21st Annual Fred Scott Feline Symposium

July 24–26, 2009

Veterinary Education Center
Cornell University
Ithaca, New York

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Photo by Alexis Wahski Roberts

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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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General Information and Logistics

21st Annual Fred Scott Feline Symposium
July 24-26, 2009

Course Overview

This year's 21st Annual Fred Scott Feline Symposium will educate and update veterinarians in gastrointestinal diseases, modern diagnostic medicine, feline diabetes, feline obesity, feline vaccine controversies, infectious diseases, feline nutrition, feline kidney diseases, and feline anesthesiology.

Accreditation and Continuing Education Credit

The College of Veterinary Medicine at Cornell University accredits this symposium for a maximum of 17 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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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 25. The certificate verifies your attendance at the 21st 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. Michael Lappin on Friday in S1 007 Schurman Hall. If you signed up to have lunch with Dr. Lappin on Friday please turn in your ticket to the staff member at the room entrance.
- Lunch with Dr. Jacquie Rand on Saturday in S1 007 Schurman Hall. If you signed up to have lunch with Dr. Rand on Saturday please turn in your ticket to the staff member at the room entrance.

Tours

If you registered to participate in a tour of the college during lunch on Friday you will find an admittance ticket in the back of your nametag. Please meet in the Atrium at the beginning of your lunch break.

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

21st Annual Fred Scott Feline Symposium
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- All lectures will be held in Lecture Hall I in the Veterinary Education Center.
- Continental Breakfasts and breaks will be located in the Hagan Room.

Friday, July 24, 2009

7:30 - 8:00 am	Registration Continental Breakfast **SPONSORED BY MERIAL**
8:00 - 8:15	Welcome - *Carolyn McDaniel*
8:15 - 9:15	Update on the Management of Feline Infectious Gastrointestinal Diseases (Part 1) *Michael Lappin*
9:15 - 9:30	Break
9:30 - 10:30	Update on the Management of Feline Infectious Gastrointestinal Diseases (Part 2) *Michael Lappin*
10:30 - 10:45	Break
10:45 - 12:15 pm	Feline Vaccine Controversies *Michael Lappin* **James R. Richards, Jr. Memorial Feline Lecture**
12:15 -1:30	Lunch in the Cafeteria
1:30 - 2:30	Pet Ownership for Immune Suppressed Individuals *Michael Lappin*
2:30 - 2:45	Break
2:45 - 4:15	Diagnostic Medicine: Use of Molecular Assays in Feline Infectious Diseases (Part 1) *Michael Lappin*
4:15 - 4:30	Break
4:30 - 5:30	Diagnostic Medicine: Use of Molecular Assays in Feline Infectious Diseases (Part 2) *Michael Lappin*
6:30 - 9:00	**Annual Picnic** at the Six Mile Creek Winery Directions are available at the registration desk.

Saturday, July 25, 2009

7:30 - 8:00 am	Continental Breakfast
8:00 - 9:00	Feline Obesity *Jacquie Rand*
9:00 - 9:15	Break
9:15 - 10:15	Feline Diabetes Mellitus: Pathogenesis & Principles of Therapy *Jacquie Rand*
10:15 - 10:30	Break
10:30 - 11:30	Feline Diabetes Mellitus: Which Insulin Do I Choose and How Do I Adjust the Dose? *Jacquie Rand*
11:30 - 12:30 pm	Feline Diabetes Mellitus: What Diet Should I Choose and How Do I Manage Problem Cats *Jacquie Rand*
12:30 - 1:30	Lunch in the Cafeteria **SPONSORED BY INTERVET SCHERING-PLOUGH ANIMAL HEALTH**
1:30 - 2:30	The State of Feline Nutrition: Where Are We and What Do We Know about Disease Management and Prevention? *Joseph Wakshlag*
2:30 - 2:45	Break
2:45 - 3:45	Feline Pancreatitis: Where Are We? *Kenneth Simpson*
3:45 - 4:00	Break
4:00 - 5:00	A New Perspective on Feline Inflammatory Liver Disease *Sharon Center*
6:00 - 9:00	**Optional Cayuga Lake Dinner Cruise**

Sunday, July 26, 2009

8:00 - 8:30 am	Continental Breakfast
8:30 - 10:00	What's New in Feline Kidney Disease? *Richard Goldstein* **SPONSORED BY IDEXX**
10:00 - 10:15	Break
10:15 - 11:45	Update on Feline Anesthesia and Analgesia *Andrea Looney*

Corporate Sponsors and Exhibitors

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James R. Richards, Jr. Memorial Feline Lecture

The James R. Richards Jr. Memorial Feline Lectures were established to honor the outstanding contributions that the late Dr. James R. Richards Jr., made to the field of feline medicine to improve the health and well being of cats everywhere. A series of state-of the-art lectures on various areas of feline medicine will be held (1) periodically at the College of Veterinary Medicine, (2) at the annual New York State Veterinary Conference, and (3) at the annual Fred Scott Feline Symposium.

Dr. Richards was Director of the Cornell Feline Health Center (1997-2007), and Past President of the American Association of Feline Practitioners. Funds contributed to the James R. Richards, Jr. Memorial Fund for Feline Health at Cornell University by his many friends and colleagues are being placed in an endowment fund, and the income from this fund will support these memorial lectures in perpetuity.

Annual Picnic

The annual picnic will be held at the Six Mile Creek Vineyard and includes a wine tour for those who are interested. Wines served at the picnic are from Six Mile Creek Vineyard and the vineyard is offering our guests a 20% discount on wine purchases.

Exhibitors

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Faculty

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Sharon A. Center, BS, DVM, Dipl ACVIM

With a background in biology and chemistry, Dr. Center completed her veterinary training at the University of California at Davis, a rotating Internship in Small Animal Medicine and Surgery, Residency in Internal Medicine at the New York State College of Veterinary Medicine, Cornell University, Ithaca, NY, and thereafter achieved board certification in the American College of Veterinary Internal Medicine. She spent 3 years in private practice and joined the veterinary faculty at Cornell in 1983 where she currently is a Professor of Internal Medicine. Her responsibilities include co-managing the Internal Medicine referral service, providing didactic lectures in the areas of hepatobiliary, renal and hematologic disorders to 3rd and 4th year veterinary students, training hospital Interns and Medicine Residents in the area of Veterinary Internal Medicine. She conducts research focused in the area of canine and feline hepatobiliary disorders, including disease characterization, diagnostic evaluations, and therapeutic interventions, nutritional management, and provides consultations in the area of hepatobiliary disease including histopathologic disease characterizations. Dr. Center's current research activities include investigation of energy utilization and body composition in clinically ill cats and dogs with the objective of refining recommendations for drug dose adjustments and nutritional support; a nationwide prospective study of chronic hepatitis in the dog, and metabolism and systemic effects of glucocorticoids in the cat. She has authored numerous research and clinical manuscripts and book chapters in the area of hepatobiliary metabolism and disease, diagnostic evaluations and treatments and has lectured widely on these topics.

Richard E. Goldstein, DVM, Dipl ACVIM, Dipl ECVIM-CA

Richard Goldstein graduated from the Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Israel in 1993. He completed an internship at the same institution and he completed a residency in Small Animal Internal Medicine at the University of California, Davis, in 1998. Goldstein spent two years in a private specialty practice in Southern California and one year as a faculty member at the Koret School in Israel, before joining the faculty at Cornell in September of 2001. He is currently an Associate Professor of Small Animal Internal Medicine at Cornell and is board certified in Small Animal Internal Medicine by the American College of Veterinary Internal Medicine and is certified by the European College of Veterinary Internal Medicine - Companion Animals. His clinical and research interests include small animal nephrology and the effects of renal disease on other body systems, infectious disease, endocrine disease, and canine and feline genomics.

Michael R. Lappin, DVM, PhD

After graduating from Oklahoma State University in 1981, Dr. Lappin completed a rotating internship in small animal medicine and surgery at the University of Georgia. After 2 years in a small animal practice in Los Angeles, he returned to the University of Georgia where he completed a small animal internal medicine residency and a PhD in Parasitology. Dr. Lappin was board certified by the American College of Veterinary Internal Medicine in 1987. He is currently Professor of Small Animal Internal Medicine at the College of Veterinary Medicine and Biomedical Sciences at Colorado State University. Dr. Lappin studies feline infectious and immune-mediated diseases and has written many primary research manuscripts and book chapters. His principal areas of interest are prevention of infectious disease, vaccine associated side effects, the upper respiratory disease complex, infectious cause of fever, infectious causes of diarrhea, and zoonoses of cats. Dr. Lappin is on the editorial board of Feline Medicine and Surgery and Compendium for Continuing Education for the Practicing Veterinarian and is the editor of the textbook, *Feline Internal Medicine Secrets*. Dr. Lappin has received the Beecham Research Award and the Norden Distinguished Teaching Award. He is the Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine at Colorado State

University and is the Assistant Department Head for Research. He was the chairperson of the AAFP Panel on Feline Zoonoses and the AAFP Bartonella Panel Report. Dr. Lappin is the director of the "Center for Companion Animal Studies."

