Cornell University
College of
Veterinary Medicine

CORNELL FELINE HEALTH CENTER

## 17th Annual

# Fred Scott Feline Symposium

## July 29–31 2005

**Veterinary Education Center**
**Cornell University**
**Ithaca, New York**

Cornell University
College of
Veterinary Medicine



Cornell Feline Health Center

## 17th Annual

# Fred Scott Feline Symposium

## July 29–31 2005

**Veterinary Education Center**
**Cornell University**
**Ithaca, New York**

Information about this conference and other continuing education programs offered by the College of Veterinary Medicine at Cornell University are available by contacting:

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Information about the Cornell Feline Health Center at the College of Veterinary Medicine at Cornell University contact:

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# General Information and Logistics

## 17th Annual Fred Scott Feline Symposium
## July 29 - 31, 2005

### Course Overview

This year's 17th Annual Fred Scott Feline Symposium will educate and update veterinarians in the latest developments in feline dermatology, systemic hypertension, renal disease, liver and pancreatic disorder, and nutrition, including nutritional management of sick cats.

### Accreditation and Continuing Education Credit

The College of Veterinary Medicine at Cornell University accredits this symposium for a maximum of 16 hours of continuing education credit. Each attendee should claim only those hours of credit that he/she actually spends in the educational lectures. You are asked to sign-in at the registration desk on the first day so that there is evidence of your attendance.

For questions about accreditation and continuing education credit please contact:

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| Cornell University | Website | www.vet.cornell.edu/extension/conedu |
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### Evaluation

It is important for the Cornell Office of Continuing Education, faculty, corporate sponsors, and exhibitors to receive your feedback. We ask that you complete the evaluation form and return it to the registration desk before you leave the symposium. The information you provide us is essential in the development of future educational programs. We welcome and encourage your comments on all aspects of this symposium.

### Certificate of Participation

You will receive a certificate of participation, which will be available at the registration desk during lunch on Saturday, July 30. The certificate verifies your attendance at the 17th Annual Fred Scott Feline Symposium.

### Meals

Meal tickets are in the back of your nametag for:

- Lunch on Friday and Saturday. These lunch meal tickets are to be turned into the cafeteria cashier after you select your lunch on Friday, and at the cafeteria entrance on Saturday.
- Lunch with Dr. Zoran: If you signed up to have lunch with Dr. Zoran on Saturday please turn in your ticket to the staff member at the meeting room entrance.

## Tours

If you registered to participate in a tour of the college during lunch on Friday or Saturday you will find an admittance ticket in the back of your nametag.

## Course Materials

The course materials that are distributed during this symposium are under the auspices of the Office of Continuing Education at the College of Veterinary Medicine at Cornell University. Duplication of these materials is prohibited.

## Disclaimer

The lectures offered during this symposium will include some discussion of off-label use and commercial products and/or services. The opinion and recommendations expressed by the faculty are their own.

Agenda

# Agenda

## 17th Annual Fred Scott Feline Symposium
## July 29 - 31, 2005

- All lectures will be held in Lecture Hall I in the Veterinary Education Center.
- Continental Breakfasts and breaks will be located in the Atrium.

### Friday, July 29, 2005

| | | |
|---|---|---|
| 7:30 - 8:00 am | Registration | James Law Lobby |
| | Continental Breakfast<br>*Sponsored by IDEXX Laboratories* | |
| 8:00 - 8:15 | Welcome - *James Richards, DVM* | |
| | **Dermatology**<br>*Danny Scott, DVM*<br>*Sponsored by Vétoquinol USA* | |
| 8:15 - 9:15 | Feline Dermatology Part I | |
| 9:15 - 9:30 | Break | |
| 9:30 - 10:30 | Feline Dermatology Part I (cont'd) | |
| 10:30 - 10:45 | Break | |
| 10:45 - 11:45 | Feline Dermatology Part I (cont'd) | |
| 11:45 -1:15 pm | Lunch | Cafeteria |
| 1:15 - 2:15 | Feline Dermatology Part II | |
| 2:15 - 2:30 | Break | |
| 2:30 - 3:30 | Feline Dermatology Part II (cont'd) | |
| 3:30 - 3:45 | Break | |
| 3:45 - 5:15 | Feline Dermatology Part II (cont'd) | |
| 6:30 - 9:00 | Annual Picnic | Baker Institute |

## Saturday, July 30, 2005

| | | |
|---|---|---|
| 7:30 - 8:00 am | Continental Breakfast<br>*Sponsored by Merial* | |
| 8:00 - 9:00 | Feline Pancreatitis I<br>*Debra Zoran, DVM, PhD* | |
| 9:00 - 9:15 | Break | |
| 9:15 - 10:15 | Feline Pancreatitis II<br>*Debra Zoran, DVM, PhD* | |
| 10:15 - 10:30 | Break | |
| 10:30 - 11:30 | Inflammatory Liver Disease in Cats<br>*Debra Zoran, DVM, PhD* | |
| 11:30 - 1:00 pm | Lunch<br>*Sponsored by Schering-Plough Animal Health* | Cafeteria |
| 1:00 - 2:00 | Staged Management of Feline Chronic Kidney Disease<br>*Scott Brown, VMD, PhD*<br>*Sponsored by Heska Corporation* | |
| 2:00 - 2:15 | Break | |
| 2:15 - 3:15 | Proteinuria and Microalbuminuria: Much Ado about What?<br>*Scott Brown, VMD, PhD* | |
| 3:15 - 3:30 | Break | |
| 3:30 - 5:00 | The Renal - Hyperthyroid Connection<br>*Scott Brown, VMD, PhD* | |

## Sunday, July 31, 2005

| | | |
|---|---|---|
| 8:00 - 8:30 am | Continental Breakfast<br>*Sponsored by The Iams Company* | |
| 8:30 - 10:00 | Diagnosis and Treatment of Feline Systemic Hypertension<br>*Scott Brown, VMD, PhD* | |
| 10:00 - 10:15 | Break | |
| 10:15 - 11:45 | Feeding Cats: Obesity, IBD, and the Carnivore Connection in Cats<br>*Debra Zoran, DVM, PhD* | |

# Corporate Sponsors and Exhibitors

17th Annual Fred Scott Feline Symposium
July 29 - 31, 2005

## Corporate Sponsors

### Heska Corporation
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Heska Corporation, headquartered in Fort Collins, Colorado, was founded in 1988. Our passion is to create and deliver innovative, high-value products and services to benefit the health and well being of companion animals. We are driven by our respect for the human-animal bond and to that end we apply cutting-edge technologies and veterinary expertise to solve important problems related to companion animal health. Heska markets a broad line of pharmaceuticals, vaccines and diagnostic products, as well as instruments, reagents and services for the diagnosis and monitoring of companion animal health.

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For more than 40 years, Schering-Plough Animal Health has provided some of the world's best-known animal health products. Their global animal health business comprises a range of pharmaceuticals, biologicals and parasiticides for food-producing and companion animals. As a result of their commitment to excellence in this area, Schering Plough ranks sixth largest in world animal health markets.

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For nearly 80 years the Vétoquinol group has been dedicated to animal health and the veterinary surgeons that work in it. As a result of its own research and in collaboration with partners, Vétoquinol regularly provides new and innovative products to the profession. Now the 14th largest veterinary company in the world, we continue to seek solutions to the problems in veterinary practice.

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### IDEXX Laboratories, Inc.
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## Annual Picnic

Hazlitt 1852 Vineyards, Inc., a part of the Fingerlakes Wine Trail, generously donated the wine provided at the Feline Symposium Annual Picnic.

# Exhibitors

Banfield, The Pet Hospital

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# Faculty

## 17th Annual Fred Scott Feline Symposium
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### Scott A. Brown, VMD, PhD, Diplomate ACVIM

Scott Brown received his veterinary degree in 1982 from the University of Pennsylvania. He completed an internship and residency in Small Animal Internal Medicine at the Teaching Hospital of the University of Georgia in 1986 and received Board Certification in Internal Medicine in 1987. From 1984-1989, Dr. Brown received a PhD in Renal Pathophysiology from the University of Georgia and was a post-doctoral research fellow at the University of Alabama-at-Birmingham School of Medicine. Since 1989, he has been a faculty member of the University of Georgia with a joint appointment in the Departments of Physiology and Small Animal Medicine where is currently a Professor of Physiology. He is presently the Acting Associate Dean for Academic Affairs. Dr. Brown has been recognized for excellence in research and teaching, having received numerous awards including the AVMA Excellence in Research Award and the National Norden Distinguished Teacher Award. His research interests are progression of chronic kidney disease and systemic hypertension.

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### Danny Scott, DVM, Diplomate ACVD

Danny Scott is a 1971 graduate of the University of California, Davis, and is presently Professor of Dermatology and Co-chief of the Dermatology Service at Cornell University. Dr. Scott's activities include teaching (students, interns, and residents), clinical service, diagnostic dermatopathology, clinical research, consultation service, and committee work. He is the author or co-author of over 490 publications and has presented over 340 continuing education seminars around the world.

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## Debra L Zoran, DVM, PhD, Diplomate, ACVIM

Dr. Zoran graduated from the Kansas State University, College of Veterinary Medicine in 1984 and became a Diplomate of the American College of Veterinary Internal Medicine in 1993. She received her PhD in Nutrition from Texas A&M University where she became an assistant clinical professor in 1997. Dr. Zoran is currently a clinical associate professor at Texas A&M University and her research interests include gastroenterology, small animal (feline) nutrition, and nutritional management of inflammatory and allergic intestinal diseases. She has presented at over 25 regional and national meetings since 2001.

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## July 29 - 31, 2005

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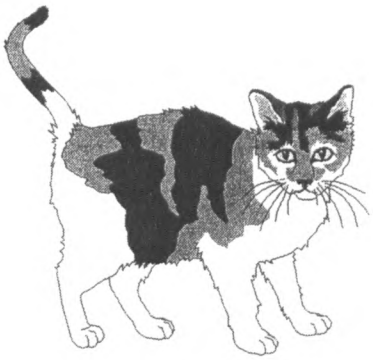

# 17th Annual Fred Scott Feline Symposium

Ithaca, New York
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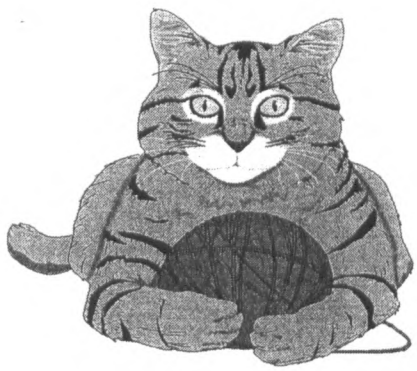
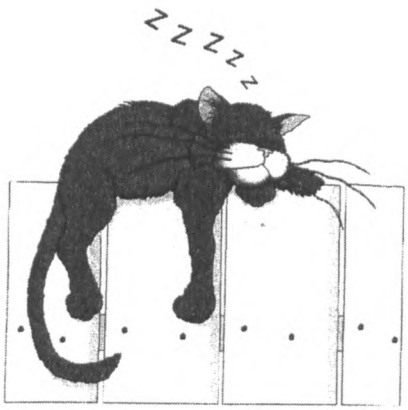
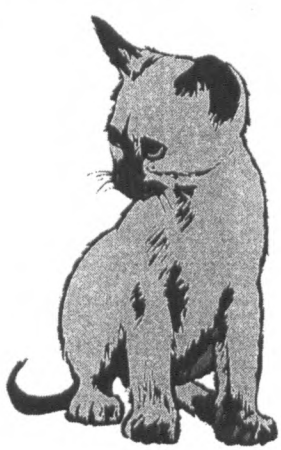





Danny W. Scott, DVM
Diplomate, ACVD



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# *Feline Dermatology: Are We Confused Yet?*

*Danny W. Scott, DVM, Diplomate, ACVD*
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## STAPHYLOCOCCAL SKIN DISEASE

Staphylococcal skin disease is said to be uncommon to rare in cats. I believe it is more common than we think.

Early studies indicated that *S. simulans* was the most commonly isolated coagulase-negative *Staphylococcus* from normal cats, and could be considered a normal resident.[1] Recent studies indicate that this organism was actually *S. felis* (*S. felis* differs from *S. simulans* in that it ferments mannose, produces a strong alkaline phosphatase reaction, and is susceptible to bacitracin).[2] In like fashion, early studies indicated that *S. aureus* was the common coagulase-positive *Staphylococcus* isolated from cats.[1] Recent studies indicate that this organism was actually *S. intermedius* (formerly biotypes E and F of *S. aureus*).[2]

Both *S. intermedius* and *S. felis* are isolated from cats with skin disease.[1,2] As these organisms are not particularly virulent, any staphylococcal infection is presumably secondary to some cutaneous, metabolic, or immunologic abnormality. Cats with the following dermatoses should be examined for the presence of staphylococci: "resistant acne"; "resistant ringworm"; "resistant eosinophilic granuloma complex lesions"; "resistant miliary dermatitis"; "resistant allergic dermatitis"; and paronychia.

Diagnosis is based on history, physical examination, cytology, skin biopsy, and response to treatment. Cytological examination of samples from superficial infections reveals neutrophils, many of which are degenerate and show nuclear streaming, with phagocytosed cocci. Samples from deep infections show, in addition, numerous lymphocytes, macrophages, plasma cells, and eosinophils. As the antibiotic susceptibility of these staphylococci are stable and predictable, culture and susceptibility testing is rarely done.[1]

Topical therapy can be challenging, but chlorhexidine-containing sprays and shampoos, as well as mupirocin ointment are useful.[1] Systemic antibiotics are usually indicated. Remember to consider mechanisms of action ("static" versus "cidal"), user friendliness, food or no food, and penetration. Antibiotics must be given until the disease is gone (visually and palpably) plus another 7 to 10 days (superficial infections) or 14 to 21 days (deep infections). To this end, product labels are rarely adequate. Never underdose antibiotics when treating skin disease. Useful antibiotics include amoxicillin-clavulanic acid (14 mg/kg q12h), clindamycin (11 mg/kg q24h), enrofloxacin (5 mg/kg q24h), and orbifloxacin (2.5 mg/kg q24h).

**References**

1. Scott DW, et al. *Muller & Kirk's Small Animal Dermatology*, 6th ed. WB Saunders, Philadelphia, 2001.
2. Thoday KL, et al. *Advances in Veterinary Dermatology IV*. Blackwell Science, Oxford, 2002.

## FELINE LEUKEMIA VIRUS INFECTION

The feline leukemia virus (FeLV) is an oncogenic immunosuppressive retrovirus.[1] Although it can induce skin tumors (lymphoma, fibrosarcoma), FeLV most commonly affects the skin by its cytosuppressive actions. Clinical signs include chronic or recurrent gingivitis or pyoderma (folliculitis, abscess, paronychia), poor wound healing, seborrhea, exfoliative dermatitis, generalized pruritus, and cutaneous horns. The viral origin of the cutaneous horns was proved by positive gp70 immunochemical staining and electron microscopy.

A pruritic crusting dermatitis has been described in FeLV-positive cats.[1,2] The lesions are [1,2] scaly, erosive, and crusted, and vary in distribution. All cases have some involvement of the face or head, either around the lips or perioral skin, pinnae, or preauricular skin. Other commonly involved sites include the feet or footpads, mucocutaneous junctions of the anus or prepuce, legs, or trunk. At presentation, the cats usually are otherwise healthy. The skin lesions respond poorly to treatment with antibiotics, glucocorticoids, interferon, or other agents. With time, the cats often show signs of internal disease, e.g., anorexia, lethargy, weight loss, but none is usually found at necropsy.

All cats are FeLV positive on serology, but skin biopsies are necessary to prove that the skin lesions are viral in origin. Histologically, the epidermis is irregularly hyperplastic and usually heavily crusted. A characteristic feature is syncytial-type giant cell formation in the epidermis and outer root sheath of the hair follicles to the level of the isthmus. Keratinocytes within and around the giant cells often are apoptotic. Involved skin shows positive gp70 staining while nonlesional skin from these cats or other FeLV-positive cats with no skin disease is negative.

Therapy has been ineffective to date.

### References


1. Scott DW, et al. *Muller & Kirk's Small Animal Dermatology*, 6th ed. WB Saunders, Philadelphia, 2001.
2. Scott DW. Dermatoses à cellules géantes associées aux rétroviroses chez le chat. Méd Vét Québec 32:19, 2002.


## FELINE IMMUNODEFICIENCY VIRUS INFECTION

Feline immunodeficiency virus (FIV) is another retrovirus that causes a variety of cytosuppressive disorders in the cat.[1] The most common clinical sign is chronic or recurrent oral disease (gingivitis, periodontal disease, stomatitis). Reported dermatologic signs include chronic or recurrent abscesses, chronic bacterial infections of the skin and ears, an increased frequency of infection with *Cryptococcus neoformans*, *Candida albicans*, or *Microsporum canis*, and demodicosis.

A generalized skin disorder has been recognized in FIV-positive cats which might have a direct association with the virus.[1,2] All cats had a generalized papulocrustous eruption with alopecia and scaling, which was most severe in the head and limbs. Pruritus was variable. On skin biopsy, a hydropic interface dermatitis was present. Occasional giant keratinocytes were

seen. In addition, a peculiar pallor of the basal epidermal cells was seen. The cause and significance of this finding remains to be seen. No treatments benefited the cats.

