasing in both human and veterinary medicine.
- An appropriate and careful use of antimicrobials is mandatory.
- Before prescribing an antibiotic consider few things:
  - Spectrum of action
    - Broad vs narrow
    - Cocci vs rods
  - Bactericidal vs bacteriostatic
    - Bactericidal are to be preferred
  - Dose
  - Toxicity
    - Dose, species, breeds
  - Underlying diseases
    - Allergies, endocrinopathies, etc.
  - Superficial vs deep pyoderma
    - Length of treatment, intracellular vs extracellular, culture
  - Client compliance
    - Route of administration
    - How often needs to be administered
    - Cost
- The ideal antibiotic should have the following characteristics:
  - Bactericidal
  - Very low toxicity/side effects
  - Easy route (oral for dogs) of administration
  - Given every 24 hours
  - Not very expensive

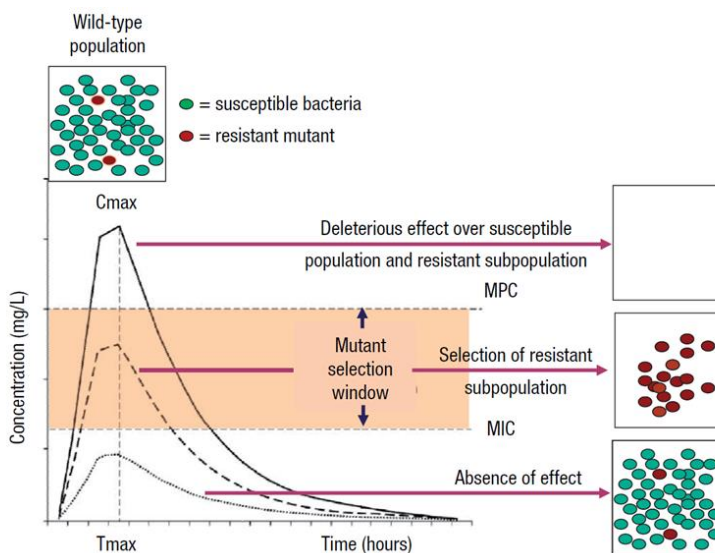
### Spectrum of action and dose

- **Always prefer the narrow spectrum antibiotics.** The use of broad spectrum antibiotic has been associated with an increase in drug resistant strains of bacteria. It is also very important use an appropriate antibiotic keeping in mind the bacterial target (cocci vs rods) and the tissue to treat (skin vs internal organs). The majority of the pyoderma are due to *Staphylococcus pseudintermedius* and for this reason, if cocci are seen on the cytology, antibiotics like macrolides and cephalosporins should be considered as first line antibiotics. In case rods are seen on the cytology, a bacterial culture is indicated to



better identify the microorganism (*Pseudomonas spp.*, *Escherichia coli*, *Proteus spp.*, etc) and use the right antibiotic based on the sensitivity panel.

- The **dose** of an antibiotic is also extremely important. Please keep in mind that in dermatology generally it is used the high range of the approved dose for that specific antibiotic. This is due to many factors including tissue distribution, blood supply, and lipophilia. It is even more important using a very high dose in concentration depend antibiotics (e.g. fluoroquinolones) to reduce the presence of resistant mutants. **Resistant mutants** are a part of the normal microflora that emerges at a constant rate depending on the bacteria and the antibiotic. It is known that when administered, an antibiotic is able to kill all the susceptible microorganisms; however, the resistant mutants may persist and become the dominant population overtime. The continuous use of antimicrobials accelerates this selection process. This is due to a stimulation of the **acquired resistance**. Acquired resistance is due to acquisition of mutations or resistant gene expression by horizontal genetic transfer. The *acquired resistance by mutation* naturally occurs in a bacteria population at a rate of  $<10^{-9}$ . An example of resistance by mutation is quinolone resistance due to mutations in chromosomal *gyrA* and/or *parC* genes. The *acquired resistance by horizontal gene transfer* is due to an efficient transfer of genes (mobilization elements – plasmids and transposons/ insertion sequences) among bacterial populations. In this environment, antibiotics can push the bacteria evolution and increase the selection for resistant mutants. In addition, mutations or resistant genes can accumulate in specific lineages or clones allowing them to survive to various antimicrobials (*selection and co-selection process*). For these reasons it is very important to use an adequate dosage and strive to reach the highest dose possible and even go above the MIC (minimum inhibitory concentration) and the MSW (mutant selection window) achieving the MPC (mutant prevention concentration). *The risk of selection for resistant mutants is virtually impossible above the MPC.*



Cantóna R, Horcajadad JP, Oliverb A, et al. Inappropriate use of antibiotics in hospitals: The complex relationship between antibiotic use and antimicrobial resistance. *Enferm Infecc Microbiol Clin.* 2013;**31(Supl 4)**:3-11.

### **Methicillin resistant Staphylococci (MRS)**

- Methicillin resistant Staphylococci have been identified since the discovery of the penicillin.
- They are NOT more virulent than the methicillin susceptible Staphylococci, but they require the use of appropriate antibiotics (no  $\beta$ -lactam antibiotics).
- Caused by the activation of the *mecA* gene with synthesis of penicillin binding protein (PBP)2a. When present the resistance is towards ALL the  $\beta$ -lactam antibiotics except tabtoxinines because their effect is not based on the interaction with the PBP protein.
- Many MRS strains can undergo to co-selection process and become multi drug resistant (MDR).
- MRS can be strongly correlated with previous use of antibiotics.

### **Length of treatment, intracellular vs extracellular, culture**

- In dermatology the use of antibiotic is more prolonged than in other specialties due to the chronicity of the infectious process.
- As rule of thumb a superficial pyoderma should be treated for not less than 3-4 weeks or at least 1 week after clinical resolution. On the other hand, a deep pyoderma should be treated for not less than 6-8 weeks or at least 2 weeks after clinical resolution.
- The use of GC is contraindicated during pyoderma, however if GC are necessary increase the time of exposure to antibiotics (an additional 7-10 days).
- The use of antibiotics (e.g. clindamycin, rifampin, macrolides, and fluoroquinolones) that accumulate intracellularly (highly lipophilic) is preferred (if possible) in cases of chronic or deep pyoderma when a fibrotic tissue/capsule is present.
- The bacterial culture is always indicated in cases of deep pyoderma (through skin biopsy if possible), of recurring superficial pyoderma, of not responding pyoderma, or in cases in which a previous exposure to antibiotics is present in the history.

### **Topical therapy**

- In cases of multidrug resistant (MDR) bacteria, it is very important to remember the use of topical antimicrobials. In fact, in dermatology it is relatively easy to treat an infection due to the fact that the skin is easy to access.
- There are many options to choose from including topical antibiotics or antiseptics.
- The former are generally not preferred due to their possibility to select for resistance, although not proven yet. These include 2% mupirocin ointment, 2% fusidic acid, and 3% tetracycline.
- Topical antiseptics are a better option since have not been associated with a high rate of resistance. This phenomenon is due to the fact that antiseptics act on physical structures of the microorganisms and not on physiological mechanisms (e.g. phospholipid formation or efflux pumps). These include 0.3-2% triclosan, 0.3-4% chlorhexidine, sodium hypochlorite (different dilutions), benzoyl peroxide, and metals (micro-nanosilver).

**\*\*\*NOTE: please read the following articles before this lecture\*\*\***

- Cantóna R, Horcajadad JP, Oliverb A, et al. Inappropriate use of antibiotics in hospitals: The complex relationship between antibiotic use and antimicrobial resistance. *Enferm Infecc Microbiol Clin*. 2013;**31(Supl 4)**:3-11.
- Summers JF, Brodbelt DC, Forsythe PJ, et al. The effectiveness of systemic antimicrobial treatment in canine superficial and deep pyoderma: a systematic review. *Vet Dermatol* 2012; 23: 305–e61.
- Jeffers JG. Topical therapy for drug-resistant pyoderma in small animals. *Vet Clin North Am Small Anim Pract*. 2013 Jan;43(1):41-50.
- Hillier A, Lloyd DH, Scott Weese J, et al. Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Vet Dermatol* 2014; 25: 163–e43.

## Approach to crusting and scaling dermatoses

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### Introduction

- Most of the crusting and scaling disorders are due to a keratinization disorder.
- Keratinization is the process by which keratinocytes differentiates from a basal cell to a corneocyte.
- Most keratinization disorders are secondary whereas only few of them have been recognized as primary.
  - Primary keratinization disorders are hereditary (associated with specific breeds).
  - Secondary keratinization disorders are resulting from a skin disease.
- Primary seborrhea due to:
  - Canine and feline idiopathic primary seborrhea, ichthyosis, acrodermatitis, exfoliative cutaneous lupus erythematosus of the German Shorthaired pointer, familiar paw pad hyperkeratosis, zinc responsive dermatosis type I, sebaceous adenitis, feline idiopathic facial dermatitis, Schnauzer comedo syndrome.
- Secondary seborrhea due to:
  - Parasitic diseases (e.g. scabies), infectious (e.g. pyoderma, dermatophytosis), allergies, autoimmune diseases (e.g. pemphigus complex), nutritional disorders, endocrinopathies (e.g. Cushing's, hypothyroidism, sex hormones imbalance), neoplasia (e.g. cutaneous lymphoma), environmental conditions.
- In this lecture we will cover only few of these as the most common primary defects seen in practice.

### Primary seborrhea

- Present in specific breeds like Coker spaniel, cavalier king Charles, shar pei, Labrador retriever, west highland white terrier, etc.
- The pathogenesis is not completely understood, but an acceleration of the keratinization has been shown (normal dogs ~21 days, affected dogs ~8 days).
- Clinically, these dogs present with very greasy skin with scales, comedones, follicular casts, otitis and dry skin (Dobermans and Irish setters). The lesions increase in severity with age. Secondary infections are common. The diagnosis is by exclusion of secondary seborrhea.
- The treatment of choice is the management of the scaling, greasiness and infections with topical treatments (keratolytic/keratoplastic and antimicrobial shampoos), associated with systemic retinoids and fatty acid. Treat otitis externa if present. The prognosis is guarded.