Andrea Looney, DVM, Dipl ACVA

Dr. Looney graduated from the College of Veterinary Medicine at Cornell University in 1989. She was an instructor at Cornell University Hospital for Animals from 1990-1993 in the Department of Anesthesiology and then an instructor in the Department of Community Practice Medicine for three years. In 2001, she received board certification from the American College of Veterinary Anesthesiology and currently is a Senior Lecturer for the College's Section of Anesthesiology. Dr. Looney's interests include emergency medicine, perioperative care and pain management.

Jacquie Rand, (Melb), DVSc (Guelph), Dipl ACVIM (Internal Medicine)

Professor Rand was appointed Professor of Companion Animal Health in 2001, and in 2002 became founder and director of the Centre for Companion Animal Health at the University of Queensland, Australia. She is an internationally recognised leader in diabetes and obesity research in cats and dogs. She has published extensively in these areas, and is the author of many book chapters, and is editor of the best-seller Problem-based Feline Medicine.

In addition to her diabetes and obesity research, Professor Rand is currently involved in developing programs in areas that enrich human-animal relationships, and prevent unwanted and problem pets, as well as fundraising to support a wide variety of research in companion animal health throughout the veterinary school. Professor Rand has attracted extensive and ongoing support for Centre studies from industry groups in the US and Europe.

Professor Rand graduated from Melbourne University in 1975, and worked in practice for 8 years before doing a residency and doctorate at the Ontario Veterinary College, Canada, followed by 3 years as a senior registrar at the University of Zurich, Switzerland. She became a Diplomate of the American College of Veterinary Internal Medicine in 1989; and in 1990 returned to Australia to take up a senior academic position at the University of Queensland.

Jacquie is married with a teenage daughter, Lisette, and lives with her husband Tom in Brisbane. Two other wonderful family members are her dog Mescha and a Burmese cat, Merlin. Jacquie's leisurely pursuits include orienteering and cross country skiing.

Kenneth W. Simpson, BVM&S, MRCVS, Dipl ACVIM, Dipl ECVIM-CA

Kenneth W. Simpson is a 1984 graduate of the Royal (Dick) School of Veterinary Studies at the University of Edinburgh. In 1989 Dr. Simpson received his PhD from the School of Medicine at the University of Leicester in England. He completed an internship at the College of Veterinary Medicine at the University of Pennsylvania in 1989 and a residency in Small Animal Internal Medicine at the Ohio State University in 1991. He is board certified by the American College of Veterinary Internal Medicine and the European College of Veterinary Internal Medicine.

Dr .Simpson has been a faculty member the Cornell's College of Veterinary Medicine since 1995 and has been a mentor, supervisor, and adviser to many interns, residents, and graduate students. He is currently Chief of the Section of Small Animal Medicine in the Cornell University Hospital for Animals. His clinical sub-specialization and research interests are in gastroenterology and host-bacterial interactions. Dr. Simpson is the recipient of several awards including the National Phi Zeta Award and Pfizer Award for Research Excellence and is a past-President of the Comparative Gastroenterology Society.

Joseph Wakshlag, DVM, PhD, Dipl ACVN

Dr. Wakshlag joined the clinical faculty approximately three years ago as a clinical nutritionist. He received his DVM in 1998 from Cornell University and continued training in pathology before embarking in a combined PhD and residency in Clinical Nutrition. Since receiving his PhD in 2005 he worked in private practice before returning to Cornell in 2006. Since then he has received board certification by the American College of Veterinary Nutrition. His research interests include metabolism of obesity and performance as well as nutritional intervention during cancer.

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FELINE INFECTIOUS GASTROINTESTINAL DISEASES

Michael R. Lappin, DVM, PhD, DACVIM
The Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine
College of Veterinary Medicine and Biomedical Sciences
Colorado State University, Fort Collins Colorado

Clinical problem and differentials. Vomiting is the forceful ejection of stomach and proximal duodenal contents through the mouth. Vomiting can be induced by vestibular, vagal, chemoreceptor trigger zone, or direct input to the emetic center. Diarrhea is a characterized by increased frequency of defecation, increased fluid content of the stool, or increased volume of stool. Markedly increased frequency of defecation, small volume stools, tenesmus, urgency, hematochezia, and mucus are consistent with large bowel diarrhea. Slight increase in frequency of defecation, large volume, melena, steatorrhea, and polysystemic clinical signs are more consistent with small bowel diarrhea. Mixed bowel diarrhea is a combination of characteristics or clinical signs. Gastrointestinal (GI) signs can be the result of primary diseases of the GI system or secondary GI diseases. The secondary GI diseases are generally those of the kidneys, liver, pancreas (pancreatitis or exocrine pancreatic insufficiency), endocrine system (hypoadrenocorticism; diabetic ketoacidosis; hyperthyroidism), or central nervous system. Differential diagnoses for primary GI diseases are often grouped into obstruction (masses, foreign body, and intussusception), dietary intolerance, drugs/toxins (garbage gut), inflammatory gastric and bowel diseases, neoplasia, infectious diseases, and parasites. The primary bacteria associated with gastrointestinal tract disease in cats include *Salmonella* spp., *Campylobacter jejuni*, *Clostridium perfringens*, *Helicobacter* spp., bacterial overgrowth syndrome, bacterial peritonitis, and bacterial cholangiohepatitis. The primary viral agents include feline coronaviruses, feline leukemia virus, feline immunodeficiency virus, and feline panleukopenia virus. The primary nematodes are *Ancylostoma/Uncinaria, Strongyloides cati*, *Dirofilaria immitis* (vomiting), *Toxocara cati*, *Toxascaris leonina*, *Ollulanus tricuspis*, and *Physaloptera* spp. Enteric protozoans include *Giardia* spp., *Cystoisospora* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, and *Tritrichomonas foetus*. The cestodes *Taenia*, *Dipylidium*, and *Echinococcus* generally cause subclinical infection.

DIAGNOSTIC PROCEDURES FOR INFECTIOUS DISEASES

Direct smear. Liquid feces or feces that contains large quantities of mucus should be microscopically examined immediately for the presence of protozoal trophozoites, including those of *Giardia* spp. and *Tritrichomonas foetus*. A direct saline smear can be made to potentiate observation of these motile organisms. The amount of feces required to cover the head of a match is mixed thoroughly with one drop of 0.9% NaCl. Following application of a coverslip, the smear is evaluated for motile organisms by examining it under 100X magnification. The sample should be fresh. The material for evaluation should be collected from the surface of the fecal material, preferably mucous if present. Alternately, a rectal scraping can be used.

Stained smear. A thin smear of feces should be made from all cats with large or small bowel diarrhea. Material should be collected by rectal swab if possible to increase chances of finding white blood cells. A cotton swab is gently introduced 3-4 cm through the anus into the terminal

rectum, directed to the wall of the rectum, and gently rotated several times. Placing a drop of 0.9% NaCl on the cotton swab will facilitate passage through the anus, but not adversely affect cell morphology. The cotton swab is rolled on a microscope slide gently multiple times to give areas with varying smear thickness. Following air drying, the slide can be stained. White blood cells and bacteria morphologically consistent with *Campylobacter jejuni* or *Clostridium perfringens* can be observed after staining with Diff-Quick or Wright's-Giemsa stains. *Histoplasma capsulatum* or *Prototheca* may be observed in the cytoplasm of mononuclear cells. Methylene blue in acetate buffer (pH 3.6) stains trophozoites of the enteric protozoans. Iodine stains and acid methyl green are also used for the demonstration of protozoans. Acid-fast or monoclonal antibody staining of a fecal smear should be performed in cats with diarrhea to aid in the diagnosis of cryptosporidiosis. *Cryptosporidium parvum* is the only enteric organism of approximately 4 to 6 μ in diameter that will stain pink to red with acid-fast stain. Presence of neutrophils on rectal cytology can suggest inflammation induced by *Salmonella* spp., *Campylobacter* spp., or *Clostridium perfringens*; fecal culture is indicated in these cases. Fecal enterotoxin measurement should be considered for cats with spore-forming rods morphologically consistent with *C. perfringens*.