**References**


1. Scott DW, et al. *Muller & Kirk's Small Animal Dermatology*, 6th ed. WB Saunders, Philadelphia, 2001.
2. Scott DW. Dermatoses à cellules géantes associées aux rétroviroses chez le chat. Méd Vét Québec 32:19, 2002.


## FELINE HERPESVIRUS INFECTION

Feline rhinotracheitis is an infection with an α-herpesvirus resulting in upper respiratory disease. Occasionally, a cat develops oral and cutaneous ulcers.[1] The cutaneous ulcers are usually superficial and multiple, and can occur anywhere on the body, including the footpads. Stress or trauma to the skin might precipitate the development of the ulcers. Skin biopsies reveal epidermal ulceration with subjacent dermal necrosis and a mixed inflammatory infiltrate. Intranuclear inclusion bodies may be visualized in the keratinocytes or dermal histiocytes. Herpesvirus can be cultured from the skin; more diagnostically, it can be seen in the keratinocytes via electron microscopy.

An ulcerative and necrotizing facial dermatitis or stomatitis has been associated with herpesvirus 1 infection in cats.[1] Affected cats may or may not have active or historical ocular or respiratory signs. The disorder is recognized most often in adult cats but kittens can be affected. All adult cats had been vaccinated. Typically, crusted skin lesions involve the nasal planum, bridge of the nose, and periocular skin. When the crusts are removed, the exposed skin is inflamed and ulcerated. Similar lesions can be found elsewhere on the body. Pruritus is variable.

With intercurrent respiratory signs, the diagnosis is straightforward. Cytology and histopathology often contain numerous eosinophils, which has been misinterpreted as indicative of an allergic or ectoparasitic disease.[1] Diagnosis is via skin biopsy. Serologic test results do not confirm active infection nor that the skin disease is due to the virus. In skin biopsies, an ulcerative, often necrotic, dermatitis and suppurative folliculitis and furunculosis is seen. There is a perivascular-to-interstitial mixed inflammatory cell dermatitis with many eosinophils. In the surface and follicular epithelium, multinucleated keratinocytic giant cells can be seen and intranuclear (Cowdry type A) inclusion bodies can be seen in the giant cells and other keratinocytes. A unique feature of this disease is necrosis of epitrichial sweat glands. Ultrastructural studies demonstrate intranuclear virions consistent with herpesvirus. Polymerase chain reaction (PCR) testing in affected cats was strongly positive for herpesvirus 1. However, the use of PCR as a diagnostic test for feline herpesvirus–associated disease is of limited value because of the occurrence of healthy carriers. An immunohistochemical test was reported to be accurate.

In adult cats, the disorder can be triggered by stress or corticosteroid usage. Correction of these problems with the use of antibiotics and other symptomatic treatments may allow for spontaneous healing. Other agents suggested include lysine (250 mg of the formulation without propylene glycol orally q24h), α-interferon, and acyclovir. These treatments may or may not be beneficial.

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## DERMATOPHYTOSIS

The prevalence of dermatophytosis in cats varies with environmental circumstances.[1] Thus, it may be rare (0.26% of all patients) to common (5.6% of all patients).[1] The clinical signs attributable to dermatophytosis are also highly variable, reflecting possible differences in: (1) dermatophyte genera and species, (2) dermatophyte strains, and (3) host immunoreactivity.[1]

Because the infection is almost always follicular, the most consistent clinical sign is one or many annular areas of alopecia with variable surface abnormalities (scale, crust, erythema, hyperpigmentation, papules, pustules, erosions, collarettes, hair casts). Lesions most commonly occur on the face, pinnae, paws, and tail. Pruritus is usually mild to absent. Examples of unusual dermatophyte clinical reaction patterns include the following:

1. "Miliary dermatitis"-like.
2. Chin folliculitis/furunculosis.
3. "Stud tail"-like.
4. Onychomycosis of one paw.
5. Kerion.
6. Pseudomycetoma (especially Persians).[2] Nodular lesions (mostly subcutaneous) occurring commonly over the trunk, with or without "typical" dermatophyte skin lesions. Treatment often disappointing.
7. Widespread exfoliative/seborrheic eruption (especially Persians).
8. Ceruminous otitis externa.[3]

*M. canis* infections have great zoonotic potential.[1]

The differential diagnosis can be lengthy.[1] History-taking may be of limited value unless exposure is known to have occurred (veterinary clinic; animal shelter, contagion). Definitive diagnosis is obtained via Woods lamp examination (about 50% of *M. canis* infections), trichography (40% to 70% of the cases in experienced hands; definitive evidence), and fungal culture (plucking or brushing; beware mechanical carriage).[1] Skin biopsies are useful in all cases, especially kerions, pseudomycetomas, and "epidermotrophic" dermatophytosis.[1]

Dermatophytosis in healthy shorthaired cats often undergoes spontaneous remission within 3 months.[1] Animals with generalized infections require aggressive therapy. Even long-haired cats undergo spontaneous remission, but it may require 1½ to 4 years!

The goals of therapy are to: (1) maximize the patient's ability to respond, (2) reduce contagion, and (3) hasten resolution of the infection. A critical feature of clinical management is the treatment of all in-contact cats and dogs, and, especially in multiple-animal dwellings, environmental decontamination.

## ***Topical Therapy***

Every confirmed case should receive topical therapy.[1] Hair is ***gently*** clipped/trimmed around localized lesions (where practical) or total body in long-haired animals or animals with widespread infections. Although clipping (preferably performed by the owners in their own already contaminated environment!) may spread the lesions, it is more important to get rid of infected hairs. Hair is carefully disposed of. Focal treatments (ointments, creams, lotions) are of no proven benefit.

For cats with multifocal or widespread lesions, and ***all*** cats with *M. canis* infections, total body treatment is indicated.[1] Rinses (dips) are preferred as rubbing of the hair coat (potential dispersion of spores into the coat and environment) is minimized, and the antifungal agent is allowed to dry on (residual effect). Lime sulfur 2% and enilconazole 0.2% - applied once weekly - are the most effective.[1,4-6] Topical therapy is continued until two consecutive fungal cultures (by brush) taken at weekly intervals are negative.

Enilconazole is a much ballyhooed topical treatment in Europe and Canada, but is not approved for use in cats in the United States. A poultry premise disinfectant in the United States containing 13.8% enilconazole was used to treat dermatophytosis in Persian cats. The product was well-tolerated, all cats were culture-negative within 28 days, but all became culture-positive again after treatment was stopped. The U.S. poultry product is ***not*** the same as the licensed European/Canadian product (benzoyl alcohol in U.S. product), and is registered by the EPA (off-label use restricted).

## ***Systemic Therapy***

Cats that have multi-focal lesions, all long-haired animals, and those in multiple-animal settings should receive systemic therapy.[1] Animals that are not responding to topical therapy after a 2- to 4-week course of treatment should also receive systemic therapy.

### Griseofulvin

Griseofulvin (Fulvicin U/F) is the drug of choice, and the only one labeled for this use in the United States.[1,7] A common protocol would be 25 mg/kg PO, q12h, with a fatty meal. Side effects are usually mild, but may be life-threatening in FIV-infected cats. Griseofulvin is highly teratogenic and should never be used in the first two-thirds of pregnancy.

### Ketoconazole

Ketoconazole (Nizoral) is effective, but not labeled for use in cats in the United States.[1,7] The typical protocol is 10 mg/kg PO, q24h, with a meal. Up to 25% of cats experience side effects (usually mild at this dosage). Ketoconazole is also teratogenic. Its usage is usually reserved for animals that cannot tolerate griseofulvin, or in "resistant" infections (rare!!).

### Itraconazole

Itraconazole (Sporanox) is effective, but is not labeled for use in cats in the United States.[1,7] The typical protocol is 10 mg/kg PO, q24h, with a meal.[1] Itraconazole is well-tolerated,

but is teratogenic. It is very expensive and usually reserved for animals that cannot tolerate griseofulvin and ketoconazole.

**Fluconazole**

Fluconazole (Diflucan) is effective, but is not labeled for use in cats in the United States.[1,7] The typical protocol is 10 mg/kg PO q24h. Fluconazole is well-tolerated. It is very expensive and has no advantage over itraconazole.

**Terbinafine**

Terbinafine (Lamisil) is effective, but not labeled for cats in the United States.[1] Studies in experimental and natural *M. canis* infections in cats indicate that the drug is effective (30 to 40 mg/kg PO q24h) and well-tolerated.[7,8] Terbinafine is expensive, but fungicidal.

***Lufenuron***

Lufenuron (Program) has received a lot of attention - principally anecdotal - since the astonishing article by Ben-Ziony and Arzi in 2000.[9] In this article, the authors treated 159 cats with dermatophytosis (***none*** with generalized disease!) with lufenuron at 51 to 266 mg/kg PO once with a 100% clinical cure (mean 12 to 21 days) and 100% mycological cure (mean 8 to 14 days!). The same authors later indicated that the lower dosage (~60 mg/kg with a meal) had failed in some cats, especially those in catteries, and recommended 80 mg/kg for house cats and 100 mg/kg in catteries.[10] In another study involving 100 cats in two catteries, lufenuron (60 mg/kg PO, twice), topical enilconazole, and environmental enilconazole applications provided good clinical and mycological improvements which were beginning to deteriorate 2 months post-treatment.[11] Recent studies showed that lufenuron (30 to 140 mg/kg PO, once monthly; or 40 mg SQ every 6 months) did not prevent infection nor accelerate healing.[12-15]

## *Vaccination*

A killed *M. canis* vaccine (Fel-O-Vax MC-K) was released for the treatment and prevention of dermatophytosis in cats in 1994 . . . with no peer-reviewed, published evidence of its efficacy.[1] Extensive studies with other killed *M. canis* vaccines in laboratory cats showed no success in preventing or accelerating the healing of dermatophytosis.[1] A recent study with Fel-O-Vax MC-K showed that it also did not prevent infection or accelerate healing of *M. canis* infection in cats.[16]

## *Environmental Decontamination*

In multianimal dwellings (especially catteries) with *M. canis* infections, the environment becomes severely contaminated (floors, walls, inanimate objects, transport vehicles, ventilation systems), and current decontamination strategies often fail.[1] The challenge is daily cleaning and disinfection until two consecutive cultures (at weekly intervals) from animals and environment are negative. The most effective disinfectants are 0.525% sodium hypochlorite (1:10 bleach), stabilized chlorine dioxide (Oxygene), glutaraldehyde and quaternary ammonium chloride (GPC 8), potassium monoperoxysulfate (Virkon), and enilconazole (Clinafarm EC).[1,7,18] However, enilconazole foggers used weekly for 4 weeks did ***not*** eliminate environmental contamination.[11]

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## FELINE DEMODICOSIS

Demodicosis is a nonseasonal, variably pruritic infestation caused by 3 different mites.[1] *Demodex cati* is long (about 219 μm) and inhabits hair follicles. Details of its life cycle are not known, and it is assumed to be a normal resident of feline skin, transmitted to nursing kittens within the first few days of neonatal life. *D. gatoi* is shorter (about 108 μm) and inhabits the stratum corneum of the surface epidermis. Details of its life cycle are unknown, but it is contagious to other cats. The third, presently undescribed, demodicid on cats resembles *D. gatoi*, but is longer (about 170 μm) and has other anatomical differences.

*D. cati* is usually associated with typical folliculitis lesions: annular areas of peripherally enlarging alopecia, scaling, and variable erythema, crusts, and papules.[1,2] Lesions may be localized or generalized, and are particularly common on the face, head, pinnae, chin, neck, and paws. Pruritus is uncommon and, when present, is usually attributable to secondary staphylococcal infection. Some cats have a variably pruritic ceruminous externa.[1,3] Affected cats frequently have concurrent predisposing disorders: hyperadrenocorticism (iatrogenic or spontaneous), diabetes mellitus, FeLV and/or FIV infection, and others. *D. cati* infestation has also been reported in the lesions of squamous cell carcinoma *in situ* (Bowen's disease) with or without concurrent FIV infection.[1,4]

*D. gatoi* is usually associated with widespread - especially trunk and limbs - traumatic hair loss, scaling, and pruritus. Multiple cats in the same household may be affected.[1,5] Most affected cats are otherwise healthy.

The differential diagnosis for *D. cati* typically includes other causes of folliculitis: dermatophytosis, staphylococcal infection, and pemphigus foliaceus/erythematosus. Typical ruleouts for *D. gatoi* include atopy, food hypersensitivity, and adverse drug reaction. Skin scrapings are diagnostic for demodicosis caused by *D. cati*. *D. gatoi* can be missed if you do not use the 10X objective and close down the diaphragm. In some cases of *D. gatoi*-induced disease, the diagnosis is confirmed by finding mites on normal in-contact cats, or by response to therapy.

Therapeutic options include topical 2% lime sulfur (*D. gatoi*) or off-label topical 125-250 ppm amitraz (*D. gatoi* and *D. cati*). Demodectic otitis externa can be treated with various ear mite otic preparations as well as off-label applications of amitraz in mineral oil or propylene glycol (1:9). In case of *D. gatoi* infestations, all in-contact cats need to be treated. Weekly treatment with selamectin was not curative for *D. gatoi* infestations.[7] Milbemycin (2 mg/kg q24h PO) may be effective in *D. cati* infections.[6]

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## ATOPIC DERMATITIS

Feline atopic dermatitis ([FAD]; atopy, allergic inhalant dermatitis) owes its birth and current level of interest and recognition to Dr. Lloyd Reedy, whose landmark article on intradermal ("skin") testing and allergen-specific immunotherapy ("hyposensitization") in cats was published in 1982. Atopic dermatitis is defined as a genetically-predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features, that is most commonly associated with IgE antibodies to environmental allergens.[2,3]

A complex pathogenesis of immune dysregulation in interplay with genetic, environmental, anatomical, microbial, climactic, and physiological factors is envisioned.[4,5] A summary of current thought as to the possible pathogenesis of atopic dermatitis in humans, dogs, and cats is presented in Table 1.[3-5]

No detailed study has been reported on the hereditary aspects of FAD. However, in one study,[6] 5 of 16 (31.9%) atopic cats had close relatives with atopic-like skin disorders. In another study,[7] FAD was diagnosed in related Abyssinian cats. Most recently,[8] FAD was diagnosed in 3 littermates, at the same age, living in the same household. There are presently no apparent age, breed, or sex predilections, although over 75% of the atopic cats in 2 studies[6,8] developed their clinical signs between 6 months and 2 years of age.

The prevalence of FAD is unknown, but it is generally thought to be the second most common allergic skin disease in cats (after flea allergy).[3] FAD accounted for 12.1% and 16% of the cases of "miliary dermatitis" in 2 studies,[6,9] 17%, 35%, and 73% of all allergic cats in 3 studies,[10-12] and 5.6% of all feline dermatoses seen over a one-year period at a university clinic.[13]

The clinical signs of FAD may be initially seasonal (warm weather in association with pollens and outdoor molds; cold weather in association with house dust, danders, and indoor molds) or nonseasonal, or progress from seasonal to nonseasonal.[3,10,14,15] The most common dermatologic findings are presented in Table 2.[3,10,14,15] These cutaneous reaction patterns may be seen in various combinations in any given cat.