### Ichthyosis

- Epidermolytic ichthyosis
  - Present in Labrador retriever, Norfolk terriers, and Rhodesian ridgeback dogs.
  - The pathogenesis is related to a defect in the presence of keratins synthesis (autosomal recessive mutation of keratin 10 in Norfolk terriers) leading to an abnormal cytoskeleton and lysis of keratinocytes.
  - Clinically they present with scaling, multifocal hyperkeratosis, erosions and hyperpigmentation of the skin. This form of ichthyosis is best recognized and described in Norfolk terrier. In this breed, lesions may appear very early (hours from birth) and are characterized by sloughing of the skin leaving erosions after mild mechanical trauma. These lesions are accompanied by hyperpigmentation and dark grey hyperkeratosis.
- Non-epidermolytic ichthyosis
  - Present in a variety of breeds, but mainly in Terriers and retrievers.
  - The pathogenesis is not completely understood, however a defect in transglutaminase I, or intercellular lipid or in the cornified envelope have been hypothesized.
  - Clinically these dogs are presented with tightly or loosely adherent large white-to-grey scales on the body. In Golden retriever, it has been reported affecting both sexes and having an age of onset varying from 8 weeks to 12 years.
- The treatment of choice is the management of the scaling and infections with topical treatments (keratolytic/keratoplastic, moisturizing and antimicrobial shampoos), associated with systemic retinoids and fatty acid.

### **Zinc responsive dermatosis**

- Type I:
  - The pathogenesis is based on an inherited impairment of dogs to absorb and metabolise zinc. This form is mainly recognized in Alaskan malamute, Samoyeds, and Siberian husky.
  - Clinical signs develop between 1 and 3 years of age and include erythema, alopecia, tick tightly adherent white-to-grey scales and crusts and hyperkeratotic foot pads. The majorly affected areas are the muco-cutaneous junctions of the face and pressure points. Secondary yeasts and bacterial infections are common.
- Type II:
  - This form is mainly present in rapidly growing large breed puppy using a non-well balance diet with high content of phytates (plant proteins) or minerals (calcium) that chelate zinc interfering with its absorption.
  - Clinical signs include thick, well demarcated plaques and crusts mainly localized on the face (periocular and perioral areas) and genital region. Enlargement of the lymph nodes have also been reported. Secondary yeasts and bacterial infections are common.
- The diagnosis is based on history and signalment, and confirmed by histopathology. Possible differentials may include demodicosis, dermatophytosis, and immune-mediated diseases.

- The treatment of choice is the supplementation of zinc. Three formulations of zinc are available: zinc sulphate, zinc methionine, and zinc gluconate. Of those the one that has been associated with a better success is the zinc methionine.

### **Sebaceous adenitis**

- Commonly seen in Akita, Standard Poodle, Vizsla, and German Shepherd dogs. It is due to an autosomal recessive defect in Standard Poodle and Vizsla.
- Clinical signs include adherent scales, follicular casts and areas of alopecia and poor hair coat. The lesions generally start from the head and progress caudally. Differential diagnoses may include superficial pyoderma, demodicosis, dermatophytosis, endocrinopathies, and follicular dystrophy.
- Histologically are characterized by destruction of the sebaceous glands by lymphocytes.
- Treatments available include oral cyclosporine and fatty acids. Topical treatments include fatty acids, phytosphingosine and moisturizing shampoos. Tacrolimus has also been used for localized lesions.

### **Feline idiopathic facial dermatitis**

- Predominantly seen in Persians and Himalayans
- Clinically characterized by thick black scaling and discharge forming crusts. Mainly localized around the eyes, mouth, and chin in a very symmetrical way. Facial pruritus and ceruminous otitis can also be present. Secondary infections are also common. Possible differentials include demodicosis, dermatophytosis, and allergies.
- Treatments include removal of the scales and crusts, use of cleaning agents (keratolytic/keratoplastic and antimicrobial products).

### **Schnauzer comedo syndrome**

- Specifically reported in miniature Schnauzers.
- Clinically it is characterized by the presence of multiple comedones on the dorsal midline. The comedones can be associated with alopecia and erythema. Crusted papules and follicular cysts have also been reported. Differential diagnoses may include demodicosis, dermatophytosis, endocrinopathies, and follicular dystrophy.
- The treatment is the management of the comedones and secondary infections with topical treatments (keratolytic/keratoplastic and antimicrobial shampoos), associated with systemic retinoids if necessary.

### **Scabies**

- Etiology: *Sarcoptes scabiei var canis*
- Clinically it is associated with intense pruritus, erythema, and scaling on the margins of the ears, elbows and ventrum.
- The diagnosis is achieved with multiple superficial skin scrapings, although the mites are not always seen (only 50% of cases). Thus a therapeutic trial is necessary to rule out the disease. Differential diagnoses may include allergies, pyoderma, and other parasitic diseases.

- Therapeutic options include ivermectin, moxidectin, milbemycin, amitraz, lyme sulphur, fipronil. The treatment should be performed every 2 weeks for 6 weeks.

### **Cutaneous lymphoma**

- It can affect many breeds at any age, although elder patients are more affected.
- It is divided in epitheliotropic and non-epitheliotropic lymphoma. The former also called mycosis fungoides, which is also the most common form of cutaneous lymphoma.
- Slow chronic progressive neoplasia with very low risk of metastases.
- Clinically the epitheliotropic lymphoma is characterized by 4 different stages/forms: pruritic erythroderma (pruritus, erythema, alopecia and scaling), plaques, masses, and muco-cutaneous (depigmentation and ulceration). Differential diagnoses may include allergies, auto-immune diseases, demodicosis, dermatophytosis, and other neoplasia.
- Treatments available include GC, lomustine, and nitrogen mustard. For more info, please refer to oncology lectures.

### **Necrolytic migratory erythema**

- Also known as diabetic dermatopathy, hepatocutaneous syndrome, superficial necrolytic dermatitis [SND] and metabolic epidermal necrosis [MEN].
- 90% of cases reported in the literature are associated with chronic hepatic disease. Other causes of NME are pancreatic glucagonomas, administration of phenobarbital, primidone, ingestion of mycotoxins, and gastroenteritis.
- It is present mainly in middle-aged to older dogs without a sex (one study showed 75% of cases in males) or breed predisposition, although large breeds seem to be more affected.
- The pathogenesis is unknown. In people, in which is mainly associated to glucagon-secreting pancreatic tumours, it is hypothesized that hyperglucagonaemia stimulates hepatic gluconeogenesis leading to depletion of amino acids from body stores. This depletion has major impact on the epidermis, in constant need of amino acids, resulting in epidermal necrosis. Also hyperglucagonaemia increases inflammatory mediators (arachidonic acid) within the keratinocytes resulting in increased inflammation and necrosis.
- Clinical signs include erosions, ulcers, and thick crusts, hyperkeratosis of the foot pads, alopecia, and erythema. Secondary yeast infections are very common and associated with pruritus. Systemic signs may include lethargy, anorexia, weight loss, polyuria and polydipsia, and difficulty walking (pain). Differential diagnoses may include superficial pyoderma, demodicosis, dermatophytosis, pemphigus foliaceus, drug reaction, EM-SJS-TEN, epitheliotropic lymphoma, zinc responsive dermatosis.
- Diagnosis is based on history and clinical signs and confirmed by bloodwork, skin biopsy, and abdominal ultrasound.
- Treatments include slow infusion of intravenous amino acids, fatty acids, administration of egg yolk, and treatment of secondary infections. In glucagonoma associated NME octreotide has also been reported successfully. **\*\*\*Very poor prognosis\*\*\*.**

### **Feline acne**

- May affect any breed.

- Primary defect of keratinization localized to the chin.
- Clinically is characterized by comedones, scaling, erythema, oedema, and follicular casts on chin and lip. Secondary infections may develop associated with pustules and draining tracts. Nodules have also been reported. Differential diagnoses may include eosinophilic granuloma complex, dermatophytosis, demodicosis, and allergies.
- Treatments include oral fatty acids and topical and/or systemic antimicrobials. Topical keratolytic/keratoplastic products can be very useful.

#### **Feline thymoma-associated exfoliative dermatitis**

- Very rare paraneoplastic syndrome in cats.
- Pathogenesis is unknown.
- Clinically it is associated with non-pruritic, generalized exfoliative dermatitis with alopecia, lichenification, and multifocal crusting (mainly on the head). Mild pruritus and erythema have been also reported. Systemic signs may include lethargy, anorexia, and weight loss. Generalized twitching, obsessive grooming and pica have been reported in one cat.
- Ideal treatment is surgical removal of the thymoma which leads to resolution of the clinical signs.



## Erosive and Ulcerative Conditions

Rosanna Marsella, DVM, DACVD

Many of these conditions are explained elsewhere in the notes. The primary problem of an ulcerative or erosive condition may be crusts if the lesion(s) are crusted over or the condition may begin as macules or papules. Vesicles may also result in erosions but vesicles are very short-lived in the dog and cat. Autoimmune skin diseases can have a variety of presentations.