Fecal flotation. Cysts, oocysts, and eggs in feces can be concentrated to increase sensitivity of detection. Most eggs, oocysts, and cysts are easily identified after sugar or zinc sulfate centrifugal flotation. These procedures are considered by many to be optimal for the demonstration of protozoan cysts, in particular, *Giardia* spp. and so is a good choice for a routine flotation technique in practice. Sugar centrifugation can be used for routine parasite evaluation and may be superior to many techniques for the demonstration of oocysts of *Toxoplasma gondii* and *Cryptosporidium* spp.. *Giardia* cysts are distorted by sugar centrifugation but can still be easily identified. Fecal sedimentation will recover most cysts and ova, but will also contain debris. This technique may be superior to flotation procedures for the documentation of *Eurytrema procyonis*, the pancreatic fluke. *Strongyloides cati* larva may be easier to identify after concentration using the Baerman funnel technique.

Culture. Culture of feces for *Salmonella* spp., *Campylobacter* spp., and *Clostridium perfringens* is occasionally indicated in small animal practice. Approximately 2-3 grams of fresh feces should be submitted to the laboratory immediately for optimal results, however, *Salmonella* and *Campylobacter* are often viable in refrigerated fecal specimens for 3-7 days. Appropriate transport media should be available through your laboratory. The laboratory should be notified of the suspected pathogen so appropriate culture media can be used. More than 1 culture may be needed to prove infection. *Tritrichomonas foetus* can be cultured from feces of cats in general practice using a commercially available kit (InpouchTM, Biomed Diagnostics). Some *Giardia* spp. isolated from cats will grow on culture media, but this technique is not generally performed in small animal practice.

Immunologic techniques. Parvovirus, *Cryptosporidium parvum*, and *Giardia* spp. antigen detection procedures are available for use with feces. Canine parvovirus antigen assays appear to detect feline parvovirus antigen. A fluorescein-labeled monoclonal antibody system is available that contains monoclonal antibodies that react with *Cryptosporidium* spp. oocysts and *Giardia* spp. cysts. However, the assay was developed for detection of human isolates and it is possible that cat isolates may not always be detected. In addition, a fluorescence microscope is

required and so the assay can only be performed in diagnostic laboratories. Antigens of *Giardia* spp. or *Cryptosporidium* spp. can be detected in feces by enzyme-linked immunosorbent assays. Most fecal antigen studies in cats have evaluated with kits developed for use with human feces and so it is possible that cat isolates may not always be detected. This appears to be true for *Cryptosporidium* spp. assays and they should not be used with cat feces. Recently, an in clinic *Giardia* spp. antigen test for use with dog and cat feces was released and seems to detect feline isolates. Giardia antigens are indicated for use with cats with small bowel diarrhea. Whether or not to screen healthy cats for *Giardia* antigens is controversial. Serum antibodies against *D. immitis* can be measured in cat serum but positive test results do not prove current infection or disease induced by *D. immitis*. If a vomiting cat is suspected to have D. immitis infection, it should be screened with both antigen and antibody assays. FeLV can cause lymphoma and induces the panleukopenia-like syndrome. FIV has been associated with lymphoma and can cause enteritis. Detection of FIV antibodies or FeLV antigen in serum documents exposure, but does not prove that clinical disease is due to the virus. The only way to document that gastrointestinal signs are due to FeLV or FIV is to exclude other known causes.

Endoscopy or exploratory laparotomy. *Ollulanus* and *Physaloptera* rarely pass ova in feces and so frequently are diagnosed only by endoscopy. Diagnosis of diffuse inflammatory diseases can be made by evaluation of endoscopy or surgically obtained tissue samples. Endoscopically obtained biopsies are small; I generally take at least 8-10 biopsies from stomach, duodenum, colon, and ileum if possible. Even if a lesion is present, endoscopically obtained biopsies can be falsely negative requiring full thickness biopsies. Gastric biopsies should be placed on urea slants to assess for urease which is found in the cell wall of *Helicobacter* spp.. The combination of inflammation, exclusion of other causes of inflammation, presence of gastric spiral bacteria, and positive urease testing can be used as a presumptive diagnosis of gastric helicobacteriosis. There is no benefit to performing duodenal aspirates for quantitative bacterial cultures or *Giardia* trophozoite evaluations in cats; the normal bacterial count range is very broad in cats and *Giardia* is found in the distal small intestine. Regional enteritis due to feline infectious peritonitis can be confirmed by documenting the organism in tissue after immunohistochemical staining.

Polymerase chain reaction. Polymerase chain reaction (PCR) is currently available to detect *Giardia* spp., *Cryptosporidium* spp., and *T. foetus* in feline feces. For *Cryptosporidium* spp., PCR is 10 to 1,000 fold more sensitive than IFA. *Giardia* PCR assays are less sensitive than IFA or antigen tests. I personally only recommend PCR for these two organisms if genotyping is desired. Most kittens with clinical illness from T. foetus infection will have trophozoites seen on wet mount examination and so PCR is usually not needed. PCR for *Giardia* spp., *Cryptosporidium* spp., and *T. foetus* can also detect subclinical carrier cats and so the assays have low positive predictive value. Some larger diagnostic laboratories also test for *Salmonella* spp. by PCR but if bacterial GI disease is suspected (*Salmonella* spp. and *Campylobacter* spp.) the feces should be cultured instead of being assessed by PCR to provide antibiotic susceptibility testing. Testing for genes of *Clostridium* spp. in feces has minimal predictive value unless combined with enterotoxin assays. Parvovirus can be detected by antigen testing and so fecal PCR for this agent is not needed. Reverse-transcriptase PCR can be used to detect coronavirus RNA in feces of cats but is not specific for feline infectious peritonitis.

INFECTIOUS DISEASE TREATMENT OPTIONS

There are multiple drugs used in the treatment of gastrointestinal parasitic infections. For all kittens, the strategic deworming recommendations for the control of hookworm and roundworm infections from the Centers for Disease Control and the American Association of Veterinary Parasitologists should be followed by veterinary practitioners. (http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm). Kittens should be administered an anthelmintic at 3, 5, 7, and 9 weeks of age and then periodically monitored or treated. If the kitten is not presented to the clinic until 6-8 weeks of age, administer the anthelmintic at least 2-3 times, 2-3 weeks apart. Pyrantel pamoate and fenbendazole are usually effective drugs for use in strategic deworming programs and for the treatment of nematodes causing gastrointestinal tract disease. Albendazole is more likely to cause hematologic side-effects than fenbendazole and so should not be used in cats. Even if anthelmintics for hookworms and roundworms are administered, a fecal flotation should be performed to evaluate for other parasites.

Monthly *D. immitis* preventatives can help control or eliminate some nematode infections as well as prevent heartworm infection. Ivemectin at heartworm preventative doses is effective for control of hookworms but not roundworms. Thus, selamectin, milbemycin, or moxidectin should be used in regions where roundworm infections are common. Selamectin and imidocarb-moxidectin have the advantage of controlling fleas as well and so may lessen the potential for *Bartonella* spp., *Rickettsia felis*, and *Haemobartonella* (*Mycoplasma*) spp. infections. In a recent study in our laboratory, administration of imidacloprid-moxidectin monthly blocked flea transmission of *B. henselae* amongst cats. *Dipylidium* and *T. taeniaformis* infestations usually are eliminated by praziquantel or espiprantel; fenbendazole is effective for *Taenia taeniaformis*. Since *Echinococcus multilocularis* can be a significant zoonosis transmitted to cats by carnivorism, hunting cats in endemic areas should be treated up to monthly. Administration of a pyrantel/praziquantel combination may be effective in these cats since praziquantel is approved for the treatment of *Echinococcus* and roundworms are also transmitted by carnivorism.