Reactions to house dust mites (*Dermatophagoides farinae* and *D. pteronyssinus*) and storage mites (*Acarus siro, Blomia tropicalis, Glycyphagus domesticus, Lepidoglyphus destructor, Tyrophagus putrescentiae*) are the most common in FAD, followed by pollens, molds, and danders.[1,3,10-12,14-16] House dust and storage mites are related to *Otodectes, Sarcoptes, Notoedres, Cheyletiella*, and other mites. Not surprisingly, false-positive reactions (intradermal and serological) can occur in cats with these parasites.[3] Whereas most atopic humans react to low molecular weight house dust mite allergens (Derf I and II, Derp I and II), most cats react to higher molecular weight allergens.[3,16]

The diagnosis of FAD is first and foremost ***clinical***, and is based on compatible history, physical findings, elimination of other causes, and response to therapy.[3] "Allergy testing" (***NOT!***) is performed - ***not*** to establish a diagnosis - but to determine allergens to be considered for avoidance and immunotherapy protocols.[3]

Allergen-specific immunotherapy based on carefully selected and prepared patients, and carefully interpreted intradermal test results, "benefit" (total control, or marked reduction in required medicines) 50% to 73% of atopic cats.[1,3,6,8,10,11,17-20] Intradermal testing remains the "cadillac", as false-positive reactions are less common, and positive reactions more frequently make sense with the cat's history.[3] However, this technique is more labor-intensive, and requires sedation, clipping, and expertise. Short-acting glucocorticoids (oral, topical) must be withheld for at least 3 weeks, repositol glucocorticoids pending the product (at least 6 to 8 weeks), antihistamines and omega-6/3 fatty acids (including Eukanuba® diets) for at least 10 days.[3]

Although *in vitro* serological allergen-specific IgE tests have been available since 1985, and new companies and techniques continue to come on the scene, rarely is scientific information available on the methodologies, specificities, and utility of the tests.[3] Despite "refinements" and "improvements" in serological tests, false-positives, false-negatives, and lack of correlation with intradermal test results persist.[3,21] Manufacturers tout the benefits of their methodologies - liquid-phase immunoenzymatic assay (VARL), FcεRIα-based ELISA (HESKA), enzyme-linked immunosorbent assay (ELISA), radioallergosorbent test (RAST) - with little or no peer-reviewed science to back them.[3] Serological tests are also influenced by glucocorticoids and season. Attempts to create in-office "screening tests" have always been a dismal failure and should be avoided like the plague.[3]

The keys to maximizing the success of ***any*** "allergy testing" are: (1) choosing a good test, (2) patient selection (rule-outs, drug withdrawal), (3) observing seasonal influences, and (4) matching test results with patient.[3] If money and availability were no problem, it is probable that the best results of allergen-specific immunotherapy would be achieved by performing both skin and serological testing on every patient.[3]

**Table 1. Pathogenesis of Atopic Dermatitis[3-5]**

| |
|---|
| Genetic predisposition |
| Complex |
| This not sufficient alone |
| Environment |
| "Hygiene hypothesis" |
| Epidermal barrier dysfunction |
| ↓Lipids/ceramides in stratum corneum |
| Percutaneous allergy absorption |
| Lesional and normal skin |
| Th2-biased response |
| Antigen-presenting cells armed/↑ expression of IgE |
| IL-4, IL-5, IL-13 |
| Eosinophils |
| Ig switch |
| "Extrinsic" versus "intrinsic" forms |
| "Good" and "bad" IgE |
| Late-phase response |
| Mast cell/basophil releasibility |
| Overactive phosphodiesterase isoforms |
| Stem cell factor |
| ↑ in lesional/normal skin |
| Keratinocytes |
| ↓ defensins |
| Secondary factors |
| *Staphylococci (adhesion; superantigen; upregulate IgE synthesis; infection) |
| **Malassezia* (adhesion; hypersensitivity; infection) |
| *Autoimmunity (epidermal/dermal components) |

**Table 2. Clinical Features of FAD**

| |
|---|
| Age of onset: 6 months to 2 years |
| Familial history |
| Seasonality |
| Dermatoses |
| Self-induced hypotrichosis ("fur-mowing") |
| Papulocrustous dermatitis ("miliary dermatitis") |
| Eosinophilic granuloma complex |
| Itch that rashes (face, pinnae, neck, paws) |
| Conjunctivitis |
| Rhinitis |
| Peripheral lymphadenopathy |

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## FOOD HYPERSENSITIVITY

Food hypersensitivity (food allergy, food intolerance, adverse food reaction) is common in cats, accounting for 11% of all cats with "miliary dermatitis",[1] 17% to 23% of all cats with allergic skin disease,[2,3] 1% of all patients seen in general practice,[4] 7.6% of the cases in private dermatology referral practice,[5] 5.8% of the dermatology cases seen in university practice,[6] or 10% of all allergic skin diseases.[7] The pathogenesis of adverse reactions to foods in cats is poorly understood, with "immediate" and "delayed" reactions recognized.[7] The most commonly incriminated food items are fish, beef, and dairy products.[7] However, a wide variety of substances are capable of being antigenic (see Table 1).[7]

Food hypersensitivity has no sex predilection, and occurs in cats 3 months to 14 years of age (up to 50% of the cases occur in animals < 1 year old).[7] Most authors report no breed predilections, while others incriminate Siamese cats.[8] Most animals have nonseasonal pruritus, though episodic or seasonal disease can be seen, reflecting antigenic exposure or concurrent atopy. In cats, reaction patterns include pruritus of the face/neck/ears/paws/tail, "miliary dermatitis", eosinophilic granuloma complex, and self-induced hypotrichosis ("fur mowing").[5-9] Cats may develop exfoliative dermatoses, pruritic or non, with histologic lymphocytic mural folliculitis.[7,10] Gastrointestinal disturbances are seen in about 15% of the cases.[7] Malaise, dullness, and lethargy may be seen.[7,11]

At present, the definitive diagnosis of food hypersensitivity can only be achieved on the basis of elimination diets and provocative exposure testing.[7] Novel protein ("hypoallergenic") diets must be individualized for each patient on the basis of careful dietary history. The objectives are to feed the patient substances not commonly encountered and to avoid additives (colorings, flavorings, preservatives).[7,12] Home-prepared diets are best.[7] Such diets are nutritionally inadequate for maintenance and should not be used in growing animals.[13] Don't forget to eliminate "chewable," "flavored,' "gelatin encapsulated," etc. substances (e.g., vitamin-mineral-fatty acid supplements, heartworm preventive). Owners and veterinarians must become vigilant ingredient label readers and pick out those "hidden" allergens: animal digest, animal by-products, poultry by-products, natural vitamin A (fish oil), proteinate, mixed vegetable oils, animal fats, bone meal, and modified food starch. Animals with rapidly relapsing bacterial and yeast infections may need to be kept on antimicrobials during the dietary trial.

Very little information is available on the "sea" of novel protein and hypoallergenic diets that veterinarians are besieged with. When known food hypersensitive cats were fed commercial novel protein diets, 20% to 65% of the animals became pruritic and dermatitic.[14,15] Additionally, when food hypersensitive cats were fed "all" available commercial novel protein diets, 7.7% to 31% became pruritic.[6,8,16]

The necessary duration of a novel protein diet is controversial, with some authors indicating that 10 to 13 weeks are necessary.[6,8,9] Myself and others[7] would expect to see some signs of response within 4 to 6 weeks, though maximum improvement may take longer. The diagnosis is confirmed when (1) there is at least a 50% reduction in pruritus, (2) feeding the previous diet causes a relapse (within 14 days), and (3) refeeding a novel protein diet "rescues" the animal.[7] Animals rarely become allergic to something in their novel diet in the future. About 8% to 30% of food hypersensitive cats are also atopic.[3,6,8,16] This can obviously complicate the diagnostic workup and therapy.

Skin and serologic "allergy tests" are worthless for the diagnosis of food hypersensitivity in cats.[7,11,18]

Therapy is most effective when based on novel protein diets. Unfortunately, from 7.7% to 31% of food hypersensitive cats could eat no available commercial diet without relapsing.[6,8,16] Steroidal and nonsteroidal agents are useful, but about 50% of food hypersensitive cats are poorly responsive to glucocorticoids.[7]

**Table 1. Reported Food Allergens in Cats**

| | |
|---|---|
| Barley | Eggs |
| Beef | Fish (variety) |
| Benzoic acid | Food additives |
| Chicken | Food preservatives |
| Clam juice | Horse meat |
| Cod liver oil | Lamb |
| Commercial diets | Lactose |
| Corn | Pork |
| Cow's milk | Rabbit |
| Dairy products | Whole meat |

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# Notes

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# *PANCREATITIS IN CATS: HOW DO WE DIAGNOSE IT AND WHAT DO WE DO WITH IT?*

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Feline pancreatitis is a very difficult disease to definitively diagnose antemortem and treatment remains symptomatic and supportive. This partly due to the lack of specific clinical signs in cats, as well as the lack of a specific and sensitive test for diagnosis of the disease – especially in cats with chronic pancreatitis. This talk will review the salient features of both acute and chronic pancreatitis in cats and discuss the treatment of cats with pancreatitis – a problem intensified by the complications that develop in anorectic cats.

**Diagnosis**

The clinical signs of feline pancreatitis are quite different from those in dogs. Acute pancreatitis is frequently encountered in obese dogs fed a high fat diet, while cats are more likely to be underweight, and high fat diets do not appear to be an important predisposing factor. Cats of all ages, sexes and breeds are affected, although Siamese cats are reported to have pancreatitis more frequently. Finally the clinical signs of pancreatitis in cats are more vague, with the most common signs being lethargy (reported in 100% of cats in one study), anorexia, dehydration and abnormal body temperature (either fever or hypothermia can be observed). Vomiting and anterior abdominal pain, which are common clinical signs in dogs with acute pancreatitis, occur in only 35% and 25% of cats, respectively. Cats with severe necrotizing pancreatitis may be icteric or in shock. Other conditions that may occur concurrently with pancreatitis in cats include hepatic lipidosis, cholangiohepatitis, inflammatory bowel disease, interstitial nephritis, diabetes mellitus or vitamin K responsive coagulopathy. Thus, the clinical signs may be quite variable, and this must be taken into consideration with each patient. In addition, with increases in liver enzymes and bilirubin, the signs and abnormalities can easily be attributed to liver dysfunction, which further delays the diagnosis.

Routine evaluation of cats with suspected pancreatitis may include hematology, a serum biochemistry profile, urinalysis, abdominal radiography and/or ultrasound, and serum assays of pancreatic function (e.g. feline trypsin like immunoreactivity –fTLI, or feline pancreatic lipase immunoreactivity – fPLI). Hematologic findings in cats with pancreatitis are nonspecific, but may include a nonregenerative anemia, leukocytosis or leukopenia (less common). In a recent study, cats with pancreatitis consistently had an elevated WBC (20,300 cell/uL) and mild decreases in platelets (mean = 180,000 platelets/uL). Reported changes in the serum chemistry profile include elevated serum alanine aminotransferase (ALT), elevated serum alkaline phosphatase (ALP), hyperbilirubinemia, hyper- or hypocholesterolemia, hyperglycemia, azotemia, and hypokalemia. In a recent study, the most common abnormalities in cats with severe pancreatitis were hyperglycemia (180 mg/dL), hyperbilirubinemia (2.5 mg/dL), hypocholesterolemia (130 mg/dL), and hypoalbuminemia (1.8 g/dL). Liver enzyme elevations were more common in cats with mild pancreatitis (determined by surgical biopsy), and GGT ALP, and ALT were all moderately elevated in these cats. Hypocalcemia is less commonly observed, but when present may be a poor prognostic sign seen in cats with severe pancreatitis or multiple organ dysfunction. Serum lipase may be increased early in acute pancreatitis, but in a recent study amylase and lipase were found to be of little diagnostic value in distinguishing

normal cats from those with pancreatitis. There are no changes in the urinalysis consistently observed or specific for pancreatitis in cats.

The fTLI was developed years ago as the definitive test for diagnosis of exocrine pancreatic insufficiency, and the data and follow up have confirmed its utility for this condition. In recent years, others have evaluated the fTLI as a diagnostic test for acute pancreatitis – working on the premise than an elevation in serum concentrations were consistent with pancreatic leakage or inflammation. While an increase in fTLI can be found in cats with acute pancreatitis, a normal fTLI does not rule out pancreatitis. This is because the leakage of enzymes tends to decrease or is controlled by the body's peptidases (macroglobulin, etc) within12-24 hours following an acute insult. Further, in chronic or low grade pancreatitis, the leakage is not great enough to be detected by this assay. Thus, while an increase in fTLI is specific for pancreatic enzyme leakage, it is not sensitive enough to be a definitive test for pancreatitis. More recently, an ELISA for pancreatic specific lipase (feline pancreatic lipase immunoreactivity –fPLI) was developed by the GI lab at Texas A&M University. The assay is species specific, has been used to detect elevations in pancreatic lipase in clinical cases, and appeared to be more specific and sensitive for diagnosis of pancreatitis in cats than fTLI. However, the assay had a relatively low sensitivity (33%) and specificity (<80%) when a cut off value of 100 ug/L was used for diagnosis. To improve upon this assay, a radioimmunoassay (RIA) was developed and validated in 30 healthy cats. In a recent paper, the sensitivity and specificity of this assay was tested in cats with mild pancreatitis and in cats with moderate to severe pancreatitis. The sensitivity in mild pancreatitis was found to be 80% while the specificity in healthy cats 75%. However, in severe pancreatitis (determined by pancreatic biopsy) the sensitivity and specificity were both 100%. These findings underscore the utility of this test in cats with acute pancreatitis, however, there still is a problem with detection of low grade or chronic pancreatic inflammation in cats with this assay. In cats with chronic pancreatitis it will still be necessary to evaluate the combined historical, physical exam, lab data and imaging information along with the fPLI when making a diagnosis.

Imaging studies are frequently used to help identify cats with acute pancreatitis, however, the changes are not consistent and can be particularly subject to interpretation and operator expertise. The most common radiographic abnormalities include a generalized or focal (upper right quadrant) loss of peritoneal detail (suggesting peritonitis or peritoneal effusion), presence of a mass in the area of the pancreas, hepatomegaly, dilated intestinal loops, or a fluid-filled duodenum. However, these findings are not specific for pancreatitis, and the sensitivity of radiography for diagnosing pancreatitis is low in cats. Ultrasonography may reveal a hypoechoic pancreas, hyperechoic mesentery, a mass effect, a dilated common bile duct or it may be normal. In previous studies, the sensitivity of ultrasound for diagnosis of pancreatitis was reported to be 24%. In a recent study, mild pancreatitis was still shown to be difficult to diagnose via abdominal ultrasound. However, in that same study, ultrasound had 80% sensitivity and 88% specificity in cats with moderate to severe pancreatitis. In humans, the "gold standard" for a noninvasive diagnosis of pancreatitis, but in this study, only 2 of the 10 cats showed evidence consistent with pancreatitis and there was large variability in the ability of this imaging technique to assess pancreatic size. As such, the cost, availability, the difficulties in imaging the normal feline pancreas using CT, make this method less attractive and unrealistic for use in the diagnosis of feline pancreatitis. The most reliable method for making an accurate diagnosis of pancreatic disease remains direct visualization and histopathology. However, this can be expensive, increase the risk of complications (anesthesia/surgery), and in cases with focal lesions, the lesions may be missed on visual or histopathologic inspection.

**Treatment of Pancreatitis**

Acute pancreatitis in cats can be a significant therapeutic challenge. As with the treatment of dogs, the therapy is supportive and aimed at restoring circulating blood volume while allowing the pancreas to "rest". If an inciting cause can be identified, it should be corrected; however, greater than 90% of cases are idiopathic. The mainstay of treatment is aggressive fluid therapy, and if the cat is vomiting, withholding food and water for 2-3 days. Colloid support can be obtained with hydroxyethyl starch (Hetastarch) or plasma if it is available. Plasma can be especially beneficial, as it provides additional alpha macroglobulins which are important scavengers of pancreatic enzymes. If the cat is unable to tolerate water or food after the 2-3 day period, alternative routes of nutritional support must be considered to prevent development of hepatic lipidosis or protein/calorie malnutrition and immunosuppression. The preferred method of nutritional support for cats with severe pancreatitis is via a jejunostomy (J) tube, but this requires an invasive procedure and may not be possible in all cats. Partial or total parenteral nutrition are viable alternatives. If the cat is not vomiting, placement of an esophagostomy (E) or percutaneous endoscopic gastrostomy (PEG) tube are reasonable alternatives – especially in cats with known or suspected hepatic lipidosis as a concurrent problem. The key point is this: you can't starve cats with pancreatitis – if they are not vomiting, use low fat enteral nutrition and "feed through" the pancreatitis. In cats with chronic, low grade pancreatitis this is even a more important aspect of long term management.

Other aspects of therapy that must be considered in cats with pancreatitis are pain management (whether or not they show overt pain this is important). Careful palpation in most cats will reveal cranial quadrant pain in cats with significant pancreatic inflammation. Pain relief can be achieved with buprenorphine (0.005-0.01 mg/kg IV, or IM q 4-8 hr), meperidine (1-2 mg/kg IM q2-4 hr), or butorphanol (0.2-0.4 mg/kg IM q2-4 hr). In addition, low dose CRI ketamine or lidocaine infusions are effective in reducing somatic pain, and lidocaine at these low doses has prokinetic activity. Morphine should be avoided as it can cause pancreatic duct spasm.

Other aspects of supportive therapy to consider are antibiotic therapy, control of vomiting, use of pancreatic enzymes, anti-coagulants (for cats in DIC), and finally, anti-inflammatory (steroid) therapy. Antibiotic therapy is generally indicated in all cats with severe pancreatitis, anorexia for long periods, or in cats with systemic inflammatory response syndrome (SIRS) as the risk of bacterial translocation and secondary sepsis are considerable. In general, broad spectrum antibiotics that cover intestinal aerobes and anaerobes should be chosen. Cefotaxime at a dose of 50 mg/kg administered intramuscularly every eight hours prevents bacterial colonization of the pancreas.

- Anti-emetic agents – Nausea and vomiting may be severe in affected animals. The $\alpha_2$ adrenergic antagonists and 5-$HT_3$ antagonists appear to be the most effective anti-emetic agents in the cat. Cats may be treated with chlorpromazine ($\alpha_2$ adrenergic antagonist) at a dose of 0.2-0.4 mg/kg administered subcutaneously or intramuscularly every 8 hours, or with any of the 5-$HT_3$ antagonists (ondansetron 0.1-1.0 mg/kg, granisetron 0.1-0.5 mg/kg, or dolasetron 0.5-1.0 mg/kg, orally or intravenously every 12-24 hours). Dopaminergic antagonists, e.g., metoclopramide, are less effective anti-emetic agents in the cat, and because they antagonize dopamine, may potentially reduce pancreatic blood flow (this effect has not been proven in cats with pancreatitis).