### Focal Erosive/Ulcerative Lesions

#### **Pyotraumatic Dermatitis (see sophomore notes)**

**Etiology:** Self trauma and possibly infection leading to a rapidly progressing self induced lesion

**Lesion distribution:** Often on the face or rump

#### **Acral Lick Dermatitis (Lick Granuloma): see Nodular notes**

**Etiology:** Often has a significant bacterial component

**Lesion:** Raised nodule with an ulcerated, moist dishd out center

**Lesion distribution:** Almost always on the carpus or tarsal region of an extre



#### **Feline Indolent Ulcer**

**Etiology:** suspect allergy but frequently undocumented

**Lesion:** Skin and mucous membrane of the upper lip, well-demarcated sishlike ulcers with elevated margin

**Biopsy:** variable dependant on age of lesion

#### **Feline idiopathic Ulcerative Dermatitis**

**Etiology:** unknown; differentiate from allergy

**Lesion:** Focal ulcerated well demarcated lesion usually on the dorsal neck

**Nodular Conditions which may Ulcerate: These include deep fungal infections, pithiosis, lagenidium, deep bacterial infections, foreign bodies....**

#### **Herpes viral infection (feline)**

**Etiology:** keratinocyte infection with herpes virus

**Lesions:** Ulcerative lesions

**Distribution:** Face

**Diagnostics:** Biopsy, viral serology, virus isolation

**(Bowens Disease) multicentric squamous cell carcinoma in situ ( see Crusting)**

**Etiology:** Papilloma virus (cat) + sun exposure?

**Lesions:** Ulcerative , crusted lesions

**Distribution:** Ears, nose, paws, face

**Diagnosis:** Biopsy

**Rx:** Antiviral treatment, surgery, Imiquimod (topical immunomodulatory drug)

**Mucocutaneous Pyoderma (Dog)**

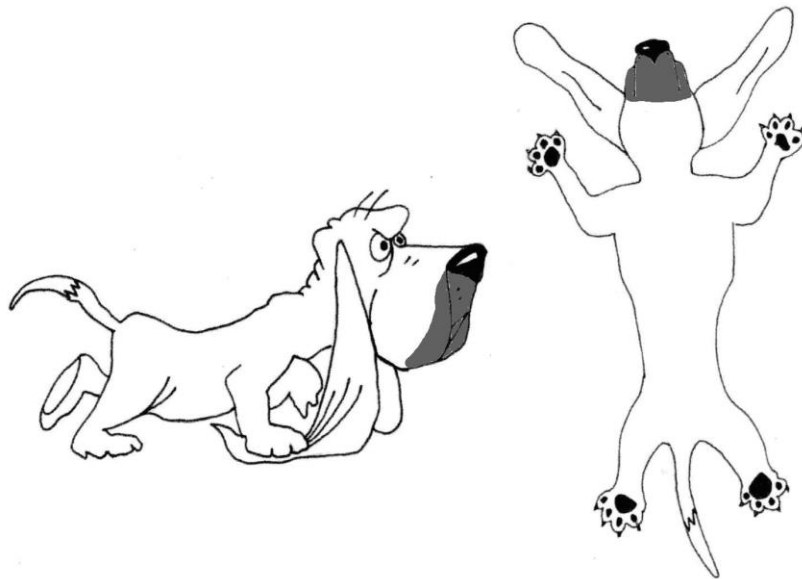
**Etiology:** staphylococcal infection of the lips that looks like autoimmune disease (DLE) and MF

**Lesions:** Ulcers

**Distribution:** Mucocutaneous; lips

**Diagnostics:** cytology, biopsy

**Rx:** Systemic Antibiotic Therapy for 4-12 wks



**DLE (Discoid Lupus Erythematosus) (Cutaneous Lupus)**

**Etiology** : Autoimmune condition where the skin is attacked

**Lesions** Erythema, scaling, sometime ulceration and erosion, often depigmentation

***Lesion distribution*** Facial esp nasal planum where it alters the architecture

***Diagnostics:*** biopsy (lichenoid infiltrate) and rule outs of other

**Dermatomyositis** (See Alopecia section vasculitis ) Dogs can present with erosive lesions but mostly appears “scarred” and alopecic

### **Calcinosis Cutis**

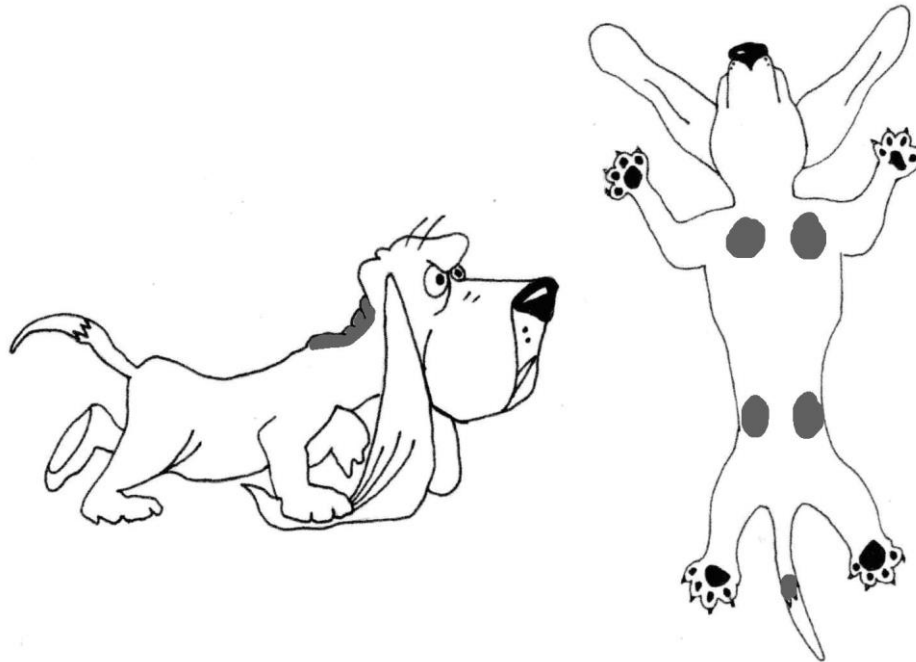
**Etiology:** Exogenous or Endogenous corticosteroids

**Lesion:** fine scale to crusted plaque to ulcerated pruritic lesions

**Lesion distribution:** Often found in fold or intertriginous areas, inguinal or groin region, top of tail and dorsal neck

**Diagnostics:** Biopsy, ACTH stimulation testing

**Rx:** Antibiotics for secondary pyodermas, DMSO topical (watch for hypercalcemia)



**Uveodermatological syndrome ( Vogt-Koyanagi-Harada like syndrome: VKH) : See Pigmentary Changes**

### **Burns**

**Etiology:** Burn injuries can result from heat, sun, flames, scalding liquids, friction, and electricity. The history usually identifies the source of injury. Burns can cause significant necrosis and loss of skin. Depending on the depth of the burn, necrosis may involve only the epidermis or may extend deeper into the tissues.

**Lesion:** Clinical signs usually include pain, erythema, and eschar formation with full-thickness burns. Deeper burns may result in shock, electrolyte and protein disturbances, and life-threatening secondary bacterial infection.

**Diagnosis:** Biopsy and history

**Rx:** Treat burns according to their depth (partial- or full-thickness) and extent over the body. Apply intensive and aggressive topical therapy in severe cases. Give medications such as morphine to control pain. Cleanse, debride, and cover burns with an antibacterial cream (e.g., Silvadene, Marion). Fluid replacement and protein supplementation are important. Because secondary bacterial (e.g., Pseudomonas) infection is common, systemic broad-spectrum antimicrobial drug therapy is essential. Skin grafts may be necessary for extensive full-thickness burns. The prognosis depends on the extent of surface area involved.

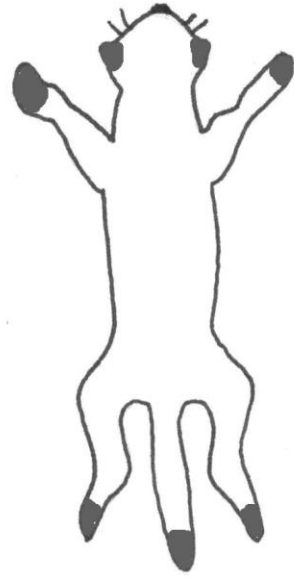
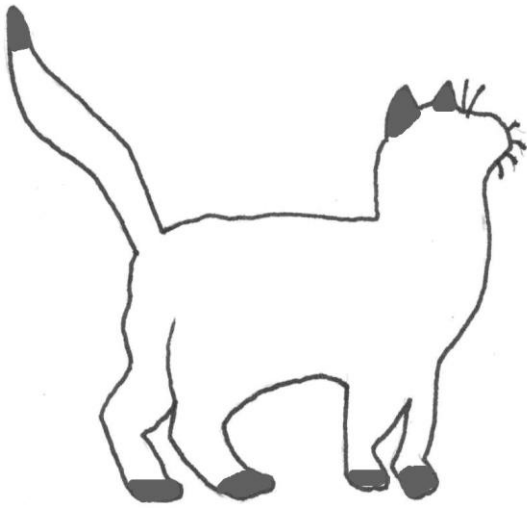
### **Frostbite**

**Etiology:** Frostbite occurs when exposure to environmental cold results in vasoconstriction so severe that the effects are not totally reversible on rewarming of the tissues.

**Lesion:** Frostbite most often results in necrosis and sloughing

**Distribution:** tips of the ears or tail. In the dog, the scrotum can also be affected. Debilitated animals are more susceptible because of immobility and poor circulation.

**Rx:** Frostbite-affected animals usually are presented long after the damage has occurred, and supportive care with debridement may be necessary. In early cases, rapidly rewarm the tissues in water heated to 40°–42°C. Whirlpool therapy can be helpful. Medication for pain may be necessary. If self-trauma can be minimized, the lesions are best left uncovered. Systemic antibiotics are necessary to manage secondary infection.