Withholding food for 24 to 48 hours is indicated in cats with acute vomiting or diarrhea. Highly digestible, bland diets are used most frequently if vomiting and small bowel diarrhea are the primary manifestations of disease. High fiber diets are generally indicated if large bowel diarrhea is occurring. Diarrhea associated with *Giardia* spp. generally resolves during or after administration of metronidazole. In a recent study, cyst shedding resolved in 26 cats after the administration of metronidazole benzoate at 25 mg/kg, PO, q12hr for 7 days. Metronidazole also helps correct the anaerobic bacterial overgrowth that commonly accompanies giardiasis. If inflammatory changes exist, metronidazole may also be beneficial due to inhibition of lymphocyte function. Central nervous system toxicity occasionally occurs with this drug; it is unlikely if no more than 50 mg/kg, PO, total daily dose is given. Fenbendazole has not been studied extensively for treatment of giardiasis in cats. In one experiment study of cats coinfected with *Giardia* spp. and *Cryptosporidium* spp., four of eight cats treated with fenbendazole at 50 mg/kg, PO, daily for 5 days stopped shedding *Giardia* cysts. The combination product of febantel, pyrantel, and praziquantel has been shown to have anti-*Giardia* activity in dogs. When given at the febantel dose of approximately 56 mg/kg, PO, daily for 5 days, *Giardia* cyst shedding was eliminated in some cats. Metronidazole and fenbendazole can be given

concurrently in resistant cases. Albendazole has been evaluated for treatment of giardiasis in a limited number of dogs, but has been associated with neutropenia. Furazolidone (4 mg/kg, PO, q12hr, for 7 days) and paromomycin (appropriate dosing interval for cats is unknown) are other drugs with anti-*Giardia* effects but have not been evaluated extensively in cats. There are no known advantages of using tinidazole or ronidazole compared to metronidazole in cats and ronidazole has a greater risk of CNS toxicity. Previously, the feline *Giardia* spp. vaccine could be attempted as an immunotherapy but the vaccine has been discontinued. Do not use the canine *Giardia* vaccine in cats. In some cats with *Giardia* and diarrhea, administration of a probiotics or addition of fiber to the food and retreating can result in resolution of diarrhea. The primary goal of *Giardia* therapy is to resolve diarrhea. It is unlikely the infection can be eliminated in most cats and reinfection is common. If treatment is to be monitored, a fecal flotation (not antigen assay) could be performed within 14 days of ending therapy.

Multiple drugs have been evaluated for the treatment of cats with *T. foetus* infections; until recently no drug eliminated infection and diarrhea rarely resolves during the treatment period. Recently ronidazole at 30 mg/kg, PO, q24hr, for 14 days eliminated clinical signs of disease and trophozoites from cats infected with one strain of the organism. Ronidazole is more neurotoxic than metronidazole and so should be used carefully. In another one small study, administration of metronidazole and enrofloxacin lessened diarrhea in kittens but it is unknown if the organisms infecting those cats was *T. foetus*. It is possible that some cats with *T. foetus* have other enteric coinfections and so antihelmintics or drugs with activity against *Giardia* spp., *Cryptosporidium* spp., and enteric bacteria like *Campylobacter* spp. are often prescribed. Paromomycin should be avoided cats with bloody stools because of the potential for being absorbed and inducing renal disease or deafness. In one study, 23 of 26 cats with diarrhea and *T. foetus* infection had complete resolution of diarrhea a median of 9 months after initial diagnosis. *Cryptosporidium* spp. associated diarrhea sometimes resolves after administration of tylosin (10-15 mg/kg, PO, BID for at least 14 days) or azithromycin (10 mg/kg, PO, daily for at least 14 days). If the cat is responding to therapy, continue treatment for 1 week past clinical resolution. Some cats may require several weeks of treatment. Nitazoxanide at 25 mg/kg, PO, twice daily for at least 14 days has been effective for controlling *Cryptosporidium* spp. diarrhea, but is a gastric irritant that commonly induces vomiting.

The *Toxoplasma gondii* oocyst shedding period can be shortened by administration of clindamycin, sulfadimethoxine, or ponazuril. *Cystoisospora* spp. generally responds to the administration of sulfadimethoxine or other sulfa-containing drugs. Clindamycin, trimethoprim-sulfa, or ponazuril are also options. Ponazuril is very safe for kittens and can be administered once or twice.

Since many of the gastrointestinal parasites that infect cats are transmitted by carnivorism, cats should not be allowed to hunt or be fed raw meats. Additionally, infection of cats by many feline parasites results from ingestion of contaminated water. Clinical disease in some parasitized cats can be lessened by eliminating stress and providing a quality diet and clean environment.

Clostridium perfringens and bacterial overgrowth generally respond to treatment with tylosin, metronidazole, ampicillin, amoxicillin, or tetracyclines. The drug of choice for campylobacteriosis is erythromycin; however, oral administration of quinolones is often less

likely to potentiate vomiting. Salmonellosis should only be treated parenterally due to rapid resistance that occurs following oral administration of antibiotics. Appropriate antibiotics for the empirical treatment of salmonellosis while awaiting susceptibility testing results include chloramphenicol, trimethoprim-sulfa, amoxicillin; quinolones are also effective. *Helicobacter* spp. infections are usually treated with the combination of metronidazole and tetracycline or amoxicillin and metronidazole in dogs. Clarithromycin or azithromycin may be logical choices in cats since the species is often difficult to treat with multiple drugs. Whether to concurrently administer an antacid like famotidine is controversial but seems to lessen vomiting in some cats.

Cats with apparent bacteremia due to enteric bacteria should be treated with parenteral antibiotics with a spectrum against anaerobic and gram negative organisms. The combination of enrofloxacin with a penicillin or first generation cephalosporin is generally effective. Second generation cephalosporins or imipenem are also appropriate choices.

Cats that have hepatic infections and signs of bacteremia should be treated with antibiotics that kill gram positive, gram negative and anaerobic bacteria as discussed before. Non septic hepatic infections generally respond to amoxicillin, amoxicillin-clavulanate, first-generation cephalosporins, or chloramphenicol. Decreasing numbers of enteric flora by oral administration of penicillins, metronidazole, or neomycin can lessen the clinical signs of hepatic encephalopathy.

Panleukopenia virus, feline leukemia virus, feline immunodeficiency virus, and coronaviruses are the most common viral causes of gastrointestinal tract disease in cats. Viral diseases are managed by supportive treatment. Make sure to maintain hydration, correct hypoglycemia, and maintain normal potassium concentrations. Use of jugular catheters is superior to leg veins since blood samples can be drawn and CVP can be measured. Based on results in dogs with parvovirus infection, administration of plasma or serum (1 ml/kg) from your hyperimmune blood donor cat may lessen morbidity in cats with panleukopenia due to passive transfer of immunity. This is effective because parvoviruses induce a viremic state; virus particles are complexed by the antibodies transferred passively. Adminstration of interferon alpha at 10,000 U/kg, SQ, once daily may have anti-viral effects. Antibiotics effective against gram negative and anaerobic bacteria are commonly indicated. Vaccines are available for the prevention of parvovirus, coronaviruses, and feline leukemia virus infection.

Histoplasma capsulatum infection is the most common fungal infection of the gastrointestinal tract of cats in the United States. Treatment with itraconazole can be effective.

Zoonotic considerations. Infection of people by feline enteric agents is usually from contact with feces in the environment, by ingestion of contaminated food or water, or by ingestion of undercooked meat (*T. gondii*). Contact with infected cats is an unlikely way for humans to acquire infection. The following guidelines may lessen the risk of transfer of feline enteric zoonotic agents to people.

- Perform a thorough physical examination and zoonoses risk assessment on all new cats.
- Perform a physical examination and fecal examination at least once or twice yearly.
- Take all cats with vomiting or diarrhea to a veterinarian for evaluation.

- Fecal material produced in the home environment should be removed daily, preferably by someone
  other than an immunocompromised individualUse litterbox liners and periodically lean the litterbox with scalding water and detergent.
- Do not allow cats to drink from the toilet.
- Follow the CDC strategic deworming guidelines.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling cats.
- Maintain cats within the home environment to lessen exposure to other animals and their feces.
- Feed cats only commercially processed food.
- Do not share food utensils with cats.
- Avoid being licked by cats.
- Control potential transport hosts like flies, rodents, and cockroaches.
- Cook meat for human consumption to 80 C for 15 minutes minimum (medium-well).
- Wear gloves when handling meat and wash hands thoroughly with soap and water when finished.

References available on request

Table 1. Common gastrointestinal parasites of cats.