- Calcium gluconate supplementation – Hypocalcemia is a frequent complication of feline acute necrotizing pancreatitis. Calcium gluconate should be given at doses of 50-150 mg/kg intravenously over 12-24 hours, along with measurement of serum total or ionized calcium concentrations to allow adjustments in therapy.

- $H_1$ and $H_2$ histamine antagonists – Histamine and bradykinin-induced increases in microvascular permeability are associated with the development of hemorrhagic necrosis in experimental feline pancreatitis. Treatment with $H_1$ (mepyramine, 10 mg/kg) and $H_2$ (cimetidine, 5.0 mg/kg) histamine receptor antagonists protects against the development of hemorrhagic pancreatitis in these feline models. Efficacy has not been established in clinical pancreatitis, but the use of these drugs in suspected or proven clinical cases seems appropriate. Diphenhydramine (2-4 mg/kg) or dimenhydrinate (4-8 mg/kg) are examples of clinically used $H_1$ histamine receptor antagonists. Cimetidine (5.0 mg/kg), ranitidine (1.0-2.0 mg/kg), famotidine (0.5-1.0 mg/kg), and nizatidine (2.5-5.0 mg/kg) are examples of $H_2$ histamine receptor antagonists.

- Low dose dopamine infusion – Low dose dopamine infusion (5 μg/kg/min) improves pancreatic blood flow and reduces microvascular permeability in feline experimental pancreatitis. Low dose dopamine infusion is effective treatment in experimental pancreatitis even when it is given up to 12 hours after induction of the disease. Part of the appeal of dopamine as a potential treatment for feline pancreatitis lies in the diversity of its actions (cardiac, renal, and systemic pressure).

- If the cat is hyperglycemic (suggesting glucose intolerance or diabetes mellitus), regular insulin should be administered (1U/kg/day via continuous IV infusion or 0.2 U/kg IM q4-6h).

- Steroid therapy was once controversial, and is not recommended in cats with acute, necrotizing pancreatitis or pancreatic abscessation. But, there appears to be increasing evidence of an association with pancreatitis and IBD in cats, and in these cases, steroid therapy is clearly indicated.

- Ductal decompression – Surgical decompression of the pancreaticobiliary duct should be considered in cases of acute ductal obstruction, e.g., calculus, neoplasia, and fluke infection. Ductal decompression has been shown to restore pancreatic blood flow, tissue pH, and acinar cell function.

- Ductal decompression may also be useful in acute cases that have progressed to the more chronic form of the disease.

The diet chosen should be highly digestible and low fat to reduce stimulation of pancreatic secretions. In some cats, a homemade, low fat diet (e.g. chicken/turkey and rice in 2:1 proportions) may be beneficial, as there are no commercially available feline diets that are both very highly digestible and very low in fat. Ultimately, the goal is to find an appropriate diet for the cat that is both commercially available and acceptable to the cat. An important point about feeding cats during this period is to avoid force feeding – not only because it is very difficult to achieve the appropriate level of caloric intake by this method, but also because it can induce food aversion.

## Partial (Peripheral) Parenteral Nutrition (PPN)

Parenteral nutrition is nutrition delivered by an intravenous route. While enteral nutrition is always preferred, parenteral nutrition can be life saving in cats that cannot tolerate enteral feeding or are unable to meet their energy needs by enteral nutrition alone. Total parenteral nutrition, which allows provision of all the cat's daily nutritional needs intravenously, are hyperosmolar solutions and must be delivered through a central venous catheter. The logistics of stocking and compounding the required solutions, placement of central venous catheters and their care, and the provision of intensive patient monitoring around the clock have limited the use of total parenteral nutrition (TPN) to large practices and teaching hospitals. In recent years, major innovations in catheters (less thrombogenic and less prone to kinking) have made use of peripheral nutrition more practical and possible. While there are still drawbacks and limitations to PPN, the process has been greatly simplified.

In general: PPN is used in cats requiring nutritional support for less than one week, as it is intended to be "gap" nutrition – in other words, to fill the gap until better support (or complete support) can be provided.

### Key Issues

- PPN is used to provide up to 50% of the of the patient's energy needs for 24 hr. Thus, unlike TPN, it cannot be the only source of nutritional support for a patient for more than a few days.
- PPN does not require a central venous line – only a dedicated peripheral catheter is required.
- Because the PPN catheter must not be used for other purposes to reduce the risk of sepsis, a second catheter must be placed for fluids, blood draws, etc.
- Silicone elastomer or polyurethane catheters appear to be the least thrombogenic than commonly used Teflon catheters
- Placement of the catheter as a sterile procedure is a must – PPN solutions are ideal for growth of bacteria.
- Minimize changes/opening connections – change drip sets every other day – don't reuse them with new PPN solution.
- The basic solution is a protein source (8.5% amino acid solution), a CHO source (5 % dextrose), and a fat source (20% lipid emulsion), with added vitamins, minerals and electrolytes as needed.
- The key difference for PPN versus TPN is the osmolarity of the solution. TPN is often > 1200 mOsm/L, while the goal is to keep PPN solutions < 800 mOsm/L.
- 5% Amino acid solutions < 500 mOsm/L and 20% lipid solutions are 340 mOsm/L – it is the CHO solutions used that can increase osmolarity, thus 5-10% solutions are used to reduce this problem.
- PPN solutions must be mixed under aseptic conditions and in a specific order – it is best to have them formulated by a pharmacist if possible – and they must be used within 24-36 hours once administration is started.

  Order: AA + dextrose, then electrolyte and vitamin/mineral solutions, finally add lipids last – care should be taken to avoid precipitation (if it occurs, the solution must be discarded).
- Delivery of PPN solutions must be continuously via an infusion pump. Both slow initiation and slow cessation of PPN administration is essential to prevent metabolic crises (hypo/hyperglycemia, hypertriglyceridemia, etc).
- Decide the amount of calories to be administered for the patient (using the same calculations as for enteral nutrition).

Nutrient Requirements:
Cats (< 10 kg)

IER x 0.50 (50% of nutrients/day) x 0.25 (% kcal from dextrose) = kcal/day from dextrose
IER x 0.50 x 0.25 = kcal/day from amino acids
IER x 0.50 x 0.50 = kcal/day from lipid

Volume Requirements for Solutions

1. 5% Dextrose = 0.17 kcal/ml
   kcal/day ÷ 0.17 kcal/ml = ml/day dextrose
2. 8.5% amino acid solution w/ electrolytes = 0.34 kcal/ml
   kcal/day ÷ 0.34 kcal/ml = ml/day amino acids
3. 20% lipid solution = 2 kcal/ml
   kcal/day ÷ 2 kcal/ml = ml/day lipid

B complex solution = 2-4 ml/L
Add each component to give the total volume (ml) of PPN solution
Total volume ÷ 24 hr = ml/hr (approximates a maintenance rate of fluid)

- The most common complications are with catheter occlusion, premature removal, line disconnection or thrombophlebitis. These problems can be minimized with proper catheter placed and patient monitoring.

- Metabolic complications with TPN are much greater than with PPN, but still must be considered. The most common complication of PPN is hyperglycemia. Hyperammonemia and hypertriglyceridemia are much less common with PPN than TPN and if they occur, require reformulation of the solution.

- Volume overload can occur in patients with congestive heart failure or renal failure, or in very small dogs or cats – intravenous fluid rates must be adjusted to account for the volume.

- The most serious complications are venous thrombosis and septicemia secondary to catheter infection or solution contamination. Any change in body temperature should be immediately assessed and addressed.

# *Medical Management of Allergic Pruritus*

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Pruritus and the various aberrations of skin and hair coat that it provokes are, by far, the most common reasons for which cats are presented to veterinarians for dermatologic diagnosis.[1] Although many different dermatoses can be pruritic, and the differential diagnosis of pruritus is complicated, allergic (hypersensitive) skin diseases are certainly the most common causes of pruritus in cats.

Pruritus is defined as a sensation that elicits the desire to scratch.[1] The pathophysiology of pruritus is complicated and poorly understood for most diseases in most species. The literature is plethoric with information on various mediators and modulators of pruritus. However, the relative importance of these mediators and modulators in any given species, disease, or individual is rarely known.

In our practice, the most common reason for having difficulty in managing the allergic patient is failure to frequently reconsider the "threshold phenomenon" and the "summation of effects". Any "allergic" patient that is difficult to control or suddenly "comes out of control", needs to be reassessed for other problems (secondary bacterial pyoderma, secondary *Malassezia* dermatitis, flea infestation, dry skin, contact dermatitis, etc.) before its allergy medicine is adjusted.

## SYSTEMIC THERAPY

Glucocorticoids are, without a doubt, the most used and abused compounds in veterinary dermatology.[1] They are also the most consistently effective drugs in the management of allergic pruritus in cats, and can be used effectively and safely in many patients (Table 1). All glucocorticoids are not created equal. Thus, if a patient does not do well with one glucocorticoid, a different one may be more acceptable. Some cats do not appear to be able to convert prednisone to prednisolone; hence using the latter is more effective. The concept of "tolerable itchiness" must be stressed to the owners. Situations do arise wherein the use of glucocorticoids is undesirable or contraindicated. Examples would include: (1) objectionable acute or chronic side effects, (2) certain concomitant diseases (e.g., diabetes mellitus, pancreatitis, renal failure), (3) concurrent infections (bacterial, fungal, viral), (4) concurrent immunodeficiency states (e.g., FIV, FeLV), and (5) owners who are "cortisone"- or "steroid"-conscious. For these reasons, clinical and research interest in nonsteroidal antipruritic agents has "exploded" in the last several years. Although nonsteroidal antipruritic agents are often useful in the management of allergic cats, they do not have an immediate antipruritic and anti-inflammatory effects. Hence, it is often necessary to give glucocorticoids along with the nonsteroidal agents for the first 3 to 7 days.

## ANTIHISTAMINES

All "traditional" $H_1$-blockers have antihistaminic, anticholinergic, sedative, and local anesthetic effects.[1-6] They must be used with caution, if at all, in the presence of liver disease, glaucoma, urinary retention, gastrointestinal atony, seizures, pregnancy, and nursing queens.
Responses are notoriously individualized and unpredictable. Thus, one often has to try several before the one that is "right" for the patient is found (Table 2). Each antihistamine should be tried for at least

two weeks. Concurrent antihistamine administration often allows reduced glucocorticoid doses. Antihistamines are often synergistic with omega-3/-6 fatty acids.

## HETEROCYCLIC ("TRICYCLIC") ANTIDEPRESSANTS

In addition to poorly-defined behavior-modifying properties, these agents are very potent H-blockers (Table 3).[1,2] In addition to classic antihistamine side effects, these agents can also cause cardiac arrhythmias, lower seizure thresholds, and potentiate side effects of monoamine oxidase inhibitors (amitraz). Cardiac side effects have not been produced in cats with normal cardiac function. Like antihistamines, heterocyclic antidepressants often act synergistically with glucocorticoids and omega-3/-6 fatty acids.

## OMEGA-3/OMEGA-6 FATTY ACIDS

Fatty acid supplements containing omega-3/omega-6 fatty acids are potent modulators of prostaglandin and leukotriene synthesis.[1] They rarely cause side effects. Numerous clinical trials have shown that these agents are useful in many allergic cats, and may also act synergistically with glucocorticoids and antihistamines.[5,7-9] The literature is very confusing as concerns the "correct" dosage, ratio, and type of omega fatty acid to be used. Most of this is directly attributable to a failure to consider the patient's base diet.

A commercial lamb and rice dog food (Eukanuba Natural® Lamb and Rice) with an omega-6:omega-3 fatty acid ratio of 5.5:1 was fed in a single-blinded, self-controlled clinical trial to 1[illegible] atopic dogs. The pruritus in 8 of these dogs (44.4%) was controlled within 7 to 21 days, returned within 3 to 14 days after the diet was withdrawn, and was again controlled when the diet was reinstated. Some of these dogs had failed to respond to recommended doses of Derm Caps.® The dog food supplied about 6 times the γ-linolenic acid (about 6 mg/kg) and eicosapentaenoic acid (about 9 mg/kg) as what is found in the commercial supplement. When the commercial dog foods being fed to these dogs were analyzed, tremendous variation in quantity, ratio, and types of omega-6/-3 fatty acids was found. In addition, it appears that atopic dogs have a partial deficiency in Δ6- desaturase and, in some cases, Δ5-desaturase activities. Hence, simply supplying these dogs with linoleic acid (omega-6) and α-linolenic acid (omega-3) may not be adequate. If the clinician really wants to know whether or not a dog will benefit from omega-6/-3 fatty acids, a commercial diet with controlled amounts and ratios (Eukanuba® Lamb and Rice, Eukanuba® F/P, Eukanuba® K/O) is preferable. Otherwise, selecting a commercial supplement without knowledge of the dog's base diet is fraught with misinterpretation and frustration. I assume that the same applies to cats until proven otherwise.[10]

## CYCLOSPORINE

Cyclosporine is a potent inhibitor of T lymphocyte-dependent immune responses.[1] Its various effects include decreased IL-2, IL-3, IL-4, IL-5, TNF-α, and IFN-α production; inhibition of antigen presentation, eosinophil and mast cell production, histamine release from mast cells, neutrophil adherence, and growth and differentiation of B lymphocytes. The microemulsified forms (Atopica,® Novartis: capsules; Neoral,® Novartis: capsules and emulsion; generic) are preferred (bett[illegible] absorption) over the original forms (Sandimmune,® Novartis). Drugs that inhibit cytochrome P-45[illegible] enzymes (macrolides, azoles, tetracyclines, large doses of glucocorticoids) increase cyclosporine

blood levels. Recommended initial dosage is 5 mg/kg q24h PO for cats. Side effects are common (especially gastrointestinal) but usually mild. Many cats can eventually be controlled with 5 mg/kg q48h or even twice weekly.[11-13] Atopica® is not approved for use in dogs less than 6 months of age, [11-13] dogs weighing less than 4 pounds, during pregnancy or lactation, or in malignant neoplasia. Patients on cyclosporine should probably receive only killed vaccines, and ***not*** be treated with ectoparasitic doses of avermectins. Cats should be checked for FIV, FeLV, and *Toxoplasma* infection prior to therapy. Cyclosporine is effective for allergic pruritus, eosinophilic plaques, and eosinophilic granulomas in cats.

## TOPICAL THERAPY

Topicals can be useful adjuvants in the management of pruritus. Moisturizing shampoos (Hydra Pearls,® EVSCO/Vétoquinol; Epi-Soothe,® Virbac) and rinses (colloidal oatmeal) reduce pruritus by rehydrating stratum corneum and removing surface allergens, irritants, and microorganisms. Remember to use cool water. Added antipruritic effect can be attained with the local anesthetic pramoxine (Dermal-Soothe,® EVSCO/Vétoquinol; Relief,® DVM).

**Table 1. Glucocorticoid Therapy in Cats**

| Species | Drug | Dose* | Frequency* | Route |
|---|---|---|---|---|
| Cat | Methylprednisolone | 20 mg/cat | + | SQ |
| | Prednisolone/prednisone | 2 mg/kg | q24h | PO |
| | Triamcinolone | 0.4 mg/kg | q24h | PO |
| | Dexamethasone | 0.2 mg/kg | q24h | PO |

*These doses and frequencies are for induction. For maintenance, the lowest alternate evening dose achievable is indicated. In general, "safe" alternate-day doses of prednisone/prednisolone are <0.5 mg/kg. Triamcinolone and dexamethasone are not safe for alternate-day therapy in dogs, but may be acceptable in cats.

+Can be given every 2 weeks for achieving remission (up to 4 times). Chronically, no more frequently than every 3 months.

**Table 2. Antihistamine Therapy in Cats†**

| Drug | Dose | Frequency |
|---|---|---|
| Cetirizine | 5 mg/cat | q12-24h |
| *Chlorpheniramine† | 2-4 mg/cat | q12h |
| *Clemastine† | 0.67 mg/cat | q12h |
| *Cyproheptadine† | 2 mg/cat | q12h |
| Diphenhydramine | 0.5 mg/kg | q12h |
| Hydroxyzine | 1-2 mg/kg | q12h |
| Oxatomide | 10-30 mg/cat | q12h |

*Dr. Scott's favorites.

†Peer-reviewed publication(s) demonstrate efficacy.

**Table 3. Heterocyclic Antidepressant Therapy in Cats**

| Drug | Dose | Frequency |
|---|---|---|
| *Amitriptyline | 5-10 mg/cat | q24h |
| Buspirone | 2.5 mg/cat | q12h |
| Clomipramine | 1.25-2.5 mg/cat | q24h |
| Fluoxetine | 1 mg/kg | q24h |

*Dr. Scott's favorite.