## **Decubitus Ulcers**

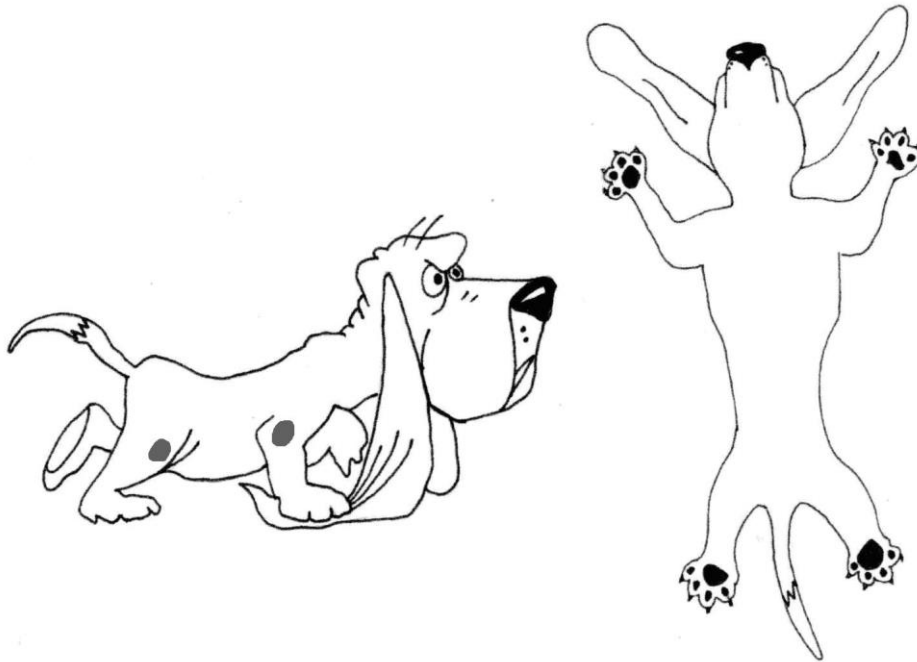
**Etiology:** Decubitus ulcers are a form of vascular compromise related to environmental conditions, characterized by loss of soft tissue cushion over bony prominences. Decubitus ulcers usually are secondary to pressure necrosis in recumbent animals.

**Lesion:** Deep ulcerated area, may have chronic firm rim of granulation tissue on periphery

**Lesions location:** Pressure points, especially stifles, elbows, hocks and hips, are common sites. These lesions are well demarcated, with full-thickness necrosis usually extending to the underlying musculature.

**Diagnosis:** Usually clinical

**Rx:** Decubitus ulcers are best treated by making the patient ambulatory, but if this is not possible, then supportive care is required. Clean and rotate the patient often. Soft bedding or a water mattress is useful. Ulcerated areas need to be kept free of fecal and urine contamination. If possible, cover affected areas with clean dressings. A wide variety of agents are available for topical use. In some cases, surgical debridement and reconstruction are indicated.

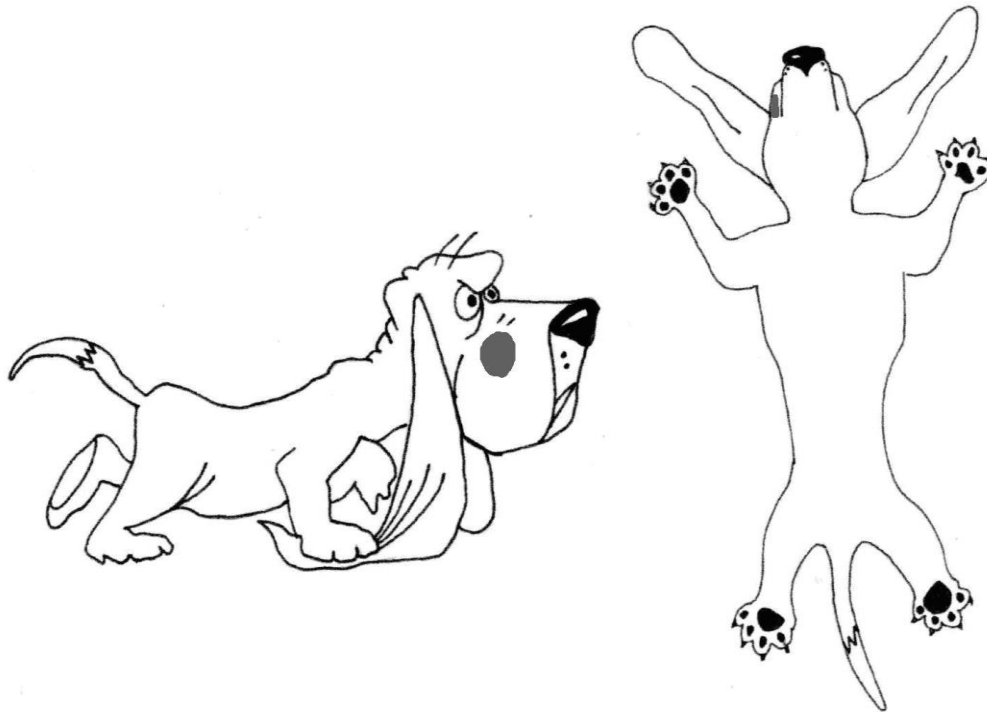


## **Spider Bite**

**Etiology** Spiders (e.g., brown recluse) cause necrotizing skin lesions by injection of a potent toxin into the tissue when they bite. The enzymes in the venom and the immunologic response of the host both play a role in dictating the clinical response. Bite wounds from the brown spider and the brown recluse spider contain potent dermonecrotic toxins. These toxins can continue to damage the surrounding tissue for an extended time after the bite.

**Lesion:** Deep ulcerative, often spreading lesion

**Distribution of lesion:** Usually facial, but could be extremity



**Diagnostics:** History and biopsy

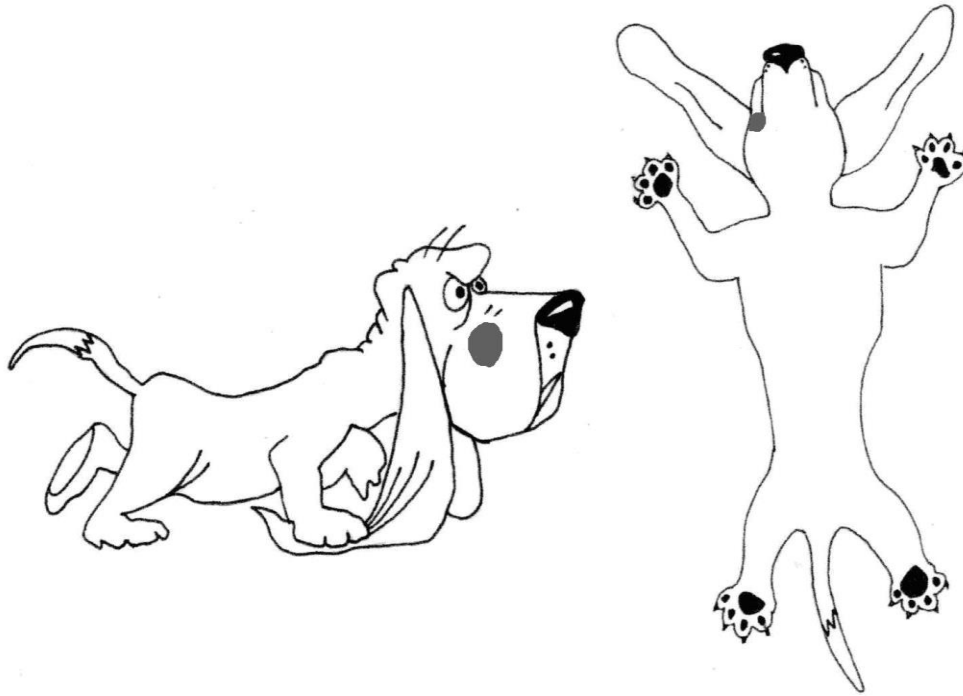
**Rx:** Excise the bite wound if the lesion is identified early as a bite from one of these spiders. Corticosteroids and antivenom do not appear to reduce local necrosis.

When systemic signs are present, corticosteroids combined with supportive care are beneficial. Intravascular hemolysis and renal failure are possible sequelae.

## **Snake Bite**

**Etiology:** Snakes, including pit vipers (copperhead, cottonmouth, and rattlesnake) and coral snakes, produce venoms that alter the integrity of blood vessels, blood cells, and coagulation; affect the nervous system; and result in necrosis at the site of envenomation.

Snake bites most frequently occur during the warmer months in geographic areas with an indigenous population of venomous snakes.



**Lesion:** Initial signs are localized soft tissue swelling that spreads rapidly. Local hemorrhage occurs, followed by necrosis of tissue and sloughing.

**Lesion distribution:** The face and extremities are the common sites of involvement.

**Diagnosis:** History and physical examination

**Treatment** varies with the severity of the clinical signs, location of the bite, type of snake, and length of time since the bite. Initially, immobilize the lesion and keep the patient quiet. Application of tourniquets is controversial, as is glucocorticoid therapy. When polyvalent antivenom (Antivenin, Fort Dodge) is indicated, give one vial slowly IV as soon as possible after the bite and repeat injections as necessary. Monitor the patient closely for anaphylaxis. Broad-spectrum antibiotics are generally indicated because both anaerobic and aerobic infections are often sequelae to the bite. Keep the lesions clean and debride wounds regularly

### **Drug-Induced Necrosis**

**Etiology:** Drug-induced necrosis of the skin followed by ulceration may occur with various drugs. Hypersensitivity may be responsible in many of these cases but proving this can be difficult. Vesiculobullous drug eruptions may precede ulceration, and purpura may occur before there is apparent tissue death.

**Lesion:** Most drug eruptions begin with generalized erythroderma or erythematous macules, followed by vesiculation and then necrosis or ulceration of the skin. These eruptions may occur during the first exposure to a drug. If they occur with first exposure, they do not usually develop clinically until after 5–7 days of drug administration.