Classification	1° clinical signs	Zoonoses
Cestodes		
Taenia taeniaformis	Subclinical	No
Dipylidium caninum	Subclinical	Yes (vector-associated)
Echinococcus multilocularis	Subclinical	Yes
Coccidians		
Cystoisospora spp.	MBD, LBD	No
Cryptosporidium spp.	SBD	Yes
Toxoplasma gondii	Polysystemic	Yes
Flagellates		
Giardia spp.	SBD	Yes
Tritrichomonas foetus	MBD, LBD	No
Fluke		
Eurytrema procyonis	V	No
Nematodes		
Ancylostoma tubaeforme	V, MBD	Yes
Strongyloides cati	V, MBD	Yes
Dirofilaria immitis	V	Yes (vector-associated)
Toxocara cati	V	Yes
Toxascaris leonina	V	No
Ollulanus tricuspis	V	No
Physaloptera spp.	V	No

V = vomiting; SBD = small bowel diarrhea; MBD (mixed bowel diarrhea); LBD (large bowl diarrhea)

Table 2. Drugs commonly used in the management feline gastrointestinal diseases

Generic drug name	Common dosage	Primary disease/organisms
Amoxicillin	22 mg/kg, daily, for 5 days, PO	*C. perfringens*, bacterial overgrowth, *Salmonella*
Ampicillin	22 mg/kg, q8hr, for 3-7 days, IV	Anaerobic sepsis
Azithromycin	7-15 mg/kg, q12hr, for 5-7 days, PO	*C. parvum*, *T. gondii*
Cefazolin	22 mg/kg, q8hr, for 3-7 days, IV	Gram positive and anaerobic sepsis
Cefoxitin	22 mg/kg, q8hr, for 3-7 days, IV	Gram positive, gram negative, and anaerobic sepsis
Cephalexin	10-30 mg/kg, q8-12hr, for 3-6 wks, PO	Bacterial cholangiohepatitis
Clarithromycin	5-10 mg/kg, q12hr, for 7 days, PO	*T. gondii, Helicobacter*
Clindamycin	12.5 mg/kg, q12hr, for 28 days PO, IM	*T. gondii*
Erythromycin	15-25 mg/kg, q12hr, for 7-10 days, PO	*C. jejuni*
Enrofloxacin	5-15 mg/kg, q8-12hr, for 3-7 days, IV, IM	Gram negative sepsis
Enrofloxacin	5-15 mg/kg, q8-12hr, for 3-7 days, PO	*Tritrichomonas foetus*
Epsiprantel	2.75 mg/kg, once, PO	*Dipylidium*, *Taenia*
Fenbendazole	50 mg/kg, q24hr, for 3-7 days, PO 30 mg/kg, q24hr, for 6 days	Nematodes, *Giardia*, *Eurytrema procyonis*
Furazolidone	4 mg/kg, q12hr, for 7 days, PO 8-20 mg/kg, q24hr, for 7 days, PO	*Giardia* *Cystoisospora* spp.
Imidocloprid moxidectin	Monthly administration topically	Hookworms, roundworms, *D. immitis*, fleas
Ivermectin	24 micrograms/kg, monthly, PO	*D. immitis*, hookworms
Itraconazole	5-10 mg/kg, q12hr, for weeks, PO	*Histoplasma capsulatum*
Metronidazole	10-25 mg/kg, q12hr, for 7 days, PO	*Giardia*, *E. histolytica*, *T. foetus*, bacterial overgrowth, *C. perfringens*
Milbemycin	2 mg/kg, monthly, PO	*D. immitis*, hookworms, roundworms
Neomycin	10-15 mg/kg, q6-24hr, for < 14 days, PO	Hepatic encephalpathy
Paromomycin	150 mg/kg, q12-24hr, for 5 days,	*Cryptosporidium* spp., *Giardia, E. histolytica*
Ponazuril	20 mg/kg, q24hr, for 2 doses	*Cystoisospora* spp.
Praziquantel	< 1.8 kg, 6.3 mg/kg, once, PO > 1.8 kg, 5.0 mg/kg, once, PO	Cestodes Cestodes
Pyrantel pamoate	5-20 mg/kg, q 14-21 days, PO	Nematodes
Pyrantel/praziquantel	< 6 months, 15 mg/kg (F) + 1.5 mg/kg (P), daily for 3 days > 6 months, 10 mg/kg (F) + 1.0 mg/kg (P), daily for 3 days	Helminths, cestodes Helminths, cestodes
Ronidazole	30 mg/kg, q24hr, PO	*T. foetus*
Selamectin	6 mg/kg, monthly, topically	*D. immitis*, hookworms, roundworms, fleas, earmites
Sulfadimethoxine	50-60 mg/kg, daily, for 5-20 days, PO	*Cystoisospora* spp.
Tylosin	10-40 mg/kg, q8-12hr, for 21 days, PO	Bacterial overgrowth, *C. perfringens, C. parvum*

FELINE VACCINE CONTROVERSIES

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A physical examination, fecal parasite screen, and vaccine needs assessment should be performed at least yearly for all cats. The American Association of Feline Practitioners (AAFP) recently published the third version of the Feline Vaccine Advisory Panel Report (www.catvets.com).[1] These guidelines are an excellent source of information for veterinarians to use when individualizing vaccination protocols. Vaccine antigens were divided into those that were considered core (FPV, FCV, FHV-1, and rabies), noncore (FeLV, FIV, *Bordetella bronchiseptica,* and *Chlamydophila felis*), and not generally recommended (*Giardia* and FIP). The *Giardia* vaccine was recently discontinued. The purpose of today's lecture is to discuss several feline vaccine controversies. Emphasis will be placed on vaccine associated side-effects and new information concerning FVRCP vaccines including use of intranasal products, use of serology to predict FVRCP need, and use of vaccines containing new FCV strains.

Overall, vaccines for cats are very safe. In my opinion, vaccines for cats undoubtedly have saved many more cats than they have hurt. Core vaccine antigens as defined by the American Association of Feline Practitioners Vaccine Guidelines Committee should be administered to all cats; non-core antigens should be selected based on needs of the individual cat.[1] The most significant problems associated with feline vaccines have been injection-associated sarcoma.[2-11] Initially, this problem seemed most apparent in cats administered adjuvanted rabies virus and feline leukemia virus vaccines. However, recent information suggests that injection site sarcomas can occur with any type of vaccine. For example, in the United Kingdom in 2006 and 2007, the majority of injection site sarcomas reported in cats occurred at the site a live vaccine (non-adjuvanted) was administered.[4,5] Studies have failed to show a link to individual products.[7,8] It is now apparent that cats that develop injection site sarcomas may be genetically predisposed and that any level of inflammation could result in malignant transformation.[3,11]

While generally very safe, modified live FVRCP vaccines have been associated with a number of clinical abnormalities including fever, infection of the fetus, induction of a chronic carrier state, polyarthritis, and upper respiratory tract disease.

We recently reported recombinant antigens of feline herpesvirus 1, calicivirus, and panleukopenia virus for use in serological assays.[12] In the same work, we showed that serology could be used to accurately determine need for FVRCP vaccination in cats based on the criteria defined in the study if validated assays are utilized. The laboratories studied included the New York State Diagnostic Laboratory and HESKA Corporation. While titrating the recombinant antigen based ELISAs by comparing to ELISAs performed using whole viruses in that study, we discovered that vaccinated cats make antibodies against a commonly used cell culture line.

The Crandall-Rees feline kidney (CRFK) cell line has been used to propagate feline viruses for years.[13-17] While isolated from a kidney, the cell line has characteristics of a fibroblast. During

virus purification for vaccine production (FVRCP) or immunoassay development, it is impossible to remove all CRFK proteins or other cell constituents. Thus, CRFK proteins contaminate the viral preparations and commercially available FVRCP vaccines grown on the cell line contain CRFK proteins. As a consequence, during the course of routine immunization, cats are exposed to CRFK proteins and may mount an immune response against those proteins. Since the CRFK cell line is derived from a feline cell line, administration of FVRCP vaccines induces antibodies that also bind to feline tissues. We have now performed several studies to assess the problem.