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# *INFLAMMATORY LIVER DISEASE IN CATS*

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Diseases affecting the liver are a common clinical problem in cats. There are four major types of liver disease in cats: hepatic lipidosis, cholangiohepatitis complex, infectious hepatitis (e.g. FIP), and neoplastic liver disease (e.g. lymphoma). As with all diseases of the liver, histopathology is required for a definitive diagnosis, and this is the most important step in determining treatment and prognosis. Although there is no universally accepted classification of inflammatory liver disease in cats, classification based on histopathologic features is one method that has been used. In general, there are two distinct histopathologic features that are used to describe inflammatory liver diseases: cholangiohepatitis (acute and chronic forms, also termed suppurative and lymphoplasmacytic forms) and lymphocytic portal hepatitis. Acute cholangiohepatitis is characterized by infiltration with large numbers of neutrophils into portal areas and bile ducts, resulting in disruption (necrosis) of hepatocytes and ultimately infiltration of neutrophils into the hepatic lobules. This syndrome is believed to be secondary to ascending bacterial infection (although bacteria are not often cultured).

The second type of cholangiohepatitis is a chronic form, and is theorized to be a late stage of the acute disease. In this form there is a mixed inflammatory infiltrate present in the portal areas and bile ducts, but the unique feature is the presence of bile duct hypertrophy and portal fibrosis. This form of cholangiohepatitis is frequently associated with inflammatory bowel disease and pancreatitis, or the so-called triad disease. The relationship these inflammatory infiltrates have to one another is still unclear, however, there is no question the relationship exists. Finally, lymphocytic portal hepatitis is distinct from chronic cholangiohepatitis in that the lymphocytic infiltration affects only the portal areas, not bile ducts, and there are variable degrees of fibrosis and ductal hypertrophy present. Many older cats (82% in one study) have hepatic infiltrates that are characterized as portal hepatitis, and many of these cats are asymptomatic, so the true clinical significance of this change is not well understood. Nevertheless, once a diagnosis is obtained, the goal for treatment of cats with severe liver disease is to provide optimal nutritional and pharmacologic support to maximize liver function, minimize future liver damage or scarring, and to promote a high quality of life for as long as possible if the disease is not curable.

## Clinical Features & Diagnosis

Inflammatory liver disease can present in cats with few external clinical signs other than inappetance or lethargy, or can cause severe illness resulting in development of ascites, icterus, hepatoencephalopathy, coagulopathy, and loss of ability to appropriately metabolize protein or carbohydrates. Thus, there is no single set of clinical signs or laboratory abnormalities that will define all liver disease patients. Nevertheless, there are some important clues that can help guide the clinician through to a definitive diagnosis.

## Key Diagnostic Features

- In addition to liver enzyme activites, there are 5 key parameters to assess in a cat with suspected liver disease: albumin, total bilirubin, glucose, BUN, and cholesterol – all of these have important ties to liver function and be very useful clinical clues to the severity of the illness. Further liver function testing (e.g. bile acid testing) is not needed in cats

with hyperbilirubinemia not due to extra-hepatic causes, as this confirms the presence of liver dysfunction.

- Icterus may indicate liver disease, but the key is to remember that hyperbilirubinemia may occur due to PREHEPATIC (hemolytic), HEPATIC, or POSTHEPATIC (biliary tree, gall bladder, and common duct) causes. All three types of cholangiohepatitis can be associated with icterus, so this is not a good sign to distinguish them.
- Ascites can also indicate liver disease, but it too, can have prehepatic (cardiac), hepatic, or post-hepatic (portal hypertension, portal vein thrombosis, GI disease). Further, leakage of fluid into third spaces can be from leaky vessels (vasculitis), lack of colloid oncotic pressure (low albumin), or increased intravenous pressure (cardiovascular, thromboembolic disease). In general, ascites is a rare finding in cats with inflammatory liver diseases, as they are rarely reach the point of liver failure.
- In cats, the half life of both serum alkaline phosphatase and alanine aminotransferase enzymes are much shorter than in dogs, so any elevation of these enzymes should be considered significant. As in dogs, neither ALP or ALT are specific for liver disease or representative of the degree of liver damage or functionality; however, elevations of these enzymes provide evidence or support for further evaluation.
- Serum gamma glutamyltransferase (GGT) is a more specific, and sensitive test of biliary tract disease in cats, and thus, is often increased in cats with cholangiohepatitis but is usually not increased in cats with idiopathic feline hepatic lipidosis.
- The liver is the major site of synthesis of most coagulation factors, coagulation inhibitors, and other essential elements of the clotting system, thus, it is highly advisable to assess a buccal mucosal bleeding time, prothrombin time, and platelet count prior to performing a liver aspirate or biopsy. However, a recent study showed that cats with significant liver disease and coagulopathy may still have normal prothrombin times, and in these cats the PIVKA test may be more reliable. Vitamin K therapy prior to surgery or biopsy is recommended in all cats with severe liver disease.
- Analysis of the liver via imaging is an important method of assessing liver size (e.g. chronicity), liver echogenicity (e.g. circulation, biliary tree, infiltrative or space occupying diseases), and the presence of other abnormalities, such as masses, gallstones, bile duct obstruction, etc.
- Despite all of these approaches, liver disease is defined and classified on the basis of histomorphologic appearance. In other words: biopsy is essential to defining the problem and making an appropriate plan for treatment.
- Whenever liver tissue is obtained for biopsy, additional tissue should be collected for culture, especially in cats with fever, acute onset of signs, or when acute (suppurative) cholangiohepatitis is suspected.

**Wedge Liver Biopsy vs. Fine Needle Aspirate/Biopsy**

Histologic evaluation of the liver is the most definitive method of diagnosing liver disease. This requires examination of enough tissue to distinguish not only changes in hepatobiliary and vascular structures, but also the regional distribution of any lesion, so that it can be better classified. Unfortunately, the invasive nature of obtaining a sample, the danger of hemorrhage due to coagulopathies, the lack of universal availability of laparoscopic equipment and expertise, and the time required for sample submission and preparation all limit the routine use of obtaining a surgical biopsy in clinical practice. For this reason, tissue aspiration or needle biopsy (using tru-cut or other similar needle biopsy instruments) to obtain tissue via ultrasound

guidance for cytologic examination are widely used alternatives. However, there are some significant issues regarding both of these techniques that should be well understood.

Fine Needle Aspiration/Cytology

- Use an 18-22 g needle with a 12 ml syringe (with or without an extension set attached to the needle for better control)
- Expel contents of needle onto a glass slide, then gently place a second slide on top of the first to spread the cells into a monolayer (do not press! – these cells are fragile and will often explode – leaving the cytologist with a gamish to read)
- The sample is air dried, then stained with Diff-Quik or other similar Wright-Giemsa stain.
- This technique works well for diagnosis of diffuse homogeneous liver disorders that exfoliate well – e.g. lymphosarcoma, hepatic lipidosis without other concurrent disorders
- However, if lesions are not diffuse (e.g. cholangiohepatitis, certain neoplasms, nodular disease, etc) or lobar in distribulation, the diagnosis may be missed or inaccurate.

Spring-triggered Needle Biopsies

- Have gained great acceptance with using ultrasound guidance due to being a rapid and relatively safe method of obtaining tissue for histopathology without laparotomy or laparoscopy.
- 18 g spring-triggered biopsy needles (e.g. tru-cut)(1 mm biopsy chamber)
- No great advantage over needle aspiration for diffuse, homogeneous, exfoliative liver diseases
- Same problems with missing the diagnosis as for aspiration – plus, there is a slightly greater risk for bleeding following this procedure.
- In human medicine, as has been found in a recent study in veterinary medicine, specimens obtained with an 18 g biopsy needle must be interpreted with caution for these reasons: 1) there is considerable variability in tissue involvement (independent of ultrasound appearance), 2) ultrasonographic targeting can overlook areas having substantial pathology, 3) obtaining a few biopsy specimens from a single liver lobe can misrepresent the overall disease process.
- In addition, in 1/3 of cases in another study, needle biopsy specimens gave a false positive result (found evidence of liver disease, especially inflammation), when examination of wedge biopsy sections of the liver were normal.
- The morphologic diagnosis assigned to a needle biopsy specimen agrees with the definitive diagnosis only 50% of the time.

Wedge Biopsies (either Laparoscopic or Surgical)

- Greater morbidity due to anesthesia and surgical procedures, which may be unacceptable for some patients.
- With laparoscopy, there is minimal invasiveness, but maximum ability to obtain large wedge biopsies from multiple liver lobes, assess appropriate hemostasis, and biopsy regions that are grossly abnormal that may have been missed at US.
- Method of choice for obtaining a definitive diagnosis in many liver disorders.
- Surgery is the method of choice (required) if one of the following conditions exists: biliary decompression is required, cholelithiasis or biliary mucocele is present, removal

of inspissated bile is needed, necrotizing cholecystitis is present or suspected, surgical removal of mass or lobe is needed.

**Treatment of Hepatic Disease: Dietary Therapy**

The key to appropriate dietary therapy in patients with chronic liver disease is to provide a diet that provides optimal nutrition for the cat while not increasing work load on the liver (e.g. protein metabolism). In addition, the ideal diet should provide additional nutritional support for liver functions and special needs (e.g. added carnitine, arginine, zinc, and vitamins B complex, E & K), while reducing the amounts of substances that may contribute to liver dysfunction or signs of failure (e.g. aromatic amino acids, methionine, sodium). One of the key's to this therapy is reducing the amount and type of proteins that cause hyperammonemia and hepatoencephalopathy, while making sure that protein is available to meet the body's needs (immune function, etc) and prevent further catabolism of muscle protein (this is especially important in cats). Further, carbohydrates must be available in a readily digestible form to decrease the need for glycogen breakdown and glucose synthesis, for which both processes may not be optimally functioning due to the liver disease. Finally, lipid metabolism (absorption, processing into bile acids, storage, etc) is also often compromised in patients with liver failure, thus, restriction of the amount of fat in the diet and providing fat soluble vitamins in water soluble forms is often necessary.

One readily available commercial diet that will meet these needs is Hill's l/d (liver) diet. Other diets that may be used to feed cats with severe liver disease include other moderate to low protein diets designed for treatment of renal disease (e.g. Hill's k/d, Purina's NF, IVD Modified, or Iam's Nutritional Kidney Formula). However, caution is advised with use of these diets, as the levels of protein may be too low or the type of protein not appropriate for liver failure. In cats that do not have signs of hepatoencephalopathy, the highly digestible diets (e.g. Hill's i/d, Purina's EN or Iam's low residue) may be completely acceptable.

<u>Nutritional Support Keys:</u>

- Place a feeding tube (either esophagostomy or PEG) as soon as possible in cats that are anorectic for > 3 days, or in cats with IHL, so that appropriate enteral nutritional support can be obtained.
- We are placing far more E tubes now than in the past – they are faster, safe, require less technical equipment, and can be left in place for as long as needed to provide nutritional support.
- Calculate nutritional needs and develop a feeding plan: start slow and work toward a feeding plan that the owner can manage.
- RER = resting energy requirement = $70(BW_{kg})^{0.75}$ or $30(BW_{kg}) + 70$ . thus, an 11 lb (5 kg) cat would need 220 kcal to meet their RER.
- a/d = 1.5 kcal/ml of food unblended, other diets (l/d for example), have to be blenderized – 1 can food with 1 can water – which makes them 0.6 kcal/ml
- To reduce nausea and vomiting, feeding should begin slowly (small meals fed often) – we recommend 4-6 meals per day at first, starting with ½ of the calculated RER the first day, then gradually increasing the amount each day.
- Ultimately, the goal is two reduce feedings to 2-3 meals per day, but this will depend on the cat. At full feed 3 times a day = 90 ml/feeding of a diet containing 1/kcal/ml. This amount of food must be administered very slowly and in some cats, may be too much at one sitting for the first few days or weeks.

**Antimicrobial Therapy**

Antibiotic therapy is frequently recommended in the treatment of liver disease; however, they may or may not be indicated depending on the diagnosis. For example, in cats with suppurative cholangiohepatitis, antibiotic therapy is essential to appropriate therapy, while in cats with lymphoplasmacytic cholangiohepatitis, antibiotic therapy may not be warranted. Antibiotic choices should concentrate well in bile in cats with significant changes in the biliary system. However, the most important consideration is that they provide broad spectrum coverage for microbes typically present (e.g. anaerobic and gram negative GI microflora). The most common isolates are *E. coli, Enterococcus, Clostridium, and Klebsiella spp.* Antibacterials that may be useful include metronidazole, clindamycin, enrofloxacin, azithromycin,and doxycycline. Because tetracycline may increase hepatic lipid accumulation, it should not be used in cats with liver disease. This effect has not been reported with doxycycline. Ampicillin/clavulonate and cephalosporins are very useful antibiotics for cholangiohepatitis but these drugs will not reach high concentrations in bile. If there is severe liver compromise and poor bile flow, the concentrations of drugs excreted by the biliary system may need to be decreased by 30-50%.

**Anti-inflammatory/Immunosuppressive Therapy**

The most common cellular infiltrate in chronic liver disease of cats is a lymphocytic plasmacytic cholangiohepatitis. Steroids have both anti-inflammatory and anti-fibrotic properties, and thus are the treatment of choice for this type of inflammatory response. The dose for anti-inflammatory therapy of liver disease is 1 mg/kg/day, but in severe disease, with fibrosis, immunosuppressive doses (2-4 mg/kg/day) must be used. Prednisolone may be preferred in cases with severe liver disease because the drug doesn't require further hepatic metabolism to be effective (the true significance of this in cats is not known). The dose should be tapered to the lowest effective dose (maintains remission of clinical signs) after an initial treatment period of 2-4 weeks. In cats requiring long term therapy with steroids or in ones that don't tolerate steroids (e.g. they have become diabetic), it may be necessary to add azathioprine to help control the progression and prevent fibrosis. Because cats are very susceptible to the neutropenic side effects of azathioprine, careful monitoring of blood counts are essential. Other drugs, such as cholchicine and zinc acetate, which are used in dogs to prevent fibrosis and hepatic scarring, have not been studied in cats. Zinc therapy must be used very cautiously, as excessive zinc supplementation can lead to acute, massive hemolysis.

**Hepatoprotectants**

**Actigall (Ursodiol, Ursodeoxycholic acid, UDCA)**

Ursodial is an unconjucated bile salt that has been used frequently dogs, cats and humans with cholestatic liver disease to improve bile flow, reduce bile sludging, prevent gallstones, and reduce the hepatocellular damage resulting from cholestasis. The recommended dose is 10 mg/kg/day for cats. The mechanism by which UDCA increases bile flow is by promoting choleuresis through the process of cholehepatic shunting. In humans, UDCA has been found to be most helpful in patients with primary biliary cirrhosis; however, no controlled trials in dogs or cats have been conducted to assess its most effective uses. Nevertheless, some experimental and antecdotal evidence suggests that UDCA improves hepatic function in cats with chronic cholangiohepatitis, and it has no known severe side effects. Evidence in humans suggests that UDCA used alone is much less effective than polymodal therapy (with SAMe, milk thistle,

vitamin E, etc), and this has been recommended in cats as well. Further, it should not be used to relieve suspected reduced bile flow in cats with gall bladder or common bile duct disease that is best dealt with surgically.

**SAMe (S-adenosylmethionine, Denosyl)**

SAMe is a naturally occurring molecule (nutriceutical) that is involved in the metabolism of methionine to homocysteine and glutathione. Glutathione is an essential cellular antioxidant/free radical scavenger, and this is the mechanism for which SAMe is used - to reduce further oxidative damage to hepatocytes. Specifically, SAMe appears to increase hepatic and mitochondrial glutathione concentrations, improves organelle and cell redox states, and restores or preserves hepatic glutathione concentrations during oxidative stress. SAMe has been widely studied in humans and is recommended for use in chronic active or cirrhotic liver disease to slow the progression or onset of hepatic failure. In addition, SAMe has been shown to have anti-inflammatory properties and promotes hepatocellular regeneration – the mechanism of which is not known. Recent studies of SAMe (e.g. Denosyl) in dogs and cats , the drug appears to protect against oxidant injury (acetaminophen and other liver oxidant injury), may improve bile flow in cats, protect from bile induced injury to hepatocytes, and may inhibit hepatocyte apoptosis. One important thing to note about use of SAMe (and other nutriceuticals) is that not all products are the same. SAMe is available in two isomer forms (R,S and S,S), and only the S,S form is active. Some companies marketing SAMe are not cautious about the purity of their SAMe, and thus, the product may contain high percentages of the R,S isomer (inactive). This information is not typically on the label and may be hard to find or is unknown. Denosyl (the veterinary product from Nutrimax Laboratories) has proven and documented the product's purity, and as such, this is the only product currently recommended for use in cats. The recommended dose is 20 mg/kg/day orally.

**Milk Thistle (Silymarin)**

Silymarin is the active extract of the milk thistle plant, which is a nutriceutical used for centuries to treat humans with liver disease. The important functions and hepatoprotective properties of silymarin include its role as an antioxidant and free-radical scavenger in the liver, it's inhibition of hepatotoxin binding, its role in increasing glutathione concentrations, it serves as an iron chelator, and it is known to promote choleuresis. Whether or not these specific effects occur in cats is not known, but studies in rats and humans, and anecdotal reports in dogs suggest that it has a beneficial effect, and side effects are extremely low. The dose recommended is 4-8 mg/kg/day.