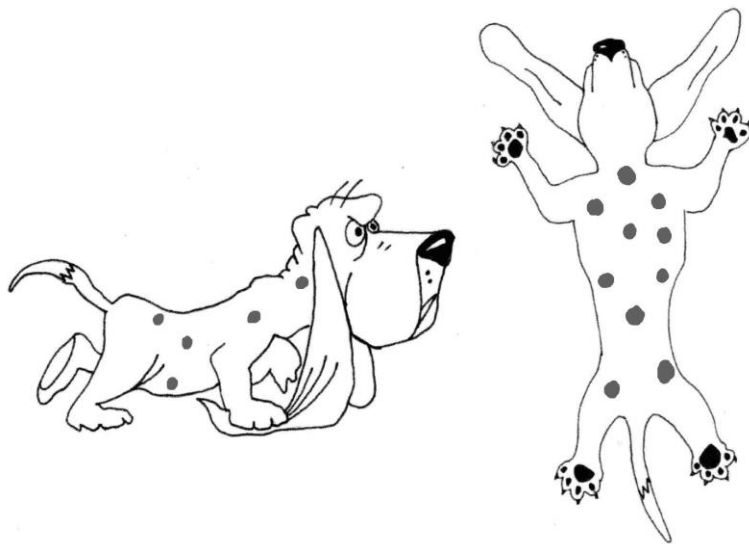
**Rx:** For treatment of drug-induced necrosis, discontinue the offending drug immediately. New lesions may continue to develop after discontinuation of the drug. If the adverse effects resolve and are known to be dosage-dependent, resume therapy at a much lower dosage if the primary disease mandates continuation of the drug. In most instances, it is preferable to substitute a different drug and to avoid giving the suspect drug to the animal in the future. The efficacy of corticosteroids, both at immunosuppressive and at anti-inflammatory levels, for drug reactions is highly controversial. Assess each case individually for potential advantages and disadvantages.

### **Erythema Multiforme (EM)**

**Etiology:** Erythema multiforme (EM) tends to be less severe than TEN but can have the same etiology as above.

**Lesions:** Multifocal clinical lesions may appear papular, macular, vesicular, bullous, or target-like, with central areas of redness surrounded by an erythematous ring. Cutaneous lesions usually progress to multifocal ulcerations and these are often in arciform or polycyclic conformations.

**Lesion distribution:** Groin, axillae, pressure points, footpads, mucocutaneous areas are generally affected. This can be more generalized.



**Diagnosis:** Biopsy: Histological examination generally shows single cell necrosis of epidermal cells at all levels of the epidermis. There often is an inflammatory infiltrate noted, even in early lesions.

**Rx:** Erythema multiforme is treated by discontinuation of any potential causative drugs as soon as possible and giving supportive care. Symptoms may continue for several days past withdrawal of the offending agent, and pain and scarring may occur. The prognosis for survival is better if the primary causative condition is not life-threatening. Although not as serious a

disease as TEN, the initial prognosis for EM should be guarded. The disease is progressive in some dogs and difficult to control in others.

### ***Toxic Epidermal Necrolysis (TEN)***

**Etiology:** necrotizing skin diseases most often caused by drugs. These conditions may also be the result of systemic diseases such as cholangiohepatitis, hepatic necrosis, and endocarditis. Other etiologies include infections, immune-mediated diseases, neoplasia and idiopathic. Some of the drugs that have been implicated in TEN and EM in dogs and cats include levamisole, penicillins, cephalosporins, sulfonamides, gold salts, 5-fluorocytosine, and antiserum.

Toxic epidermal necrolysis (TEN) may mimic EM in its early signs, but it is a much more serious disease. In early lesions and prior to secondary infection *the dermis is not necrotic* and inflammation is minimal. In this way TEN can be differentiated from chemical or thermal injuries if the lesions are biopsied early.

**Lesions:** Eventually full-thickness necrosis and sloughing of the skin occur, often involving large areas of skin. The clinical appearance can mimic a burn. There may be a positive Nikolsky sign in which normal-appearing skin can be separated away from the underlying dermis with firm manual pressure. The patient usually shows systemic signs of malaise and fever.

**Lesion distribution:** Generalized, may also involve mucous membranes

**Diagnosis:** Biopsy shows the histological lesion of TEN is full thickness coagulative necrosis of the epidermis which may extend into the hair follicles

**Rx:** Toxic epidermal necrolysis represents a true dermatologic emergency. Immediately discontinue any suspect drugs and search for systemic disease or neoplasia. Once full-thickness necrosis of the skin begins, start aggressive supportive care with intravenous (IV) fluids such as lactated Ringer's solution to replace estimated fluid loss. Keep affected tissues clean and debrided; and cover with a topical cream such as silver sulfadiazine (Silvadene, Marion) to decrease evaporation from large denuded areas. Secondary infection can result in sepsis and hypoproteinemia may be a concern when large areas are affected. Corticosteroids (prednisone or prednisolone, 2.2–4.4 mg/kg q12h PO initially, and then reduce) are recommended by some, especially early in the course of the disease. The prognosis is guarded, and in spite of removal of the causative agent or disease, TEN can continue to progress and may be fatal.

### ***Vasculitis/Vasculopathy ( see also in Alopecia)***

**Etiology:** Vasculitis is an inflammatory process that occurs within blood vessel walls which can lead to necrosis of the vessels and subsequent death of the adjacent tissue. Histopathologic evidence of vasculitis can be subtle and transient. When surrounding tissues suggest vascular compromise or there is vessel wall damage without cells, many pathologists refer to this as vasculopathy. Acute cutaneous vasculitis is most likely to result in necrotizing skin signs which include hemorrhage (echymoses or purpura), hemorrhagic bullae, necrosis (eschar), and punched out ulcers. Hemorrhage can be confirmed clinically by diascopy (the skin remains discolored when pressure is applied with a glass slide. In comparison, erythema blanches under pressure). Chronic vasculitis or cell-poor vasculitis (vasculopathy) is more likely to present with ischemic changes

such as alopecia, scaling, hyperpigmentation and some erythema. Both often involve the ears, tail tip, face, and extremities. Cutaneous vasculitis and vasculopathies are rarely primary in the dog. The list of secondary causes is quite extensive; for prognosis and treatment purposes it is useful to separate these into infectious and non-infectious etiologies. In spite of an extensive search for an underlying cause, many cases are idiopathic.

• **Non-immunologic causes:**

- Necrotizing vasculitis can be seen with a variety of infections caused by bacteria, viruses, disseminated fungi, and tickborne organisms such as *Rickettsia rickettsii*. Bacteria may directly invade the vessel walls especially with sepsis. Other infections such as *E.coli* can produce toxins that result in specific signs of vasculopathy as seen in the cutaneous and renal glomerular vasculopathy of Greyhounds.
- Neoplasia can result in vessel wall necrosis through toxin production or direct invasion of the vessel wall by neoplastic cells.
- Specific drugs can induce lesions of vasculitis in animals; the antifungal drug, itraconazole, at a dosage of 5 mg/kg q12h PO has been observed to cause vasculitis in some dogs.

• **Immunologic causes:**

- With autoimmune disease immune complex deposition may occur in vessel walls. Antibodies or cytotoxic cells may attack components of the vessel walls in other connective tissue conditions.
- Focal cutaneous vasculitis has been reported at the site of rabies vaccination. (See Alopecia).
- Post-vaccination ischemic dermatopathy and familial dermatomyositis in the acute stages may exhibit erosions or ulcerated lesions on the extremities in association with vasculitis or in more chronic cases, alopecia and evidence of a vasculopathy. (see Alopecia)

**Clinical Lesions:** usually consist of necrosis and ulceration.

**Lesion distribution:** These commonly occur on the pressure points, foot pads, pinnae, and extremities. Mucocutaneous ulcerations may be present as well as fever, lymphadenopathy, anorexia, and depression. Acute signs are more often necrotic or erosive lesions whereas chronic signs may show alopecia and scarring.

**Rx:** Vasculitis/vasculopathy is best managed by treatment of the underlying disease. Unfortunately, a specific cause of vasculitis/vasculopathy cannot be identified in a significant number of cases. • If sepsis or generalized bacterial, fungal, or rickettsial disease is identified, treat the infectious agent.

• If the vasculitis is drug-induced, discontinue the offending drug immediately.

Corticosteroids at anti-inflammatory dosages (prednisone or prednisolone, 1.1 mg/kg q12–24h PO) are advocated by some for the management of drug-induced vasculitis.

• If immune complexes are being deposited in vessel walls, give immunosuppressive doses of glucocorticoids (2-4 mg/kg q 12-24 hrs PO) or other drugs.

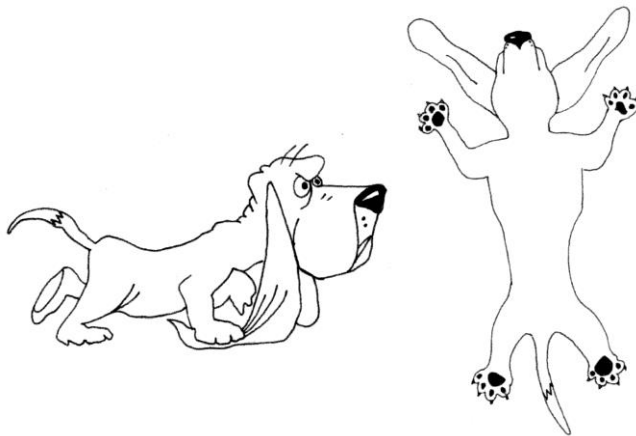
• Corticosteroids may be beneficial in some cases of vasculitis/vasculopathy. Other cases are self-limiting. In some, alternative treatments may be beneficial. Pentoxifylline (10-15mg/kg q8h PO) has a wide range of properties, few side effects, and can be used for

successful management in idiopathic cases. Dapsone (Avlosulfone, Jacobus)[dogs only] as well as sulfasalazine reportedly have been effective. The initial dosage of dapsone is 1 mg/kg q8–12h PO; when the disease is controlled, gradually reduce the dosage. Both of these drugs have potential side effects, and should be used accordingly.

### **Vascular Compromise**

**Etiology:** Vascular compromise can occur whenever there is interruption of the normal circulation to an area of tissue. This is involved in many of the aforementioned conditions and also can be the result of a thrombus, vasculopathy, or mechanical or pressure constriction (e.g., elastic bands).

**Lesion:** sloughing or ulcerated lesions. In mechanical occlusion of the circulation, the necrotic lesion is distal or beneath the obstruction. For example, an elastic band tightened around the tail over time causes underlying tissue death and sloughing of the distal tail. You can color in the tail or the neck or wherever there is constriction !