In the first, recently completed study, our objectives were to determine whether cats inoculated with FVRCP vaccines grown on the CRFK cell line develop antibodies against CRFK lysates or renal cell lysates (FRC), whether cats hypersensitized with CRFK lysate develop antibodies against CRFK cell lysates or FRC lysates, and whether FVRCP vaccination or hypersensitization with CRFK cell lysates induces clinical pathological or histopathological abnormalities over a 56 week period.[14] We assessed three FVRCP vaccines for SQ administration and one FVRCP vaccine for intranasal/intraocular administration. CBC, serum biochemical panel, urinalysis, microalbuminuria assay, and ELISAs to detect antibodies against CRFK lysate or FRC lysate were performed on samples collected at intervals during the study. Renal biopsies were assessed for abnormalities independently by two pathologists. None of the cats was positive for antibodies against CRFK lysate or FRC lysate prior to inoculation. All six cats administered CRFK lysate alone were positive in the CRFK ELISA on multiple sample dates in the CRFK ELISA. Neither of the cats receiving intranasal/intraocular vaccination achieved the positive cutoff value in the CRFK ELISA. Five of the six cats administered a parenteral vaccine were positive in the CRFK ELISA at least once during the study. All six cats administered CRFK lysate were positive on multiple sample dates in the FRC ELISA. All six cats administered a parenteral vaccine were positive on multiple sample dates in the FRC ELISA. Neither of the cats administered the intranasal/intraocular vaccine were positive in the FRC ELISA. Significant CBC, serum biochemical, urinalysis, microalbuminuria, or histopathologic abnormalities were not detected during the study. We concluded that parenteral administration of vaccines grown on the CRFK cell line and SQ inoculation of CRFK lysate alone induced CRFK antibodies and FRC antibodies in most cats in this study. However, the clinical pathological and histopathological results suggest that even hypersensitization with CRFK proteins was not associated with detectable renal dysfunction, renal inflammatory disease, or glomerular disease in the 56-week time period studied.

In the first study, renal biopsies were collected 6 weeks after the last vaccination or hypersensitization. It is possible that inflammation of renal tissues occurred but was transient and resolved by the time of biopsy. In the first follow-up study, we hypothesized that interstitial nephritis would be detected in cats hypersensitized with CRFK lysates, boosted with CRFK lysates, and then biopsied 2 weeks after the booster.[15] We documented interstitial nephritis in 3 of 6 cats hypersensitized with CRFK lysates, but not cats vaccinated with the intranasal FVRCP vaccine. None of these 3 cats had significant inflammation detected 1 year previously. One of the 6 cats recently died of interstitial nephritis. However, it is important to emphasize that the cats in the study were inoculated multiple times with CRFK proteins over the first year of the study. Whether this occurs after parenteral administration of CRFK contaminated FVRCP vaccines using routine vaccination protocols remains to be proven.

In our first study to determine CRFK antibodies in vaccinated cats, we only had 2 cats per group. Thus, a larger study was performed with 5 groups of cats (1 intranasal vaccine and 4 parenteral vaccines).[16] In that study, we showed that parenteral administration of FVRCP vaccines induces a statistically greater magnitude of antibody response to CRFK proteins than intranasal administration of a FVRCP vaccine. These findings were expected because parenteral inoculation of CRFK lysates to immunocompetent cats would be expected to induce an immune response. The viruses used in the production of the FVRCP vaccine for intranasal administration is also grown on CRFK cells. However, while the viruses in the vaccine are alive, the CRFK cell line components that contaminate the vaccine are not. Thus, we believe the reason cats inoculated with this intranasal vaccine do not develop CRFK antibodies relates to immune exclusion of the CRFK cell line components by the mucosal lining the nose and mouth. We are in the process of determining the immunodominant CRFK antigens recognized by feline antibodies.[17] We have identified 3 immunodominant antigens and will study these antigens further. Antibodies against two of the three antigens (alpha enolase and annexin A2) have been associated with autoimmune disorders in people. We recently showed that administration of parenteral FVRCP vaccines induces antibodies against these two glycolytic pathway enzymes.[18]

At this time, we have not directly linked FVRCP vaccination to auto-immune diseases in cats. To further assess for disease associations with administration of CRFK containing FVRCP vaccines, we are currently performing the following studies: 1. Determination of the source and distribution of CRFK proteins in feline tissues; and 2. Correlation of CRFK antibodies with presence of biochemical abnormalities in groups of client-owned cats of the United States. A general recommendation at this time would be to not use parenteral FVRCP vaccine at an interval shorter than every third year after the 1 year of age booster. In addition, FVRCP antigens should not be split and given yearly as that may result in increased exposure to the cell culture antigens.

Some variants of FCV induce systemic vasculitis in cats (virulent systemic calicivirus; VS-FCV) and clinical signs can be severe in some cats previously vaccinated with FVRCP vaccines.[19-24] VS-FCV strains arise spontaneously from endogenous FCV strains and outbreaks have resolved quickly after the initial cases are recognized. Currently, it is unknown how often these outbreaks occur and whether the outbreaks are increasing. The VS-FCV strains evaluated to date have been genetically and antigenically diverse.[25,26] An inactivated, VS-FCV-containing vaccine line is now available in the United States (CaliciVax™, Fort Dodge Animal Health). The product contains a routine FCV vaccine stain as well a VS-FCV strain. To date, the only challenge data is in small numbers of cats that were challenged with the homologous strain shortly after the last booster. However, cross neutralization studies show that cats inoculated with more than one FCV strain inactivate more FCV stains in vitro than cats inoculated with one FCV strain.[27,28] Thus, even if this vaccine antigen does not cross protect against other VS-FCV, it may induce superior cross protection to other FCV. The AAFP recently posted an information brief that reviewed the information currently known about this vaccine (www.catvets.com). The following are the major points the AAFP Panel believes should be considered when deciding whether to include this product in the vaccination program of individual cats.

- The incidence of VS-FCV associated disease in the United States or other countries is unknown.

- In part because of the difficulties associated with achieving a clinical diagnosis, it is currently unknown whether VS-FCV outbreaks are increasing over time.
- VS-FCV strains appear to arise from mutations; so far, each of the outbreak strains appears to be genetically and antigenically distinct from others.
- It is currently unknown whether administration of CaliciVax™ results in protection against heterologous VS-FCV strains on challenge.
- The maximal duration of immunity of CaliciVax™ for homologous or heterologous VS-FCV strains is unknown.
- Use of multiple FCV strains in feline vaccines may increase cross-protection capabilities but results of serum neutralization tests of FCV strains in vitro may not necessarily correlate to protection on challenge.
- Inactivated vaccines may induce protection more slowly than modified live vaccines and so if an inactivated FCV containing vaccine is to be used in the primary immunization period for cats at high risk of exposure to feline panleukopenia virus, it should be used in combination with a parentally administered modified live feline panleukopenia virus containing vaccine.

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PET OWNERSHIP BY IMMUNE SUPPRESSED PEOPLE

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Zoonotic diseases are defined as being common to, shared by, or naturally transmitted between humans and other vertebrate animals. Humans are infected with zoonotic agents from direct contact with the infected pet, contact via contaminated food or water, from shared vectors, and from the shared environment. Direct contact with animal feces (enteric zoonoses), respiratory secretions, urogenital secretions, or infected skin and exudates, as well as bites and scratches can result in human infections.

Most of the agents discussed in these proceedings can infect and cause disease in anyone that is exposed, but disease is generally more prevalent or more severe in those that are immunodeficient. Immunosuppression is common in humans. Humans with AIDS are discussed most frequently, but there are many more immunodeficient individuals including the very old, the very young, and those receiving chemotherapy for immune-mediated diseases, organ transplantation, or neoplasia. Humans are unlikely to contract zoonotic diseases from contact with their pets and so in most cases do not need to relinquish their animals. The Centers for Disease Control of the United States online publication, *Preventing Infections from Pets; A Guide for People with HIV Infection,* states 'You do *not* have to give up your pet'.[a] The American Association of Feline Practictioner's Zoonoses Guidelines states 'All human or animal care providers should provide accurate information to pet owners concerning the risks and benefits of pet ownership so that an informed decision about acquiring and keeping pets can be made' (Brown et al, 2003).

Veterinary health care providers are at increased risk for some zoonoses since they commonly handle animals; these agents will be discussed in depth in this articles. Since some enteric zoonotic agents are infectious when passed with feces, direct contact with infected animals can result in human infections. However, it is felt that most enteric zoonoses result from ingestion of the infectious agent in contaminated food, water, or other environmental sources. Giardia spp., Cryptosporidium spp., and Toxoplasma gondii are notable examples. Some zoonotic agents are transmitted between animals and man by shared vectors like fleas, ticks, or mosquitoes. Rickettsia rickettsii (ticks), Ehrlichia spp. (ticks), Borrelia burgdorferi (ticks), Rickettsia felis (fleas), Bartonella spp. (fleas), Dirofilaria immitis (mosquitoes), Dipylidium caninum (mosquitoes), and West Nile virus (mosquitoes) are examples of vector borne zoonoses. The pet brings the vector of the organism into the environment resulting in exposure of the human. There could be a slight increased risk of exposure to veterinary health care providers since we handle many animals infested with fleas and ticks. However, it is the vector, not direct contact with the infected animal that results with infection of the human. Flea and tick control should always be maintained on our client's animals and infested animals that are seen in the clinic should be treated immediately. Some zoonotic agents including Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Cryptococcus neoformans, and Aspergillus spp

do not usually infect humans from direct with the infected pet but are acquired from the same environmental source.