**Nutritional Supplementation**

Vitamins E and C

There is ample evidence that chronic liver injury is partly due to oxidative damage to hepatocytes. Further, there is also supporting evidence that antioxidant therapy may be beneficial in managing chronic liver diseases. One such beneficial supplement is vitamin E (d-alpha tocopherol) which has been shown to protect against oxidative damage from iron, copper, and bile acids. The dose of vitamin E recommended for use in hepatic disease is 100-400 IU/cat q 24

hr. If the water soluble formulation of the vitamin is given, there is a greater chance that the vitamin will be adequately absorbed orally. Caution is advised in over-supplementation with vitamin E because of the potential for toxicity; however, this is less of a problem with this fat soluble vitamin than it is with vitamin A.

B vitamins (complex)

In anorectic cats with liver disease, supplementation with B vitamins may improve appetite and increase the availability of these essential vitamins (e.g. cobalamin, folate, thiamine) needed to improve healing, promote normal metabolism and improve energy utilization by cells). Measurement of cobalamin levels is indicated in cats with signs of GI disease to determine if cobalamin supplementation is needed. The dose of vitamin B complex is 0.5-1.0 ml/cat IV or SQ, or 5 ml/liter bag of fluids. Cobalamin supplementation is 250 ug/cat/week.

L-carnitine

There is good evidence in cats that L-carnitine may protect against hepatic lipid accumulation, especially in obese cats that may already have some lipid metabolic disturbances. Carnitine is a nonessential amino acid that is vital in the transport of long chain fatty acids into the mitochondria for oxidation into energy (in the absence of carnitine, beta oxidation of fatty acids does not occur). Impaired energy formation leads to impaired fatty acid oxidation and urea cycle function – both of which will lead to increase production of ammonia. Carnitine supplementation for cats with liver disease is recommended at 250 – 500 mg/day.

**Other Considerations**

In addition to all of the above dietary and pharmacologic treatments, cats with liver disease may have coagulation defects for which vitamin K therapy may be needed. Patients with severe liver failure may develop ascites due to hypoproteinemia for which diuretic therapy may be indicated, and they often require therapy to control signs of hypergastrinemia (e.g. vomiting, nausea, anorexia) which may include histamine-2 receptor antagonists or specific antiemetic therapy. In conclusion, management of chronic liver disease can be challenging, and require a variety of pharmacologic and dietary intervention strategies. To achieve optimal results, both the veterinary clinician and the owner must be willing and able to provide the intensive therapy and monitoring required to adjust to the patients changing needs. However, with appropriate management, most cats can return to fully functional lives for months or years to come.

# *STAGED MANAGEMENT OF FELINE CHRONIC KIDNEY DISEASE*

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In veterinary and human medicine, renal function generally is held to be equivalent to glomerular filtration rate (GFR). We recognize that this is an oversimplification as the kidney has a wide variety of functions; disease processes can interfere with one function (e.g., urinary concentration or renin production) without significantly altering GFR. However, for clinical purposes the degree of renal injury and its clinical significance can best be judged by assessment of the degree of decline of GFR. We generally use serum creatinine concentration to assess GFR in clinical patients.

## SOURCE OF AZOTEMIA

Generally, azotemia may be pre-renal, renal, or post-renal in origin. Examples of prerenal dysfunction include systemic hypotension and dehydration. Examples of post-renal dysfunction include urinary tract obstruction and urinary bladder rupture. Regardless of the site of origin, renal dysfunction is characterized by the accumulation of nitrogenous waste, disordered electrolyte metabolism, and changes in body fluids status.

CKD is frequently present in patients presented for clinical therapy. The overall prevalence of renal disease in dogs and cats has been variously estimated at 0.5 percent to 2 percent of all animals. However, in animals presented to referral veterinary clinics, particularly older animals, the prevalence may be as high as 10 to 30 percent of all patients.

## STAGES OF FELINE CHRONIC KIDNEY DISEASE (fCKD)

fCKD is generally a progressive disease. Consequently, not all animals with fCKD should be managed similarly. One approach is to subdivide animals with chronic renal disease into four stages, as recommended by the International Renal Interest Society (IRIS; see Table 1).

### Stage I: Non-azotemic fCKD

A primary renal disease is any process that damages the kidney. Examples would include bacterial infection, hereditary nephropathy, neoplasia, and hypertensive nephropathy. Unfortunately in veterinary practice we frequently identify the consequences of destruction of renal tissue but not the cause of the destruction because we miss the early stage where there is damage but adequate renal function. This stage, here referred to Non-azotemic fCKD is defined as the initial stage of this process where renal tissue is damaged by a primary disease process but compensatory renal responses mask both the injury and its effect on the clinical patient. The animal is not azotemic but may have some compromise of urinary concentrating ability. This stage can be rather devastating to the kidney: renal functional reserve provides that an animal with 75 percent destruction of renal mass generally has no observable clinical signs!

If chronic renal disease is identified in this early stage, the primary goal is diagnostic: identify the primary cause of renal injury and this is often achieved with a renal biopsy. If renal imaging studies suggest a disease is generalized then an ultrasound guided needle biopsy is appropriate. However, animals with in this stage with focal, multifocal, and/or unilateral renal

disease are best assessed by exploratory surgery and directed biopsies of *both* kidneys. An unfortunate error is occasionally made when one presumes that a kidney appearing grossly normal is unaffected by a microscopic disease process. Therapeutic concerns in this first stage of renal disease center upon identification of clinical manifestations of renal injury such as systemic hypertension or proteinuria. Further therapeutic concerns include therapy designed to slow the progression of renal disease, such as dietary modification or the use of antihypertensive agents.

**Stage II: Mild renal azotemic**

The second stage of fCKD, herein referred to as mild renal azotemia, occurs when there is sufficient loss of renal tissue such that azotemia is present without clinical signs. During this stage, progression of the disease process is an important consideration and therapy is generally focused upon delaying this rate of progression. The rate of progression is often slow in cats (months to years) but erratic and more rapid in dogs (weeks to months). Therapy in dogs and cats with renal insufficiency would center upon dietary modification and/or the administration of antihypertensive agents, with these efforts designed to slow the progression of the fCKD.

**Stage III: Moderate renal azotemia**

The third stage of fCKD, herein referred to as moderate renal azotemia, is a transition stage. During this stage, progression of the disease process is still an important but clinical signs of uremia are often present, intermittently at first. Therapy in cats in stage III would center upon dietary modification, administration of antihypertensive agents, and supportive (symptomatic) care.

**Stage IV: Severe renal azotemia**

The fourth stage of renal disease is referred to as Severe Renal Azotemia. Animals in stage 4 fCKD often exhibit abnormalities of electrolyte balance and have markedly reduced ability to deal with changes in fluid and sodium intake. They may exhibit systemic hypertension. Poor appetite, nausea, and vomiting often lead to negative caloric and nitrogen balance causing loss of depot fat stores and depletion of lean body mass. In this advanced stage of renal disease, a nonregenerative, normocytic, normochromic anemia is often present and this complicates therapy. Animals with renal failure may have a subclinical compromise of both the immune system and hemostatic mechanisms. In stage IV, therapy focuses upon minimization of these clinical manifestations of uremia. While dietary therapy includes dietary protein and phosphorus restriction, it is often more important (and difficult) to assure adequate caloric intake.

Some of these complicating factors, such as electrolyte disorders and anemia, are readily identified by laboratory assessment of the patient. Other problems may be less readily apparent. For example, platelet function may be depressed in animals with renal failure, although this is a minor effect and, by itself, is not usually clinically important. This effect of renal failure on platelet function can be important in animals where there is another pre-existing coagulation disorder.

Systemic hypertension is often present in animals with stage IV or severe renal azotemia and BP should be assessed by appropriate direct or indirect measuring techniques to determine if hypertension is present and to plan accordingly. Animals with systemic hypertension (systolic BP>160 mmHg) are at risk for suffering an adverse event. The most common adverse events of marked systemic hypertension (systolic BP > 180 mmHg or an acute rise of systolic BP of 30 mmHg within 24 hours) include hypertensive retinopathy (intraocular hemorrhage, retinal edema, and/or retinal detachment in cats and dogs) and hypertensive encephalopathy (progressive stupor, coma, and seizures in cats). Therapeutic agents that raise BP, such as fluid and electrolyte solutions, should be used judiciously in these animals. Cats in particular, are

susceptible to the development of hypertensive encephalopathy, caused by cerebral edema. Where observed, emergency therapy is appropriate. Agents to use in this setting include amlodipine (0.25 mg/kg given orally once daily), hydralazine (2 mg/kg given orally or parenterally every 8-12 hours), or both.

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Table 1: IRIS* Classification of Feline Chronic Kidney Disease (fCKD)

| Stage | I | II | III | IV |
|---|---|---|---|---|
| | Non-azotemic fCKD | Mild renal azotemia | Moderate renal azotemia | Severe renal azotemia |
| Creatinine: | | | | |
| (μmol/L) | < 140 | 140 to 250 | 251 to 440 | > 440 |
| (mg/dl) | <1.6 | 1.6 to 2.8 | 2.9 to 5.0 | >5.0 |

*IRIS: International Renal Interest Society

# *IMPORTANCE OF PROTEINURIA AND MICROALBUMINURIA: MUCH ADO ABOUT WHAT?*

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We now recognize that proteinuria is associated with increased risk of developing end-stage renal failure in cats and with an increased risk of mortality even in nonazotemic animals. Further, studies have shown that therapies that reduce the magnitude of proteinuria are often renoprotective.

Recent findings have suggested that renal protein leak is not only a marker of severity of renal disease but also potentially could be a cause of renal injury. While the role of this protein leak in producing renal damage has not been clearly established in cats, findings in cell culture studies and investigations of rodent models of renal failure raise our concerns for the importance of separately evaluating our patients for the presence or absence of proteinuria and for monitoring patients with proteinuria to determine its magnitude, location, persistence. We should investigate proteinuria in those cases where it is present and institute appropriate therapy, if indicated. It is critical, however, that veterinary clinicians develop an enlightened approach to the diagnosis and management of proteinuria.

Proper management of proteinuria mandates two initial steps. First, a finding of proteinuria should lead to characterization (confirmation by sulfosalicylic acid or Robert's reagent or urine protein/creatinine ratio; quantification by the urine protein/creatinine ratio) and if confirmed, it should be categorized.

**Categorizing Proteinuria - Prerenal Proteinuria**

Prerenal proteinuria is caused by the presence of proteins in the plasma that are filtered through a normal glomerulus with normal permeability to macromolecules (i.e., permselectivity). These proteins may be normal proteins (e.g., hemoglobin) or abnormal proteins such as immunoglobulin light chains (e.g., Bence-Jones proteins)

**Categorization of Proteinuria - Postrenal**

Postrenal proteinuria is due to plasma proteins from hemorrhage or inflammation in the urinary tract (kidneys, ureters, bladder, urethra, and/or accessory sex glands). Many would also include extra-urinary losses such as from the accessory glands or genital tract as a postrenal cause of proteinuria..

**Categorization of Proteinuria – Three Types of Renal Proteinuria**

Most, but not all, causes of renal proteinuria are abnormal. There are some functional causes of proteinuria (e.g., fever or exercise) that are transient, mild, and reversible and considered variants of normal.

Pathological renal proteinuria is due to a renal abnormality in protein handling. It may occur from increased leakage of protein across the glomerulus (permselectivity defect causing glomerular proteinuria) or abnormal tubular handling of filtered protein (tubular proteinuria), or both. Tubular proteinuria occurs because small plasma proteins (<15,000 molecular weight) freely traverse the glomerular barrier. There are also small amounts of larger molecular weight proteins (e.g., albumin = 69,000 gm/mole) that are filtered through the normal filtration barrier. In a normal kidney, the tubules reabsorb practically all of this filtered protein. In some diseases (e.g., gentamicin nephrotoxicosis) the glomerulus is normal and permits filtering of only small molecular weight proteins and a minor amount of albumin. However, the diseased tubules are unable to metabolize these proteins and tubular proteinuria ensues.

Protein may also enter the tubular fluid from interstitial inflammation (e.g., pyelonephritis or renal neoplasia) and this is referred to as interstitial proteinuria.

**Proteinuria in cats**

Once proteinuria is identified and categorized, it is critical to ascertain whether or not it is persistent. Generally, this means assessing the urine protein/creatinine ratio on 3 occasions at 2 week intervals. In cats with chronic kidney disease, urine protein/creatinine values $\geq 0.4$ in cats are associated with an increased risk of mortality. A benefit of angiotensin converting enzyme inhibitor therapy has been shown for cats with a ratio of 1.0 or greater. Anti-proteinuric, renoprotective therapy is generally taken to be indicated in cats with kidney disease and a persistently elevated ratio which exceeds 0.5. In cats, this will initially be an angiotensin converting enzyme inhibitor (e.g., benazepril at 0.5 mg/kg once daily).

Results of recent studies suggest have heightened our concern about the importance of proteinuria in dogs and cats, as evidence suggests that persistent proteinuria is associated with progression of chronic kidney disease (CKD) and worsened mortality rates, perhaps even in animals without CKD. In veterinary medicine, we have traditionally relied upon the urine dipstick and more recently, the urine protein-to-creatinine ratio, to identify and characterize proteinuria. Now there is a renewed focus on proteinuria and more specifically on microalbuminuria as a screening test for our patients. It is altogether fitting and proper that we should do this.

It has long been known that in diabetic people, proteinuria is a hallmark of impending nephropathy. Studies to quantify protein in the urine of diabetic people demonstrated that even small quantities of albuminuria were predictive of subsequent renal disease. This small amount of albuminuria (30-300 mg albumin in a 24-hour urine collection) was less than that observed in overt proteinuria (>300 mg/24 hrs) and it became known as microalbuminuria because it was a comparatively smaller ("micro") amount of albumin observed in the urine. A 24-hour urine collection test to detect for the presence microalbuminuria test has been used for decades as a screen in diabetic people. In this nomenclature, < 30mg albumin/day is normal in people, 30-300 mg/day is defined as microalbuminuria, and >300mg/day is proteinuria.

While we often think of proteinuria originating from the glomerulus as a sign of kidney disease, recently it has been shown that in people with endothelial dysfunction small amounts of albumin can leak through the glomeruli of an otherwise normal kidney, producing microalbuminuria. This led to a new hypothesis: generalized endothelial dysfunction is manifest in the renal microcirculation as glomerular capillary albumin leak, which the clinician (veterinarian and physician) can detect as the presence of microaobuminuria. These consequent

small amounts of albumin may be detected only by sensitive tests, which may confirm the presence of microalbuminuria. Traditionally this would require a 24-hour urine collection as a screening test.

Tests for microalbuminuria became a focus in human medicine where microalbuminuria is an independent risk factor for death from cardiovascular disease and for the development of myocardial infarction and stroke in people with CKD. Indeed, these cardiovascular complications are more common end-points than uremic mortality for people with CKD. In the past decade it has become apparent that that microalbuminuria is a marker for fairly common renal and cardiovascular problems, including systemic hypertension, neoplasia, and generalized inflammatory conditions in people. As the need for a more clinically useful microalbuminuria test arose, measurement of the urine albumin/creatinine ratio (> 30 mg/gm is abnormal) or the use of albumin dipsticks became commonplace in people as a screening test for the presence of microalbuminuria.

Veterinary medicine has historically utilized the routine (traditional) urine dipstick as a screening tool for identifying proteinuria and employed the urine protein-to-creatinine ratio to provide semi-quantitative information about the magnitude of proteinuria in positive cases. This back-up test is required because the dipstick is only qualitative and is fraught with problems, particularly in specificity. There is now a commercially available albumin-detecting dipstick test (E.R.D.-Screen™ Urine Test, Heska, Ft. Collins, CO) which is more sensitive and specific than the routine urine dipstick and that could be used to confirm the presence of proteinuria in the face of a positive dipstick result. It is altogether fitting and proper that we should do this.

Critically, the traditional dipstick will generally detect urine albumin present at a concentration of ≥30 mg/dL, whereas the new albumin-specific dipstick can reportedly detect ≥ 1 mg/dL. Because this microalbuminuria is thus reportedly more sensitive than the traditional urine dipstick, it has been become possible to use this new dipstick as a test for the presence of microalbuminuria in dogs and cats. It can thus be employed as a screening test in dogs and cats, similar to the approach in people. By one method of classification in veterinary medicine, microalbuminuria is defined as a positive albumin-specific dipstick in the absence of a positive routine (traditional) urine dipstick. We could use this test to screen all dogs and cats for the presence of CKD or for the presence of endothelial dysfunction. Based on what we know today, we need to act cautiously in this regard as it is probably not altogether fitting and proper that we should do this.

First, transient microalbuminuria may be observed in a variety of transient conditions, some of which remain to be identified in dogs and cats. *Persistent microalbuminuria* is an important clinical finding. In dogs and cats, persistent microalbuminuria is defined by the ACVIM Proteinuria Consensus Panel as microalbuminuria found repeatedly in ≥ 3 specimens obtained ≥ 2 weeks apart which cannot be attributed to a postrenal cause. Persistent microalbuminuria is often due to altered glomerular permselectivity (CKD or endothelial dysfunction); but impaired tubular handling of the small amounts of albumin that traverses the normal glomerular filtration barrier can also cause microalbuminuria. There is no clinically applicable way to reliably determine the source of microalbuminuria (glomerular vs. tubular). Nonetheless, progressive increases in magnitude of microalbuminuria are likely to indicate significant renal injury.