**Lesion distribution:** Depends on etiology

**Diagnosis:** Rule out other Rx: Vascular compromise should be treated based on the etiology and the location of the necrosis. When mechanical occlusion causes incomplete circulation to the tissue, the mechanical device must be removed.



### **Dachshund Pinnal Thromboembolic**

**Etiology:** Thrombus or emboli of idiopathic origin

**Lesion:** Necrosis of the dependant portion of the ears, Dogs flap heads often spreading hemorrhage.

**Lesion distribution:** Dependant portion of pinna

**Rx** In thrombovascular necrosis of the ears, the therapy of choice is resection of all affected tissue.

### **Erosive/Ulcerative Autoimmune Skin Diseases**

#### **Pemphigus vulgaris**

**Etiology:** Autoantibody attack of intercellular adhesion molecules in the basal cell layers of the epithelium. This leads to acantholysis and blister or vesicle formation.

**Lesions:** Begin as vesicles but usually present with ulceration

**Distribution of Lesions:** oral cavity, mucocutaneous junctions, groin, axilla

**Diagnosis:** Biopsy and history

**Treatment:** See sophomore notes for management of autoimmune disease

#### **Bullous Pemphigoid (and other sub-epidermal blistering diseases)**

**Etiology :** Rare group of autoimmune skin diseases where autoantibodies attack adhesion molecules in the basement membrane zone.

**Lesion:** Vesicles but usually present with ulceration

**Lesion distribution:** oral cavity, mucocutaneous membranes, groin, axilla

**Diagnostic testing:** Biopsy, history, Rule outs

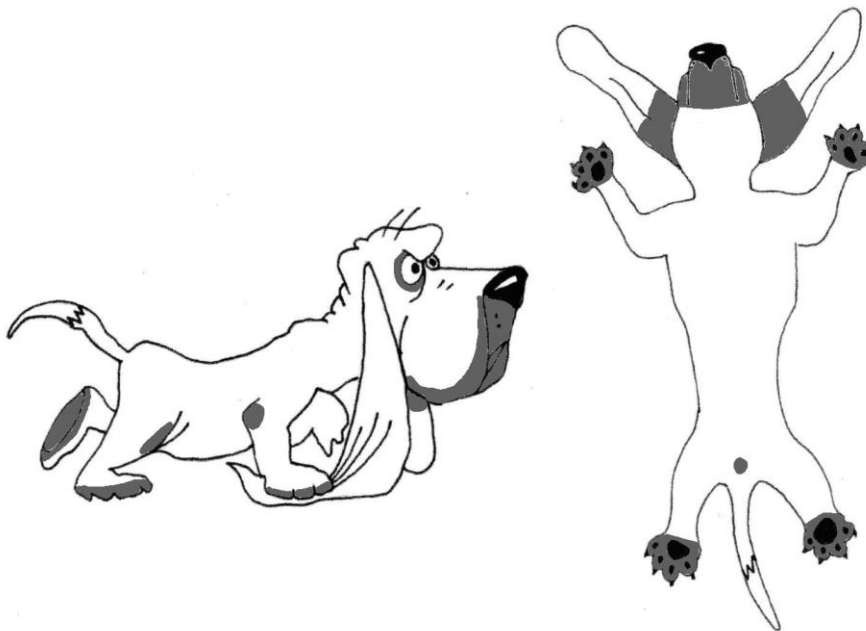
Rx: See sophomore notes

**DLE (Discoid Lupus Erythematosus) See earlier in this handout**

***Superficial Necrolytic Dermatitis (SND) Necrolytic migratory erythema (NME), metabolic epidermal necrosis (MEN), hepatocutaneous syndrome) (also in Crusting and Scaling notes )***

**Etiology:** is an uncommon canine skin disease which is a manifestation of a poorly defined error in metabolism. The histologic picture is similar to glucagonoma syndrome in humans. In a recent retrospective study affected SND dogs had a high frequency of chronic phenobarbital usage administered for idiopathic epilepsy. Liver enzyme values especially alkaline phosphatase are often elevated. Some cases (< 10% of cases reported in the literature) have had glucagonomas (i.e. similar to the disease in humans). Mean plasma amino acid concentrations for dogs with SND reportedly are lower than normal dogs or dogs with hepatitis, some amino acids are <20% of the normal values. A metabolic hepatopathy with increased hepatic catabolism of amino acids is hypothesized as the cause of this syndrome, but the exact metabolic etiology is still undefined.

**Lesions & Distribution:** The clinical findings in SND are erythema, crusting, exudation, and ulceration of the skin of the footpads, mucocutaneous junctions, and pressure points. Classically there is crusting, ulceration, and fissuring of the footpads with some patients being reluctant to walk due to pain. Although this condition may clinically mimic EM, the footpad lesions are more suggestive of SND. Systemic SND signs are quite varied and may include clinical signs of concurrent diabetes mellitus and/or hyperadrenalcorticism.



**Diagnosis:** *Biopsy: histopathological findings include a marked parakeratotic epidermis with inter- and intracellular edema, keratinocyte degeneration in the upper epidermis, and hyperplastic basal cells, forming a characteristic 'red, white and blue' histological lesion diagnostic for this syndrome.*

**Rx:** The medium- to long-term prognosis is generally poor and an outcome of euthanasia is common, often due to the painful feet of the patient. The reported mean survival time from diagnosis is less than 6 months but some dogs live for months with waxing and waning of their symptoms. Treatment with dietary supplementation of protein (high

protein diets or egg yolks) or amino acid supplements (e.g. Promod 1 scoop per 10kg), fatty acids, and zinc have generally not been rewarding. Intravenous solutions of amino acids (e.g. Aminosin 500 mls q weekly) have caused transient improvement in some cases. There is frequently a secondary bacterial and/or yeast infection of the lesions (especially interdigitally). Recognition and control of the infection (topical and systemic antimicrobial therapy) provides significant benefit (and temporarily improved quality of life) to some dogs although the primary disease will progress.

### **Neoplasia**

**Etiology** Neoplastic transformation of cells

**Lesion** Ulcers, ulcerated nodules

**Lesion distribution**

Squamous cell carcinoma: nasal planum, pinna

Epitheliotropic Lymphoma (generalized) Any tumor can be ulcerated.

**Diagnostic tests** : Biopsy , Cytology

### **Calcinosis Cutis**

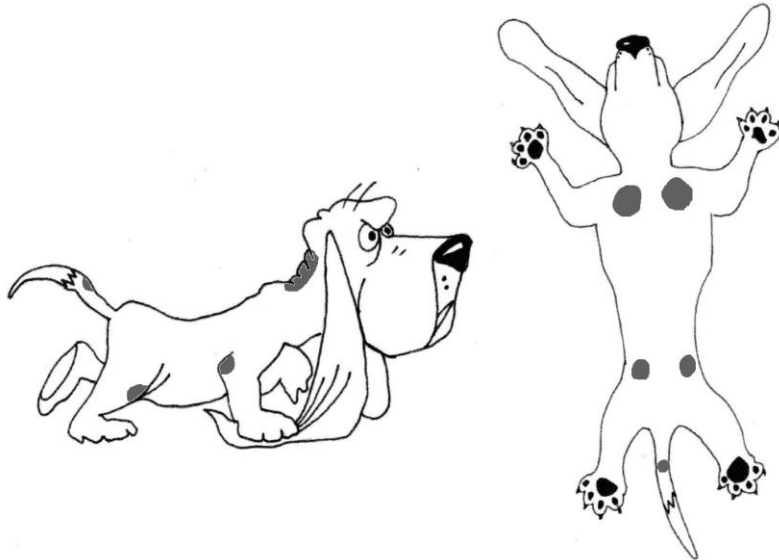
**Etiology:** Exogenous or Endogenous corticosteroids

**Lesion:** fine scale to crusted plaque to ulcerated pruritic lesion(s)

**Lesion distribution:** Often found in fold or intertriginous areas, inguinal or groin region, top of tail and dorsal neck

**Diagnostics** Biopsy, ACTH stimulation testing

**Rx:** Antibiotics for secondary pyodermas, DMSO topical (watch for hypercalcemia)





**Canine Ehlers\_Danlos (Rubber puppy, cutaneous asthenia, hyperelastosis cutis)/**

**Feline Dermatosporaxis**

**Etiology:** Defect in collagen fibrillogenesis.

**Lesions:** Skin fragility, hyperextensibility, joint laxity; Recognized at a young age as skin hyperextensibility; . Frequent lacerations, many scars. Also see joint luxations. Lacerations very hard to suture, like wet tissue paper.

**Lesion distribution** : at sites of trauma

**Diagnosis:** Clinical diagnosis which can be supported by biopsy

**Rx:** No specific treatment, avoid trauma, consider declaw in cat

**Feline Skin Fragility Syndrome**

**Etiology:** Exogenous or Endogenous excess glucocorticoids

**Lesion:** Tears in the skin

**Lesion distribution:** anywhere

## Pigmentary Changes

Rosanna Marsella, DVM,DACVD

### Hyperpigmentation

#### Postinflammatory

- Flea Allergy
- Demodicosis
- Staph pyoderma
- Yeast dermatitis
- Atopic dermatitis
- Food intolerance

#### Hormonal

- Hypothyroidism
- Hyperadrenocorticism
- Testicular neoplasia

#### Neoplasia

- Melanoma
- Basal cell tumor

#### Congenital/Hereditary

- Acromelanism
- Lentigo
- Acanthosis nigricans?
- Melanocytic nevi

### Hypopigmentation

#### Congenital/hereditary

- Albinism
- Chediak Higashi syndrome
- Waardenburg syndrom

#### Immune mediated

- Vitiligo/leukoderma/leukotrichia
- Uveodermatological syndrome
- Lupus
- Pemphigus complex?