The following is a brief description of the more common canine and feline zoonoses that are encountered in small animal practice that can be direct contact zoonoses. General guidelines for the avoidance of zoonotic transfer of disease for veterinarians and pet owners are listed in Tables 1 and 2, respectively.

Enteric zoonoses. There are multiple infectious agents of the gastrointestinal tract that can be shared between animals and humans and infection rates are as high as 40% in dogs or cats with diarrhea. These findings emphasize that diagnostic workups for enteric infections are indicated due to potential human health risks. The minimal diagnostic plan to assess for enteric zoonoses in pets with diarrhea includes a fecal flotation, Cryptosporidium spp. screening procedure, fecal wet mount, and rectal cytology. Fecal culture should be considered if Salmonella spp. or Campylobacter spp. are on the list of differential diagnoses.

Nematodes. Visceral larva migrans can be induced by infection of humans with Toxocara cati, Toxocara canis, or Baylisascaris procynosis. These common roundworms are passed as eggs in feces. The eggs larvate and become infectious after 1 to 3 weeks, and can survive in the environment for months. Thus, these are not direct contact zoonoses; humans are infected after ingesting larvated eggs in the contaminated environment. Dogs are considered more important than cats for the spread of eggs. However, areas such as children's sandboxes may be contaminated with T cati because of the defecation habits of cats. It is extremely unlikely that human infection will develop following direct contact with dogs or cats since the eggs are not immediately infectious. Dogs and cats can be subclinically affected or may develop poor haircoats, poor weight gain, and gastrointestinal signs. Following ingestion of infectious eggs, larvae penetrate the intestinal wall and migrate through the tissues. Eosinophilic granulomatous reactions involving the skin, lungs, central nervous system (CNS), or eyes then occur, potentially leading to clinical signs of disease. Clinical signs and physical examination abnormalities in humans include skin rash, fever, failure to thrive, CNS signs, cough, pulmonary infiltrates, and hepatosplenomegaly. Peripheral eosinophilia is common. Ocular larva migrans most commonly involves the retina and can cause reduced vision; uveitis and endophthalmitis can also occur. Visceral larva migrans is most common in children between 1 and 4 years of age, while ocular larva migrans is most common in older children. Diagnosis in people is confirmed by biopsy or can be presumed in cases with classic clinical manifestations, eosinophilia, and positive serology.

Ancylostoma caninum, A braziliense, A tubaeforme, Uncinaria stenocephala, and Strongyloides stercoralis have been associated with cutaneous larva migrans in the United States. Eosinophilic enteritis in humans was reported following ingestion of larvated A caninum eggs. Following the passage of hookworm eggs into the environment in feces, infectious larvae are released after incubating for 1 to 3 days; humans are infected by skin penetration. Thus, these infectious are not direct contact zoonoses but occur from contact with the organisms in the contaminated environment. Animals are either subclinically ill or have nonspecific signs such as poor haircoats, failure to gain weight, vomiting, or diarrhea. Heavily infested puppies and kittens can present with pale mucous membranes from blood loss anemia. In humans, the larvae cannot

penetrate the dermoepidermal junction and so usually die in the epidermis. Clinical signs are related to migration of the larvae which results in an erythematous, pruritic cutaneous tunnel. Cutaneous signs usually resolve within several weeks. Abdominal pain was the most common clinical sign in humans with A. caninum intestinal infection.

Prevention of hookworm and roundworm infection is achieved by control of animal excrement in human environments. All puppies and kittens should have a fecal flotation performed and should be routinely treated with an anthelmintic such as pyrantel pamoate at least three times.[b-d] Some veterinarians administer the drugs at 21 days apart during their initial vaccination period. Roundworm and hookworm infections are occasionally occult and so all puppies or kittens should receive an anthelmintic whether or not eggs are detected on microscopic examination of feces. In puppies with high worm burdens, deworming with pyrantel pamoate can be initiated at 1-2 weeks of age and repeated at 2 week intervals.[b] In heavily infected kittens, deworming with pyrantel can begin at 3 weeks of age and repeated at 2 week intervals.[b] The bitch and queen should be dewormed as well as patent infections may exist. Feces of adult dogs and cats should be periodically screened for roundworms and hookworms and anthelmintics should be administered periodically. An effective way of providing strategic deworming year round is to administration of heartworm preventatives that also control or eliminate hookworms and roundworms.

Cestodes. Dipylidium caninum, Echinococcus granulosa, and Echinococcus multilocularis are cestodes that can infect humans. Wild carnivores are more common definitive hosts of Echinococcus spp.and shed infective eggs into the environment. Echinococcus granulosa eggs can be transmitted in feces of dogs following ingestion of infected sheep tissues; Echinococcus multilocularis can be transmitted in feces of dogs or cats after ingestion of infected vole. Transmission to humans occurs following ingestion of the intermediate host (flea, Dipylidium) or by the ingestion of eggs (Echinococcus spp.). Infection of dogs and cats with cestodes is generally subclinical. Dipylidium infection is most common in children and can lead to diarrhea and pruritis ani. In people following ingestion of eggs, which are immediately infectious, Echinococcus enters the portal circulation and spreads throughout the liver and other tissues. Echinococcus multilocularis is most common in the northern and central parts of North America but seems to be spreading with the fox population (most common definitive host). Prevention or control of cestodes is based on sanitation procedures and use of taeniacides. Dogs and cats should not be allowed to hunt and should only be fed commercial foods.

Coccidians. Cryptosporidium spp. inhabit the respiratory and intestinal epithelium of many vertebrates including birds, mammals, reptiles, and fish. Once thought to be commensal agents, Cryptosporidium spp. are now known to cause gastrointestinal tract disease in a number of mammalian species including rodents, dogs, cats, calves, and humans. Cryptosporidium spp. have an enteric life cycle similar to other coccidians; it culminates in the production of environmentally resistant oocysts that are passed in feces. Oocysts (4 to 6 microns in diameter) are passed sporulated and are immediately infectious to other hosts. It is now apparent that there are multiple strains of Cryptosporidium spp. including C. parvum, C. hominis, C. felis and C. canis. While some isolates infect multiple species, others have a limited host range. For example, C. hominis of people does not infect dogs, cats, or rodents. However, strains that infect both pets and people cannot be differentiated from those that only infect pets by light microscopy

and so all Cryptosporidium spp. should be considered potentially zoonotic. The prevalence of Cryptosporidium spp. oocysts or antigens in dog and cat feces approximates that of Giardia leading to the recommendation that all dogs or cats with diarrhea in the homes of immunosuppressed people be assessed for this infection. Person-to-person contact with oocysts by fecal-oral contamination or by ingesting contaminated water are the most likely routes of exposure. Cryptosporidium spp. infection of people following exposure to infected calves has been recognized for years. Human infection associated with contact with infected dogs and cats has been reported but is thought to be unusual. In one study, cat or dog ownership was not statistically associated with cryptosporidiosis in HIV-infected people. Infection of dogs and cats by Cryptosporidium spp. is usually subclinical, but small bowel diarrhea occurs in some cases. Immunosuppression may potentiate disease; several dogs and cats had concurrent feline leukemia virus infection, canine distemper virus infection, or intestinal lymphoma. Clinical cryptosporidiosis is characterized by small bowel diarrhea and is generally self-limiting in immunocompetent humans, but fatal infection can occur in humans with AIDS. The small size (approximately 4 to 6 microns in diameter) of Cryptosporidium spp. oocysts lead to difficulty in diagnosis. Routine salt solution flotation and microscopic examination at 100X will commonly lead to false-negative results. The combination of concentration techniques with fluorescent antibody staining or acid fast staining appears to be more sensitive. Enzyme-linked immunosorbent assays for the detection of C parvum antigen in feces and immunofluorescent assay for detection of C parvum oocysts in feces are commercially available but do not consistently detect C felis or C canis. Polymerase chain reaction is the most sensitive test to date, but assays are not routinely available and are not standardized between laboratories. No drug has been shown to eliminate Cryptosporidium spp. from the gastrointestinal tract. However, clinical signs often resolve after administration of paromomycin at 150 mg/kg, q24hr, PO for 5 days, tylosin at 10-15 mg/kg, q12hr, PO for 14 to 21 days, or azithromycin at 10 mg/kg, q24hr, PO for 10 days. Avoiding exposure is the most effective prevention. Routine disinfectants require extremely long contact with the organism to be effective. Drying, freeze-thawing, and steam-cleaning can inactivate the organism. Surface water collected in the field for drinking should be boiled or filtered.