Since *persistent microalbuminuria* may be a marker of either CKD or endothelial dysfunction in dogs and cats, a microalbuminuria screening test may lead to discovery of a

treatable underlying CKD or an inflammatory, metabolic, or neoplastic condition in an apparently healthy animal.

Urine testing that for the presence of microalbuminuria should be considered for the following circumstances: animals with chronic illnesses that may be complicated by proteinuric nephropathies (e.g., systemic lupus), screening apparently healthy dogs that are ≥ 6 years old and cats that are ≥ 8 years old, animals with confirmed or suspected systemic hypertension, screening dogs or cats to detect possible onset of a hereditary nephropathy as early as possible.

Much remains to be learned about this exciting and novel approach that utilizes of the presence of small amounts of protein in the urine as a potentially valuable early marker of CKD and other conditions of clinical importance in dogs and cats. As veterinarians, we should be open to adopting this approach as we carefully scrutinize the literature for developing new information. It is altogether fitting and proper that we should do this.

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# *The Renal-Hyperthyroid Connection*

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Renal insufficiency and hyperthyroidism are relatively common conditions of older cats. Hyperthyroidism is the most common endocrinopathy of older cats and chronic renal failure (CRF) is diagnosed commonly in older cats, especially those older than 10 years of age. Chronic renal failure is estimated to be the number two cause of death in domestic cats of the USA (Morris Animal Foundation Survey). It can be difficult to accurately diagnose cats with chronic renal failure, hyperthyroidism, or both conditions as there are many overlapping clinical signs (weight loss, polydipsia, polyuria, dilute urine). It is likely that hyperthyroidism is underdiagnosed in cats with chronic renal failure since nearly half of cats with CRF and hyperthyroidism will have a normal T4 level on a single measurement. In cats with a palpable thyroid nodule and CRF or chronic renal disease, definitive diagnosis of hyperthyroidism may require thyroid scintigraphy or T3-suppression testing.

The relationship between the development of hyperthyroidism as a consequence of renal insufficiency has not been explored. The possibility that hyperthyroidism causes chronic renal disease in some cats has received little attention. Most attention has focused on the simultaneous occurrence of renal insufficiency and hyperthyroidism in a population of cats under consideration for treatment of hyperthyroidism. It has been observed that a population of hyperthyroid cats develop azotemia or display a worsening of azotemia following therapy that induces euthyroidism. Hyperthyroidism potentially could induce renal failure through effects of systemic hypertension, intraglomerular hypertension/hyperfiltration ***(Scott: Has this been looked at by you or others ?),*** atypical hyperparathyroidism, and hypercalciuria.

Thyroid hormones exert major effects on renal functions. Normal cats undergo increased GFR and RBF and decreased BUN and serum creatinine following administration of exogenous thyroxine administration for 30 days (Adams 1997). Groups of cats with hyperthyroidism often have increased GFR compared to normal cats. Plasma iohexol clearance in 12 hyperthyroid cats was 3.83±1.82 ml/min/kg (N = 13) compared to normal cats at 1.83 ± 0.56 ml/min/kg (n = 10) (Becker 2000). Similar results were found when GFR was determined using DTPA clearance nuclear medicine (2.51±0.69 ml/min/kg in 13 hyperthyroid cats vs. 2.02 ± 0.27 ml/min/kg in 11 normal cats) (Graves 1994). Hyperthyroidism is known to result in dilute urine and polyuria with polydipsia. This effect is likely due to increased RBF and medullary solute washout, though a direct effect on the collecting tubules and ADH receptor interaction cannot be excluded. Psychogenic mechanisms also cannot be excluded. Hyperthyroidism is known to result in hypercalciuria in other species due to enhanced bone calcium mobilization; this effect may have some role in the development of polyuria as well as a possible role in creating chronic renal damage by excessive exposure of renal tissue to calcium. Most cats with hyperthyroidism also have increased systemic blood pressure, which could injure renal tissue. Hyperparathyroidism was noted in 77% of 30 cats with untreated hyperthyroidism; the magnitude of increased PTH levels was very large in some instances (Barber 1996). The reversibility of hyperparathyroidism following correction of hyperthyroidism has not been reported. Though serum creatinine (and calcium) was lower in this population of hyperthyroid and

hyperparathyroid cats, the possibility of renal secondary hyperparathyroidism cannot be excluded (renal disease may still exist and not be detected).

Hyperthyroid cats (n = 12) decreased GFR (iohexol clearance) from 3.83±1.82 to 2.02 ± 0.81 4 to 6 weeks following treatment with methimazole (Becker 2000). Two of these 12 cats developed overt azotemia following treatment in this same study though as a group increases in BUN or serum creatinine did not achieve statistical significance. Twenty-two hyperthyroid cats treated with radioiodine experienced no change in GFR, BUN, or creatinine 6 days following treatment (T4 was decreased), but BUN and creatinine were significantly increased at 30 days (T4 was also further lowered) (Adams 1997). No cats with a GFR > 2.25 ml/min/kg developed post treatment renal failure in this same study. Thirteen of 15 cats with GFR < 2.25 ml/min/kg were in renal failure 30 days following radioiodine treatment (2/15 that failed to suppress T4 did not develop azotemia); 9 of these 15 were azotemic prior to treatment; the others had normal parameters initially (Adams 1997). GFR (DTPA nuclear clearance) decreased from 2.51 ± 0.69 ml/min/kg to 1.40 ± 0.41 ml/min/kg 30 days following bilateral thyroidectomy in 13 cats (Graves 1994) while creatinine increased from 1.26±0.34 to 2.05±0.60 and BUN increased from 26.62±6.83 to 34.92±8.95.

Azotemia prior to treatment of hyperthyroidism was detected in as many as 41% of cats and in 59% of cats 30 days post treatment in one study (Adams 1997). Twenty-three percent developed azotemia for the first time following treatment in the same study. Mean serum creatinine and BUN increased at 30 and 90 days post-treatment in 58 cats treated by surgery, methimazole, or radioiodine; there were no differences in the magnitude of increase by treatment group (Dibartola 1996). Nine of these 58 cats had increased serum creatinine concentration prior to treatment. Two of 12( Becker 2000) and 2 of 13 (Graves 1994) cats developed overt azotemia following treatment with methimazole or bilateral thyroidectomy respectively. Based on results of these three studies, it appears that an estimate for the development of de novo azotemia following treatment for hyperthyroidism in cats is from 15-23%. Some increase in serum creatinine concentration is expected following the development of euthyroidism due to increased muscle mass (origin of creatinine), though decreased GFR certainly contributes to increased serum creatinine concentration. It is likely that lessening the degree of hyperthyroidism results in decreased RBF and GFR that unmasks azotemia in cats with marginal renal function prior to therapy.

Serum creatinine concentration in cats with reduced lean muscle mass may seriously underestimate any degree of excretory renal dysfunction since less creatinine will be generated from these muscles. Reduced muscle mass is common in advanced hyperthyroidism and in those with chronic renal disease. In these instances, serum creatinine will be lower than it would be if muscle mass were greater. It is wise to ask the question "What would the serum creatinine likely be if muscle mass were normal ?" It is possible that cats with upper range "normal" serum creatinine concentration and poor muscle condition have underlying renal disease. It is especially important in these situations to critically evaluate the results of urinalysis. If the urinary specific gravity is less than 1.040 increased suspicion for primary renal disease is warranted. Measurement of GFR using nuclear medicine clearance methods or iohexol clearance is recommended in cats whose renal function is uncertain prior to permanently inducing a euthyroid from hyperthyroid state. Those cats with lower values for GFR are at risk to develop overt azotemia and possibly clinical signs of CRF following conversion to euthyroidism. Rarely, some cats without pre-existing azotemia and with urinary specific gravity greater than 1.040 prior to treatment

develop CRF within 6 months of treatment for hyperthyroidism – whether this is a consequence of the conversion to euthyroidism in unclear.

Should cats with overt azotemia and hyperthyroidism be treated for hyperthyroidism ? Some endocrinologists and nuclear medicine specialists advocate so. It is likely that many of these cats will increase their level of azotemia following treatments that result in euthyroidism or hypothyroidism. In some cats this increase in creatinine will be mild, while other cats will experience large increases in serum creatinine. If clinical signs related to hyperthyroidism are severe, at attempt at treatment is warranted. We recommend screening cats with obvious azotemia and those suspected of renal disease with a methimazole challenge. Some had advocated that all cats should have methimazole challenge testing whether or not renal disease is suspected or not as the best standard of care. Methimazole treatment provides a reversible means of inducing euthyroidism and observing what happens to the level of renal function. An initial dose of 2.5 mg BID is given for 2 weeks and then serum biochemistry is repeated to evaluate renal function and T4 levels. If renal function is stable, the dose is gradually increased every two weeks as needed until T4 levels have entered the normal range if renal function remains stable. The dose can be increased to 2.5 mg TID, then 5 mg BID, and 5 mg TID if needed. Methimazole is discontinued if renal function deteriorates during the methimazole challenge. If renal function remains stable, then long-term methimazole can be considered for therapy or more-definitive treatment of hyperthyroidism provided by I-131 treatment or surgery. The definition of "stable" renal function is arbitrary and in our hospital means that the creatinine increased less than 2.0 mg/dl in those without initial azotemia and less than 1.0 mg/dl in those with obvious azotemia.

Supplementation with thyroxine should be considered for those cats with worsening signs of renal disease or excretory renal function that become hypothyroid following bilateral thyroidectomy or radioiodine treatment. About 9% of cats develop low T-4 values post I-131 treatment. Anecdotal evidence suggests that excretory renal function can be supported in some post-treatment hypothyroid cats when supplemental thyroxine is supplied. As a compromise, it may be desirable to titrate the dose of methimazole in cats with marginal renal function in such a way as to partially control the hyperthyroidism without decreasing GFR too much. Other treatments to control cardiac effects of uncontrolled hyperthyroidism may be warranted (beta blockers such as atenolol).
Body condition score of 2.0 of 5


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# *DIAGNOSIS AND TREATMENT OF FELINE SYSTEMIC HYPERTENSION*

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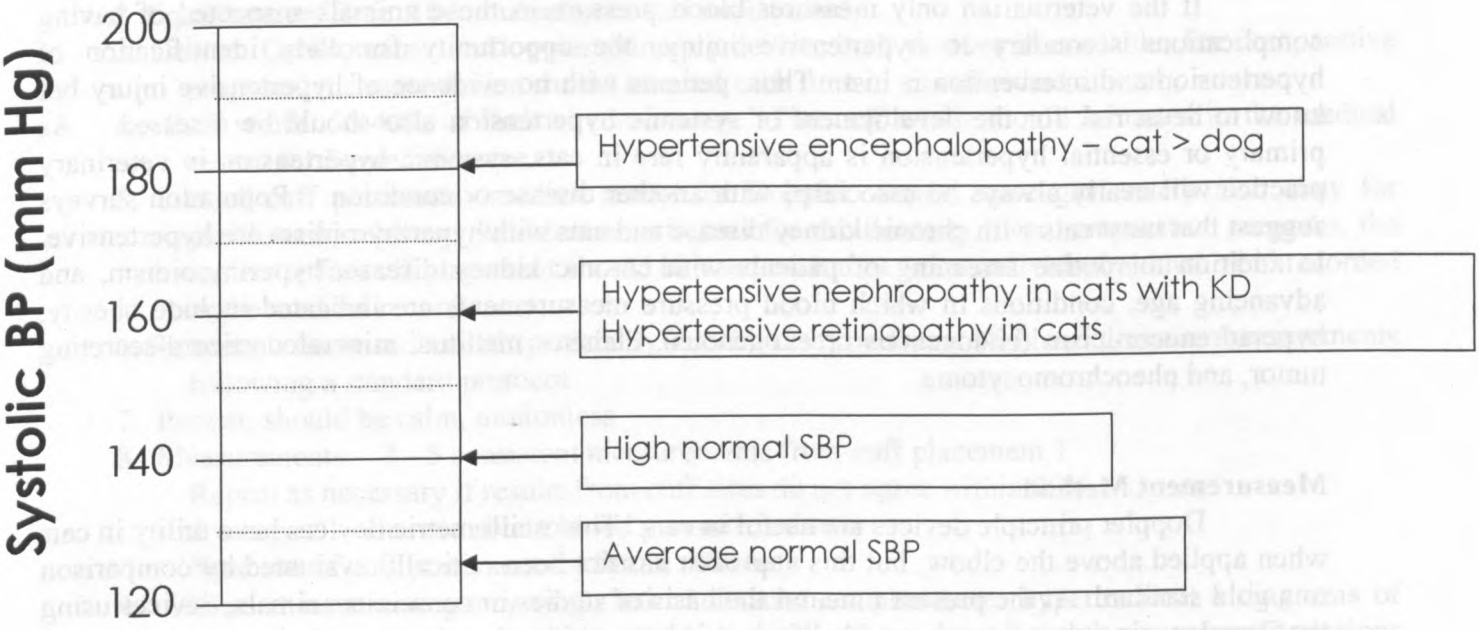
High systemic arterial blood pressure is commonly observed in dogs and cats with chronic kidney disease. In veterinary medicine, systemic hypertension has been associated with ocular pathology, progression of CKD, neurological complications, and cardiovascular changes. As our understanding of the prevalence and consequences of systemic hypertension moves forward, so must our ability to diagnose and manage this problem.

**Rationale for Diagnosis and Treatment**

Systemic hypertension can damage a variety of tissues. The kidney is susceptible to hypertensive injury. There is a clear association between ocular injury and marked systemic hypertension in dogs and cats. Findings associated with hypertensive injury include hemorrhage within the retina, vitreous, or anterior chamber; retinal detachment and atrophy; retinal edema; perivasculitis; retinal vessel tortuosity; and glaucoma.

Because the heart is working against an increased arterial pressure (i.e., afterload), left ventricular hypertrophy and secondary valvular insufficiency may be observed. Tachycardia is not a common finding with hypertension although some primary diseases that lead to secondary hypertension, such as hyperthyroidism, may also lead to elevated heart rate. Left ventricular hypertrophy may regress with antihypertensive treatment.

## Figure 1: Thresholds for adverse effects of systemic hypertension:



Signs consistent with cerebrovascular hemorrhage (head tilt, depression, seizures) have been seen clinically in cats with uncontrolled hypertension, and are often associated with a poor prognosis. However, cats suffering from systemic hypertension (systolic blood pressure >160 mmHg) occasionally develop a syndrome of progressive stupor, head pressing, and/or seizures which rapidly resolves with effective antihypertensive therapy. This syndrome is probably due to cerebral edema caused by high intracapillary hydrostatic pressure which develops once the systemic arterial pressure exceeds the autoregulatory range.

**Importance of Measurement of Blood Pressure**

A diagnosis of systemic hypertension is based upon determination of systemic arterial blood pressure. Further, the indiscriminate use of antihypertensive therapy in the absence of reliable values for systemic arterial blood pressure is inappropriate. This is highlighted by the fact that antihypertensive agents may induce a variety of side-effects, including dehydration and volume depletion; systemic hypotension leading to weakness, syncope, and renal dysfunction; or hypokalemia and associated clinical signs. Therefore, reliable measurement of blood pressure is required to establish a diagnosis of systemic hypertension and the efficacy of antihypertensive therapy must be judged upon the basis of blood pressure measurements.

**Which patients to assess?**

Blood pressure could be measured in patients with each of the following groups of patients: (i) all patients, (ii) patients with clinical signs referable to hypertensive injury, or (iii) patients at risk for developing systemic hypertension. While it is possible to measure blood pressure in all clinical patients, currently there is not sufficient rationale to do so in cats. Many hypertensive cats present with signs attributable to high systemic arterial blood pressure, such as blindness, hyphema, seizures, ataxia, or sudden collapse (signs compatible with cerebral vascular hemorrhage, edema, or stroke), or labored breathing (signs related to heart failure). It is clear that measurement of systemic arterial blood pressure should be an integral part of the management of these patients.

If the veterinarian only measures blood pressure in those animals suspected of having complications secondary to hypertensive injury, the opportunity for early identification of hypertension and intervention is lost. Thus, patients with no evidence of hypertensive injury but know to be at risk for the development of systemic hypertension also should be assessed. As primary or essential hypertension is apparently rare in cats, systemic hypertension in veterinary practice will nearly always be associated with another disease or condition. Population surveys suggest that most cats with chronic kidney disease and cats with hyperthyroidism are hypertensive. In addition to routine screening of patients with chronic kidney disease, hyperthyroidism, and advancing age, conditions in which blood pressure measurements are indicated include obesity, hyperadrenocorticism (endogenous or exogenous), diabetes mellitus, mineralocorticoid-secreting tumor, and pheochromocytoma.

**Measurement Method**

Doppler principle devices are useful in cats. The oscillometric devices have utility in cats when applied above the elbow, but this approach has not been critically evaluated by comparison to a gold standard. At the present time, on the basis of studies in conscious animals, devices using the Doppler principle are recommended for use in cats.