#### Infectious

- Leishmaniasis

#### Nutritional

- Zinc deficiency

#### Neoplastic

- Epitheliotropic lymphoma

#### Environmental

- Burns, cold, trauma, chemicals

#### Idiopathic

Nasal depigmentation

## **HYPERPIGMENTATION**

### **Endocrine hyperpigmentation:**

**Hypothyroidism**

**Cushing's disease**

**Hyperestrogenism**

**Alopecia X**

**Lesion:** Diffuse to focal hyperpigmentation of the skin, usually the trunk

**Distribution:** Symmetrical

**Seasonal Flank Alopecia :** See Alopecia

### **Non-specific Hyperpigmentation:**

**Remember that Post-inflammatory hyperpigmentation is not uncommon in the dog.**

**It can be seen in conjunction or following any chronic dermatologic condition.**

### **Melanoma, basal cell tumors and melanocytic nevi**

**Etiology:** Neoplastic proliferation of melanocytes or basal cells, or congenital accumulation of melanocytes

**Lesion:** tumors

**Distribution:**

Melanoma – head, neck, eyelids, muzzle, trunk, paws

Basal cell tumor: eyelids, nasal planum, head, neck

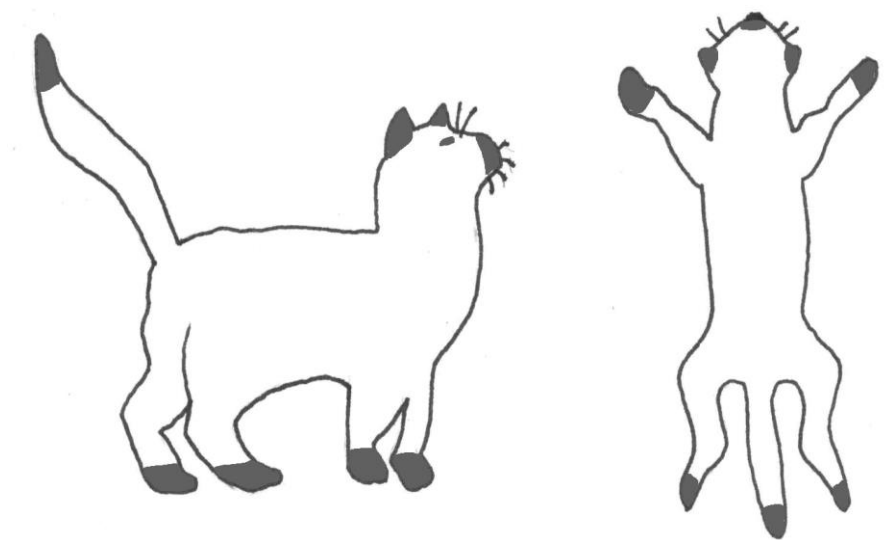
Melanocytic nevi: anywhere

## Acromelanism :

**Etiology:** Dark hairs (points) are found on the extremities of some cats due to temperature dependant effects on melanin synthesis. This can also occur after clipping because of cooling of the skin and hair follicles. This occurs due to genetic selection in Siamese cats, Himalayan cats, and rabbits. This is not a disease but normal.

**Lesions:** at site of clipping and at points

**Distribution:** Tips of ears, nose, extremities



## Lentigo

**Etiology:** genetically determined hypermelanosis in dogs and ginger cats.

**Predominant lesions:** sharply demarcated, intensely pigmented, hyperpigmented macules

### **Lesion Distribution:**

Dog: ventral abdomen

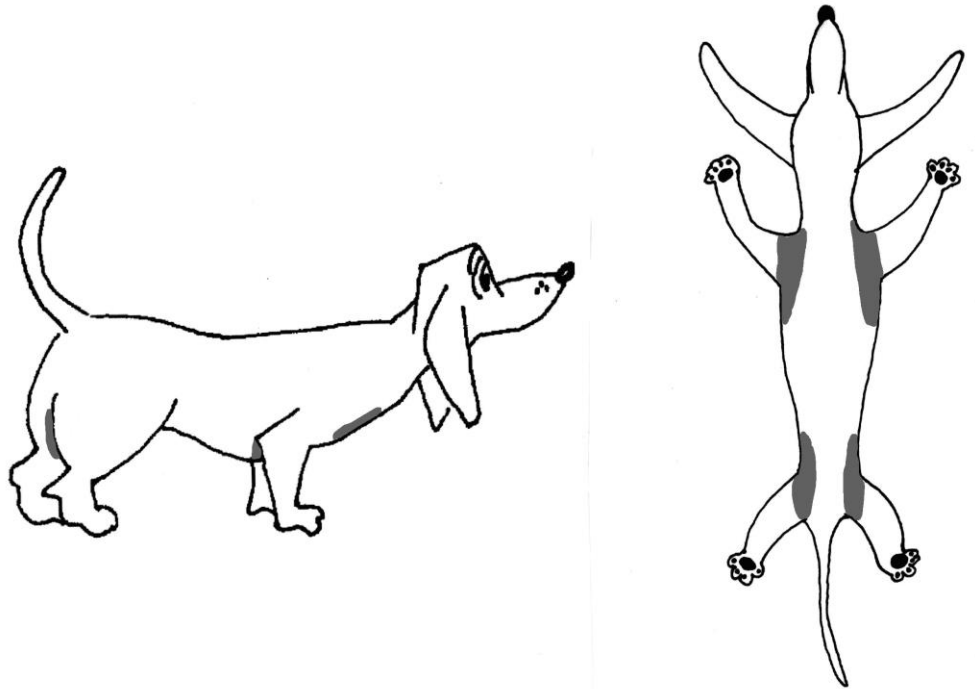
Cat (Ginger) lips, nose, gingival, eyelids

**Tests:** biopsy



**Acanthosis nigricans:**

Dachshund condition described in the older literature... in this condition there is a progressive pigmentation of the skin in the axilla and groin: likely was due to malassezia dermatitis.



**Environmental:**

Dogs that have been clipped or those that have alopecia and UV light exposure will often “tan” or pigment.

## Hypopigmentation

### **Albinism:**

**Etiology:** Rare congenital disease in dogs and cats caused by lack of melanin synthesis due to mutations affecting the gene for tyrosinase.

**Lesions:** Total lack of skin and hair pigment

**Distribution:** Generalized

**Appropriate diagnostic tests:** Clinical diagnosis



### **Chediak Higashi syndrome**

**Etiology:** inherited disorder of Persian cats with blue-smoke hair color and yellow eyes. It is due to a mutation of the beige gene.

**Lesions:** dilute coat color, non pigmented retina, increased susceptibility fo infections, bleeding disorders

**Distribution:** generalized

**Tests:** Hemogram (neutrophils and macrophages contain giant granules)  
Biopsy and trichogram

### **Waardenburg-Klein syndrome**

**Etiology** rare congenital disease in dogs (Dalmation, collie, bull terrier, and cats esp Persians caused by a defect in the migration and differentiation of melanocytes

**Lesions:** Total lack of skin and hair pigment; blue eyes and total deafness

**Lesion distribution:** generalized

**Tests:** Clinical diagnosis, hearing tests

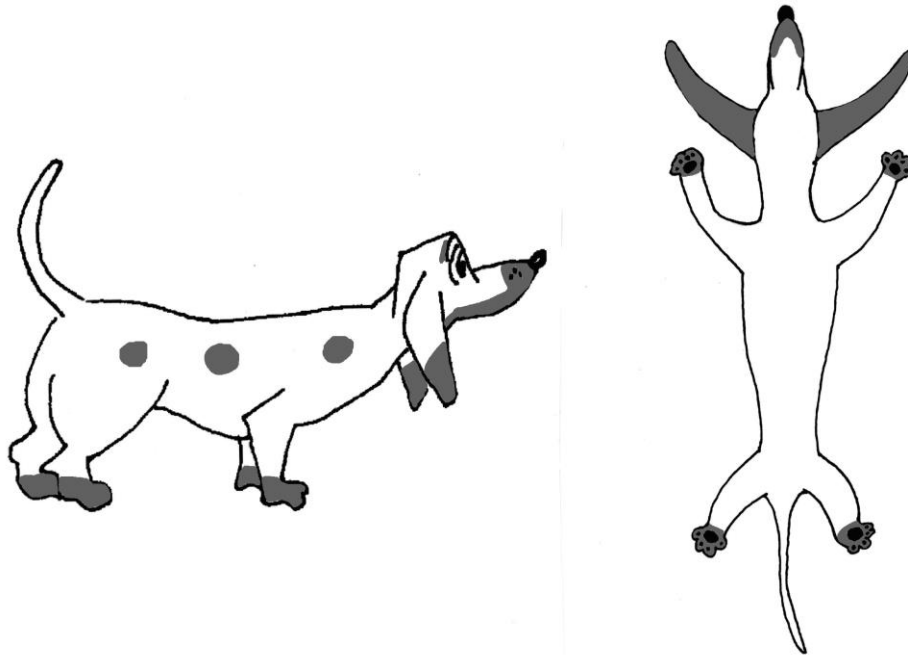
**Vitiligo**

**Etiology:** Thought to be immune mediated destruction of melanocytes. The autoimmune hypothesis is most supported. Belgian Tervurens, Rottweilers and Doberman pinschers

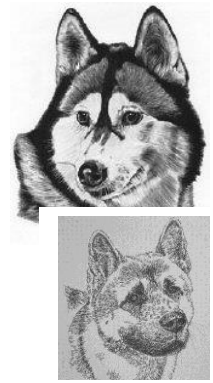


**Lesions:** Patches of symmetrical leukoderma and leukotrichia

**Distribution:** nose, lips, face, buccal mucosa, footpads, trunk



**Tests:** biopsy; usually very non-inflammatory drop off into dermis or total absence of melanin. May or may not also affect hairs