**Cuff choice and placement**

An oversized cuff may give erroneously low recordings; an undersized cuff a falsely high reading. Indirect blood pressure measurement studies should employ a cuff width that measures

30-40% of the circumference of the limb. If the ideal cuff width is midway between two available sizes, the larger cuff should be used, since it will theoretically produce the least error.

The cuff may be placed around the brachial, median, cranial tibial, or medial coccygeal arteries. Generally, for the Doppler technique the cuff is placed over the median artery and the transducer is placed between the carpal and metacarpal pad. Clipping of hair and application of acoustic gel at the site of transducer placement may enhance the signal. For the oscillometric technique, the median artery and coccygeal artery provided more reliable values than other sites in our studies.

The cuff should be placed at the level of the aortic valve. If not, a compensation can be made for gravitational effect with a 1.0 mmHg rise in blood pressure expected for each 1.3 cm of vertical distance between the level of the cuff and the level of the aortic valve.

**Anxiety and the white coat effect**

The visit to the veterinary clinic, hospitalization, presence in a strange environment, restraint in the examination room, clipper noise and vibration, cuff placement, cuff inflation, and other unusual stimuli in the setting of a veterinary hospital may induce anxiety in an animal during blood pressure measurement. As a consequence, a falsely elevated value for blood pressure may be obtained secondary to catecholamine release associated with this anxiety. Unfortunately, the magnitude of this effect varies widely between animals and between visits in the same animal. The extent of this effect may be minimized by doing the following: (a) obtain blood pressure measurements prior to a physical examination or other manipulations to which the animal may object, (b) perform all measurements in a quiet room utilizing a calm and reassuring manner, (c) allow the animal to acclimate to its surroundings for at least 5 minutes before obtaining blood pressure measurements.

**Conscious Animal Blood Pressure Measurement Procedure:**

1. Environment: Quiet, away from other animals, owner present (generally)
2. Equilibration Time: 10 minutes (quiet and undisturbed)
3. Device: Oscillometric or Doppler principle device; both devices if available. For comparative purposes, the same device should be used each time in an individual animal.
4. Cuff width: 30-40% of limb circumference. The cuff width should be noted in the medical record for future reference.
5. Site of cuff placement: median artery for Doppler device; coccygeal artery also okay for oscillometric device. Mid-humerus in cats for oscillometry. For comparative purposes, the same site for cuff placement should be used each time in an individual animal. And recorded in the medical record.
6. Personnel: Same individual (preferably a technician) performs all blood pressure measurements following a standard protocol
7. Patient: should be calm, motionless
8. Measurements: 3 - 5 consistent measurements from cuff placement 1
   Repeat as necessary if results from cuff sites do not agree within 20%
   Average all values to obtain blood pressure estimate
   Note site of cuff placement for future reference
9. Unless it is an emergency (e.g., retinal detachment plus sever hypertension) a diagnosis of systemic hypertension should be established only after at least 2 repeat measurement sessions confirm the elevated blood pressure. These sessions should be separated by at least 30 minutes.

**Which animals to treat?**

There is a clear association between end-organ injury and systemic hypertension in cats. We currently recommend the following classification system upon which to base treatment. Animals with confirmed hypertension should be treated while the animals should be treated only if there is evidence of ongoing hypertensive end-organ injury. Effective treatment of animals in stage II should be immediate. Those in Stage I can be further evaluated at the discretion of the clinician on the basis of the clinical findings. Frequent re-evaluations are appropriate in all of the higher blood pressure classes.

**Table 1: A Blood Pressure Classification System for Cats**

| Risk Category | Systolic | Diastolic | Risk of Future TOD |
|---|---|---|---|
| **I** | <150 | <95 | *Minimal* |
| **II** | *150-159* | *95-99* | *Mild* |
| **III** | *160-179* | *100-119* | *Moderate* |
| **IV** | *≥180* | *≥120* | *Severe* |

**Therapeutic Goal**

It is usually not possible to restore blood pressure to normal values when treating a hypertensive animal. It should be the veterinarian's goal to lower the blood pressure to within 25-50 mmHg of the normal ranges for blood pressure, ideally lowering pressure (systolic/diastolic) to < 160mmHg/100mmHg.

**Therapy**

An inhibitor of angiotensin converting enzyme (e.g., 0.5 mg enalapril or benazepril/kg orally every 12-24 hours) may lower blood pressure. In cats, though, the role of the renin-angiotensin system in the maintenance of systemic hypertension has been questioned and though less effective in cats, a higher dosage (1-2 mg enalapril/kg orally every 24 hours) may prove efficacious in hypertensive cats. The co-administration of an ACE inhibitor and a calcium channel antagonist (see below) may prove effective when monotherapy is not sufficient in lowering blood pressure.

Some drugs classified as calcium channel antagonists reduce total peripheral resistance, leading to a decrease in blood pressure. Amlodipine besylate, a long-acting dihydropyridine calcium antagonist, has been used successfully as a single agent in hypertensive cats at a dosage of 0.625 mg/cat orally every 24 hours. Larger cats (>4 kg) often require 1.125 mg orally every 24 hours. Blood pressure decreases significantly during amlodipine treatment, and significant adverse effects (i.e., azotemia, hypokalemia, weight loss) are not frequently identified. Because amlodipine has a slow onset of action, adverse effects such as hypotension and loss of appetite are usually avoided.

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# *FELINE OBESITY: OVERNUTRITION OR WRONG NUTRITION?*

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"The smallest feline is a masterpiece" – so said Leonardo Da Vinci. Cats are truly unique in almost every aspect of their existence, from their behavior to their biochemistry. It is those differences that bring us to our topic of discussion: the nutritional peculiarities of the feline. In particular, this review is not going to simply be an accounting of their metabolic differences, but more importantly, an overview of how not taking into account these differences lead to disease (hepatic lipidosis), disability (obesity), and possibly, nutritional problems for our sick feline patients.

**Feline Nutrition**

Cats are obligate carnivores. This statement is news to no one, and yet many don't recognize the importance of that statement. While cats can use carbohydrates (CHO) as a source of metabolic energy, they have no requirement for them (nor do dogs for that matter). But, more importantly, because cats evolved consuming prey (e.g. high protein, low to moderate fat, minimal carbohydrate), they are metabolically adapted for higher protein metabolism and lower CHO utilization. What does that mean metabolically and nutritionally? There are a number of specific metabolic and biochemical differences in feline physiology that are important. For those who are interested in the specific details of these metabolic and physiologic differences in the nutritional biochemistry of cats, the reader is referred to a recent review of this subject[1]. To summarize the major differences, cats have obligate and daily needs for additional protein, specific requirements for certain amino acids (e.g. taurine, arginine), increased requirements for many B vitamins, and reduced ability to digest, absorb and metabolize carbohydrates. This paper will discuss several important medical problems in cats that may be directly linked to, or may be specifically managed by, dietary manipulation.

**Cats and Nutrition: Key Facts**

- Cats have an obligate need for protein and amino acids in their daily diet because they are unable to down regulate their urea cycle or transaminases (protein conversion to energy) as other species can in times of starvation
- Cats utilize protein for energy, even in the face of large amounts of CHO in the diet (there is no "down-regulation" or protein sparing when CHO are plentiful in the diet as with other species)
- Taurine, arginine, methionine, cysteine, and possibly carnitine requirements for cats are greater than non-carnivores
- Arachidonic acid is also an essential fatty acid in cats (it is not in dogs), and is found only in fats from animal tissue
- Cats require vitamin A and D to be present in the active form in their diet as they are unable to synthesize adequate amounts from other dietary precursors (e.g. carotenoids or vitamin D precursors in skin)
- Cats have an increased need for many B vitamins in their diet (e.g. thiamin, pyridoxine, niacin, pantothenic acid) as they have greater metabolic needs for these vitamins and cannot synthesize or get them from other sources.

- Salivary amylase is absent in cats, and they have greatly reduced levels of intestinal and pancreatic amylases – so CHO digestion is much less efficient.
- Cats have fewer disaccharidases and other brush border enzymes in their small intestine designed to digest and absorb starches.
- The small intestine of cats is much shorter than that of an equally sized omnivore – longer GI tracts are necessary for handling of complex carbohydrates.
- Cats have greatly reduced activities of hepatic enzymes (e.g. glucokinase) designed to convert a post prandial glucose load to glycogen and thus are less able to handle this glucose load.
- There are no fructokinases in cats – they are unable to utilize fructose and other simple sugars.

**Feline Obesity**

While figures vary, recent studies indicate that greater than 35% of cats in the United States are overweight or obese. There are a large number of factors that contribute to this problem, including sex (intact vs. neutered, male vs. female), age, activity (indoor vs. outdoor), and feeding style (meal feeding vs. free choice). Nevertheless, obesity is a significant contributor to morbidity in middle aged to older cats. Further, "it is much harder to take it off, than it is to put it on" – as we are all very aware. One factor that is increasingly being considered, both in the development of and treatment of obesity, is the role of CHO in diet. Because of the metabolic requirement for cats to utilize protein as an energy source, CHO in the diet that are not immediately used for energy (e.g. via exercise or other utilization for energy) will be stored as fat. Traditional weight loss plans include feeding an energy restricted (e.g. low fat, high CHO, high fiber) diet. However, while these diets may result in weight loss, they do so to the detriment of lean body mass. Successful weight loss requires loss of adipose tissue as well as maintenance of lean body mass, as lean body mass is the driver of basal energy metabolism (loss of lean body mass is a major contributor to weight regain as appetite is not reduced and satiety not reached). Several recent studies have evaluated use of a high protein, low CHO diet (protein 45% or higher) for weight loss in cats, and in those studies, all cats lost weight, but maintained lean body mass. Importantly, high protein, low carbohydrate diets not only result in sustained weight loss in these cats, but also in normalization of appetite (reduced urge to eat constantly because they are satiated). Because dry foods must be extruded (i.e. made into a biscuit), CHO are required in the cooking process, and thus, the best commercial diets for achieving a high protein, low CHO profile are canned (e.g. kitten or growth) foods. However, there are now prescription diets formulated with a high protein/low CHO profile that are designated for weight management or, as we will talk about next, control of diabetes mellitus.

Calculating calories: Most indoor cats do not need more than their resting energy requirement (RER) to meet their daily nutritional requirements. Cats that are very obese may need to reduce their intake by 20-40% (or 60-80% of RER) to lose weight. RER = $70(BW_{kg})^{0.75}$ or if the cat is > 2kg: $30(BW_{kg}) + 70$. Thus, if a 5 kg cat needs 220 kcal for RER, but is still obese, the intake must be reduced by 20% (200 kcal/day) or 40% (160-180 kcal/day). EXAMPLE: Hill's m/d = 165 kcal/can, while Hill's m/d dry = 485 kcal/cup – thus, it is much more difficult to reduce calories using the dry food.

Key Points: The commercially available diets lowest in CHO are canned foods. The best high protein/low CHO diets are canned kitten foods or new diabetes diets (Hill's m/d, Purina DM, Purina OM). Most cats should be fed some (50% is a starting point) canned food as part of their diet – both to reduce the CHO in their diet, but also to better control calories (dry foods are very

calorie dense), and to increase the amount of water consumed daily. An important follow up point to remember about all diets is that calories count. You cannot free choice feed cats – even with high protein, low carb diets – because if they consume too many calories (and the diabetes diets are very calorie dense) they will remain obese. Also, calorie control and feeding canned foods must be started when they are kittens, as they will not learn to accept canned food (many adult cats won't eat canned food because they were never introduced to it as kittens). This is not only important for diet selection now, but if later in life the cat requires a canned prescription diet for a specific problem (e.g. kidney disease or urinary disease), they will more readily accept it if they already eat some canned food.

**Feline Diabetes Mellitus**

Approximately 65% of all diabetic cats fall into the category of Type II diabetes (obese, but may be transient, insulin or non-insulin dependent). This is in contrast to the disease in dogs, where the overwhelming majority of cases are Type I (insulin dependent) diabetes. Dietary recommendations for years (which were extrapolated from human and canine recommendations) have been to feed these affected cats with diets high in complex CHO (e.g. high fiber diets). However, with our awareness of the role of diet in management of the problem of obesity, as well as some of the dietary issues that confound treatment of feline diabetes, these recommendations have been appropriately challenged. Recent studies have shown that high-protein, low-CHO diets are beneficial in the management of diabetes in cats, resulting in a greater than 50% reduction in the amount of insulin in 8 of 9 cats in one study. In another study, complete cessation of the insulin requirement occurred in a third of the cats. Other studies have recently shown that, contrary to what is observed in dogs, fiber containing diets do not alter glucose tolerance (an important reason for feeding high fiber diets in diabetic dogs and people). Another benefit of high protein/low CHO diets is that there is a reduction in post-prandial hyperglycemia (fewer CHO in diet to lead to a smaller post-prandial surge) and, this results in a concurrent reduction in hyperglycemia induced glucose toxicity.

Key points: The best commercially available diets for diabetic cats are high protein/low CHO canned diets (e.g. Hill's m/d or Purina DM, Purina OM, or canned kitten foods). For cats that won't eat canned foods, dry formulas that are high protein/low CHO include Purina DM, Purina OM, and Hill's m/d.

**Feline Hepatic Lipidosis**

Idiopathic hepatic lipidosis (IHL) is a common hepatobiliary problem in cats that stop eating, especially in cats that are obese or undergoing stress or illness. However, recent studies suggest IHL is the result of a combination of factors: excessive peripheral lipid mobilization (due to high catecholamine release from stress or illness), and subsequent development of nutritional deficiencies that compromise the formation of lipoproteins and the mobilization of hepatic triglycerides. The individual nutrients that may be involved include taurine, carnitine, arginine, threonine, citrulline, choline and cobalamin. However, the key to treatment of IHL remains feeding affected cats, usually through a feeding tube (esophagostomy or PEG tube) until their metabolism normalizes. Feeding a high quality, moderate to high protein diet for 2-6 weeks, or until the cat begins to eat again, is the most important aspect of treatment. This cannot be over-stated: the key to treatment is for the cat to receive adequate protein and fat calories via tube feeding to correct the nutritional imbalance that has been created. Force feeding cats is not appropriate for treatment of this disease for several reasons: 1) the disease will require nutritional support for 2-4 weeks in most cats to overcome the metabolic disturbance, 2) it is very difficult to achieve the daily caloric requirement by force feeding, and 3) force feeding cats, can lead to food aversion and additional stress.

Key points: Most cats with hepatic lipidosis need a high calorie, high protein diet such as Hill's a/d, Eukanuba Maximum calorie, or other recovery diet. If the cat has severe liver failure and cannot tolerate high protein diets, use of Hill's l/d (liver diet) or one of the canned renal failure diets is an acceptable alternative.

**Juvenile Feline Diarrhea**

There are a few factors to consider in the development of diarrhea in kittens, but dietary causes are important. First, a few facts: it is believed (with the published information that we have) that cats have much higher concentrations of bacteria in their small intestine, compared to dogs and people. The reason for the increased intestinal microflora in cats is not known, but along with their shorter overall intestinal length (compared to dogs), the presence of increased numbers of bacteria may serve to enhance digestion of proteins and fats, both of which are higher in normal feline diets. Conversely, diets higher in CHO and fiber (especially soluble fibers) may predispose cats to intolerance, changes in bacterial flora numbers or species, or result in osmotic overload. This problem may become prominent when kittens are switched from milk or canned foods to dry food (because of the high CHO in dry foods). The alterations in bacterial populations or species are believed to lead to the development of diarrhea.

Key point: In young cats with diarrhea, or cats with intermittent vomiting or diarrhea that may be a result of dietary intolerance, feeding diets high in protein and low in CHO, along with antibiotic therapy, may resolve the problem.

**Feline Inflammatory Bowel Disease**

Feline inflammatory bowel disease (IBD) is an idiopathic, inflammatory disease of the intestinal tract for which dietary and immunosuppressive/anti-inflammatory therapy seems to control, but for which we still have no clear understanding of its cause or perpetuation. A wide variety of possible causes have also been investigated in humans with IBD, but current research is focused on the role of bacteria in the development and progression of the aberrant immune response that occurs in humans. This hypothesis may also be important in the pathogenesis of feline IBD as well, especially owing to the fact that cats often respond when combinations of metronidazole and steroids are used together. Further supportive evidence for a specific role of bacteria in the development of feline IBD is lacking, but several aspects of feline digestion and feline diets are suggestive of a possible role for microbes in the disease (see above). Diets higher in CHO and fiber (especially soluble fibers) may predispose cats to intolerance, changes in bacterial flora numbers or species, or result in osmotic overload. It is the alterations in bacterial populations or species that is believed to lead to the abnormal intestinal inflammatory response in humans with IBD, and may also be important in feline IBD as well. Dietary therapy may be appropriate for prevention of feline IBD, but once the disease has been initiated, these diets may not be sufficient to control the aberrant immune response. In fact, increased protein may result in an increased exposure of the gut immune system to these proteins resulting in further sensitization and inflammation. Nevertheless, this merits addition consideration and research as we continue to seek answers to perplexing issue.

**Zoran, DL.** Feline Nutrition: The Carnivore Connection, *JAVMA*, December, 2002.