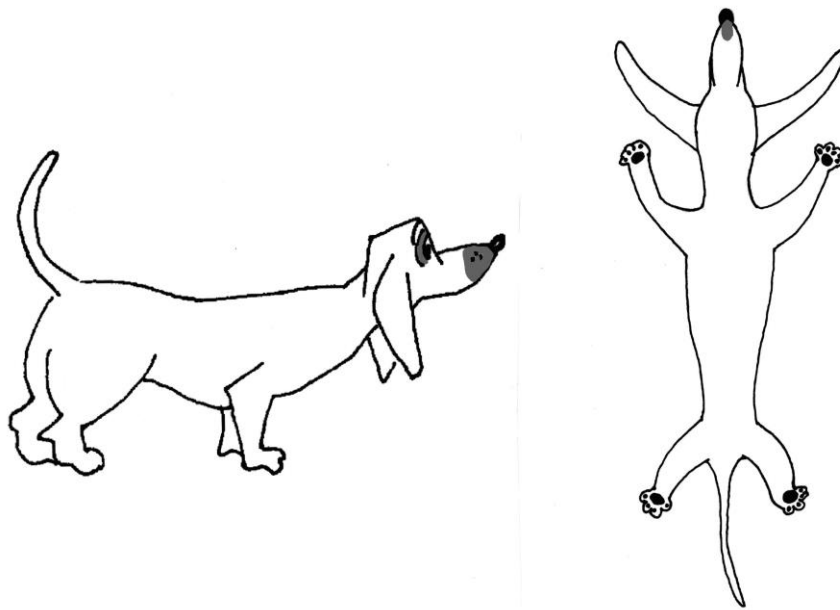
**Uveodermatological syndrome ( Vogt-Koyanagi-Harada like syndrome)**

**Etiology:** An autoimmune disease in which cutaneous and ocular melanocytes are damaged by autoantibodies and macrophages.

Akitas, chows, Samoyeds, Siberian huskies predisposed

**Lesions:** leukotrichia, leukoderma, uveitis; these dogs classically present with severe uveitis and the depigmentation may appear before, during, or after the eye signs. In many there are neurological signs but these have not been repeatedly documented in dogs.

**Distribution:** nose, lips, and eyelids, sometimes additional areas



**Tests:** Biopsy shows a granulomatous, lymphocytic infiltrate

**Rx:** Oral immunosuppressive drugs. Ophthalmological damage is often aggressive and prognosis is guarded to poor.

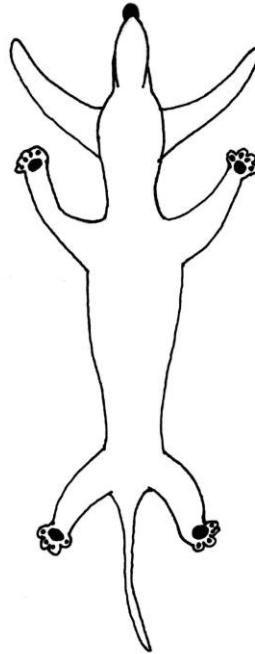
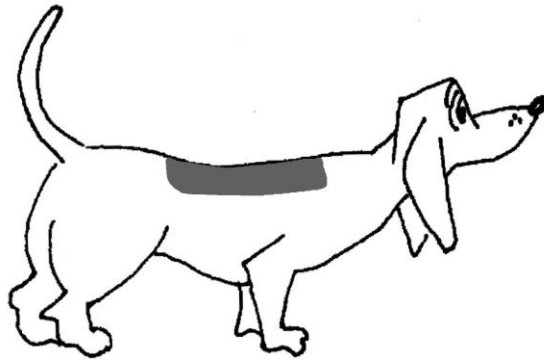


**Environmental damage (burns, cold, trauma, chemicals)**

**Etiology** : damage to melanocytes caused by physical or chemical injury

**Lesions** : patches of leukoderma and leukotrichia

**Distribution**: At site of damage



**Tests**: History

**Idiopathic nasal depigmentation (Dudley nose, snow nose)**

**Etiology**: Unknown etiology but may be associated with aging.

**Lesion**: hypopigmentation

**Distribution**: nasal planum

**Rx**: No effective Treatment, condition may wax and wane

**Idiopathic leukotrichia**

**Etiology**: unknown but may be a form of vitiligo

**Lesions**:

Patches of leukotrichia

**Distribution**: Head, trunk, legs

**Diagnostic tests:** biopsy

**Rx:** These may spontaneously regress or may be permanent

**Lupus Systemic Lupus, Discoid Lupus:**

Nasal depigmentation and loss of cobblestone appearance of the nasal planum can be a primary presentation for DLE. Some dogs with SLE will have nasal involvement and occasionally dogs will have leukotrichia/leukoderma with lupus.

**Nutritional related Pigmentary Abnormalities**

These are not well documented but may involve Zinc, or Copper metabolism.

## University of Florida College of Veterinary Medicine Syllabus

### I. Course information

Number: VEM  
Course Title: Small Animal Dermatology  
Department: Small Animal Clinical Sciences  
Course credit: 2 credits

### II. General information

Course director: Dr. Rosanna Marsella  
Office location & office hours: VC-34, by appointment  
Office phone number: 352-278-0742  
Email: marsella@ufl.edu  
Course Faculty: Dr. Rosanna Marsella

### Course description and objectives

The goals of this course are to provide advanced knowledge on how to logically and systematically approach small animal dermatological diseases with particular emphasis on problem based approach. This course will include information regarding the clinical presentations, diagnostic approach and treatment of allergic, infectious, autoimmune and immune-mediated skin diseases of small animals.

The specific objectives are for the students to become familiar with a problem based approach and learn how to approach cases in a logical step-by-step manner both in terms of diagnosis and management. Additional objectives are to provide the students with knowledge on the pathogenesis and clinical signs of skin diseases of dogs and cats that are encountered in clinical practice and were not addressed in the core dermatology course (VEM 5387). Besides providing lectures, this course also provide opportunities for case discussion in which 3 instructors (Drs. Santoro, Gram and Marsella) will encourage students to participate in discussing clinical cases. This approach has the aim to encourage application of knowledge and open discussion of the pros and cons of different approaches that could be taken on various clinical cases. There will be no laboratory time in this course.

By the end of the coursework, the student will be able to explain the necessary types of diagnostic tests and the reasons for performing them when evaluating your patients. The student will be able to discuss pros and cons of different therapy approaches for various diseases and customize the recommendations to individual cases.

**Required texts:** SCAVMA notes provided by Dr. Marsella

Recommended/ Reference texts British Small Animal Veterinary Association manual of Dermatology of dogs and Cats, 3<sup>rd</sup> Edition.

Additional Resources/ equipment: SCAVMA notes provided for the sophomore core dermatology course

**Course Outline & schedule:** This course is typically taught over the course of 5-6 weeks.

1. Introduction to Problem Based Dermatology
2. Diagnostic approach to Pruritus
3. Management of Pruritus.....
4. Steroid therapy
5. Approach to Macular/Papular Pustular/Dermatoses.....

6. Approach to Crusting Scaling Dermatoses
7. Approach to nodular dermatitis
8. Approach to Alopecia (focal/multifocal)
9. Approach to Alopecia (symmetric)
10. Endocrine Interpretation / Tests...
11. Approach to Erosive Ulcerative Dermatoses
12. Approach to Pigmentary Abnormalities
13. Regional Dermatoses 1 (perineal, pinnae, claws)
14. Regional Dermatoses 2 (nose, footpad)
14. Approach to otitis
15. Antimicrobial Resistance
17. Discussion of clinical cases
18. Discussion of clinical cases
19. Discussion of clinical cases
20. Discussion of clinical cases
21. Discussion of clinical cases
22. Discussion of clinical cases
23. Discussion of clinical cases
24. Discussion of clinical cases
25. Discussion of clinical cases
26. Discussion of clinical cases
28. Discussion of clinical cases
29. Review
30. Review

#### **IV. Evaluation/ Grading/ Testing:**

Methods by which the students will be evaluated

Students will be evaluated by 2-hour exam at the end of the course. The exam will be composed by 40 application of knowledge multiple choice questions. Each question will be weighted equally. There will be no mid-term evaluation.

Grading scheme:

The final grades assigned for this course will be based on the percentage of total points earned. The UF grading scheme will be used for this course.

Grading Policy	Percent	Grade	Grade Points
	93.4-100	A	4.00
	90.0-93.3	A-	3.67
	86.7-89.9	B+	3.33
	83.4-86.6	B	3.00
	80.0-83.3	B-	2.67
	76.7-79.9	C+	2.33
	73.4-76.6	C	2.00
	70.0-73.3	C-	1.67
	66.7-69.9	D+	1.33
	63.4-66.6	D	1.00
	60.0-63.3	D-	0.67
	0-59.9	E	0.00

For more information, please refer to:

<https://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>.

The student's grades will be posted on the course's E-Learning site. The students will be notified as soon as the grades become available.

There will be no practical assessment of clinical skills

#### **Class Attendance and Make-Up Policy**

Class attendance is strongly encouraged. Excused absences are consistent with university policies in the undergraduate catalog (<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>) and require appropriate documentation. A makeup final exam will be provided for students who miss either exam due to extreme, documented circumstances. Students should arrange with the instructor for makeup material.

#### **Students Requiring Accommodations**

Students with disabilities requesting accommodations should first register with the Disability Resource Center (352-392-8565, [www.dso.ufl.edu/drc/](http://www.dso.ufl.edu/drc/)) by providing appropriate documentation. Once registered, students will receive an accommodation letter which must be presented to the instructor when requesting accommodation. Students with disabilities should follow this procedure as early as possible in the semester.

#### **Course Evaluation**

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://evaluations.ufl.edu>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu/results/>.

#### **Class Demeanor**

Students are expected to arrive to class on time and behave in a manner that is respectful to the instructor and to fellow students.

#### **University Honesty Policy**

UF students are bound by The Honor Pledge which states, "We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment." The Honor Code (<https://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/>) specifies a number of

behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obligated to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the instructor

**Counseling and Wellness Center**

Contact information for the Counseling and Wellness Center:

<http://www.counseling.ufl.edu/cwc/Default.aspx>, 392-1575; and the University Police Department: 392-1111 or 9-1-1 for emergencies.