Toxoplasma gondii is an ubiquitous coccidian with worldwide distribution. Most seroprevalence studies performed in the United States suggest that approximately 30% of cats have been exposed. Human prevalence rates have been declining which may relate to food production changes over time. Cats are the only known definitive host of the organism and complete the enteroepithelial cycle (sexual phase) that results in the passage of environmentally resistant unsporulated oocysts in feces. Oocyst sporulation occurs in 1-5 days in the presence of oxygen; sporulated oocysts are infectious to most warm-blooded vertebrates. Following infection by T gondii, an extraintestinal phase develops which ultimately leads to the formation of tissue cysts containing the organism. Infection by T gondii occurs after ingesting sporulated oocysts, after ingesting tissue cysts, or transplacentally. Transplacental infection of humans and cats usually only occurs if the mother is infected for the first time during gestation.

In dogs and cats, clinical disease from T gondii infection occurs occasionally and is manifested most commonly by fever, uveitis, pulmonary disease, hepatic disease, and CNS disease. Infected immunocompetent humans are generally asymptomatic; self-limiting fever, lymphadenopathy, and malaise occur occasionally. Transplacental infection of humans results in clinical

manifestations including stillbirth, hydrocephalus, hepatosplenomegaly, and retinochoroiditis. Chronic tissue infection in humans can be reactivated by immunosuppression leading to dissemination and severe clinical illness; this has been commonly associated with drug-induced immunosuppression as well as AIDS. Approximately 10% of humans with AIDS will develop toxoplasmic encephalitis. Oocysts are most effectively demonstrated in cat feces following sugar solution centrifugation. Clinical toxoplasmosis is difficult to diagnose in humans, dogs, and cats but usually involves the combination of clinical signs, serologic test results, organism demonstration techniques, and response to anti-Toxoplasma drugs.

Toxoplasma gondii is recognized as one of the most common zoonoses. However, humans are usually not infected by direct contact with cats. The oocyst shedding period usually lasts several days to several weeks (approximately 7-10 days if the cat was infected by tissue cyst ingestion). Since oocysts have to sporulate to be infectious, contact with fresh feces cannot cause infection. Cats are very fastidious and usually do not allow feces to remain on their skin for time periods long enough to lead to oocyst sporulation; oocysts were not isolated from the fur of cats 7 days after completing the oocyst shedding period. There was no association between cat ownership and T gondii seroprevalence in a group of HIV-infected humans. Veterinary health care providers generally do not have increased incidence of toxoplasmosis when compared to the general population. Thus, cats do not need to be removed from households with immunodeficient or pregnant humans due to the risk of acquiring toxoplasmosis. Toxoplasma gondii infection can be avoided by avoiding the ingestion of sporulated oocysts in old feline feces and avoiding ingestion of tissue cysts in undercooked meats.

Flagellates, ameoba, and ciliates. Giardia spp. (flagellate), Entamoeba histolytica (amoeba), and Balantidium coli (ciliate) are enteric protozoans that can be transmitted to humans by contact with feces; the cysts do not require an incubation period to become infectious. Entamoeba histolytica infection extremely rare in dogs and cats; Balantidium coli infection of dogs is rare and has not been reported in cats.

Giardia spp. infection of dogs and cats is common and can be detected in feces of normal dogs and cats or those with small bowel diarrhea (and occasionally mixed bowel diarrhea in cats). Clinical signs of disease are generally more severe in immunodeficient individuals. Because the organism is immediately infectious when passed as cysts in stool, there is potential for direct zoonotic transfer. While it is known that some Giardia spp. will infect humans, dogs, and cats, that may not be the case with all species. In 1 study, cats were relatively resistant to infection by a Giardia spp. isolated from humans. Based on genetic studies, it is now known that there are multiple Giardia spp.. Assemblage A has been found in infected humans and many other mammals including dogs and cats. Assemblage B has been found in infected humans and dogs, but not cats. Dogs (C and D) and cats (F) have there own genotypes. However, as for Cryptosporidium, since it is impossible to determine zoonotic strains of Giardia spp. by microscopic examination, it seems prudent to assume feces from all dogs and cats infected with Giardia spp. are a potential human health risk. Fecal examination should be performed on all dogs and cats at least yearly and treatment with drugs with anti-Giardia activity like fenbendazole, metronidazole, or febantel/praziquantel/pyrantel should be administered if indicated. Zinc sulfate centrifugation is considered the optimal fecal flotation technique by most parasitologists to demonstrate cysts. If fresh stool is available from dogs or cats with diarrhea,

examination of a wet mount to detect the motile trophozoites may improve sensitivity. Monoclonal antibody based immunofluorescent antibody tests, fecal antigen tests, can PCR are available for use as adjunct tests. These techniques should be used in addition to, not in lieu of fecal flotation that can also reveal other parasites. Giardia vaccines for SQ administration are now available for both dogs; the feline vaccine has been discontinued. The vaccines were considered generally not recommended by the American Association of Feline Practitioners and American Animal Hospital Association vaccine guidelines committees. Vaccination against Giardia could be considered in dogs with recurrent infection and has been evaluated as a therapeutic agent with variable results. Prevention of zoonotic giardiasis includes boiling or filtering surface water for drinking and washing hands that have handled material contaminated by feces, even if gloves were worn. It is unknown whether treated dogs and cats are cured and it is likely that if a treated dog or cat is exposed again it will be reinfected.

Bacteria. Salmonella spp., Campylobacter spp., Clostridium difficile, E. coli, Yersinia enterocolitica, and Helicobacter spp. each infect dogs and cats and can cause disease in humans. Transmission from animals to people is by fecal-oral contact. Dogs can be subclinical carriers of Shigella spp. but humans are the natural hosts. While Helicobacter pylori was isolated from a colony of cats, it is unclear whether dogs and cats are a common source of Helicobacter infection for people. Based on epidemiologic studies, it is unlikely. In 3 recent enteric zoonoses prevalence studies, Salmonella spp. and Campylobacter spp. infections were uncommon in pet dogs and cats. Prevalence of Salmonella and Campylobacter infections is greater in young animals housed in unsanitary or crowded environments.

Gastroenteritis can occur in dogs or cats following infection by Salmonella spp., Campylobacter spp., or E. coli; Yersinia enterocolitica is probably commensal agents in animals but cause fever, abdominal pain, polyarthritis, and bacteremia in humans. Helicobacter infections cause gastritis which is commonly manifested as vomiting, belching, and pica. Salmonella spp. infection in dogs and cats is often subclinical. Approximately 50% of clinically affected cats have gastroenteritis; many are presented with signs of bacteremia. Salmonellosis of cats and people has been associated with songbirds (Songbird fever). Abortion, stillbirth, and neonatal death can result from *in utero* infection. Diagnosis of Salmonella spp., Campylobacter jejuni, E. coli, and Yersinia enterocolitica is based on culture of feces. Clostridium difficile enterotoxins can be measured in feces. A single negative culture may not rule out infection. Rectal cytology should be performed on all animals with diarrhea. If neutrophils are noted, culture for enteric bacteria should be considered, particularly if the animal is owned by an immunodeficient individual. Culture is preferred to PCR for Salmonella spp. and Campylobacter spp. to allow for determination of the antimicrobial sensitivity pattern. Antibiotic therapy can control clinical signs of disease from infection by Salmonella spp. or Campylobacter spp., but should not be administered orally to animals that are subclinical carriers of Salmonella due to risk of antibiotic resistance. Strains of Salmonella that were resistant to most antibiotics have been detected in several cats. Prevention of enteric bacterial zoonoses is based on sanitation and control of exposure to feces. Immunodeficient humans should avoid young animals and animals from crowded or unsanitary housing, particularly if clinical signs of gastrointestinal tract disease are occurring. Dog used for visitation can acquire and carry zoonotic agents like C. difficile (Lefebvre et al, 2009).

Bite, scratch, or exudate exposure zoonoses

Bacteria. Bartonella henselae is the most common cause of cat scratch disease as well as bacillary angiomatosis, and bacillary peliosis, common disorders in humans with AIDS. Cats can also be infected with B clarridgeiae, B koehlerae, B bovis, and B weissii (Brunt et al, 2006). Bartonella henselae has been isolated from the blood of subclinically ill, seropositive cats and also from some cats with a variety of clinical manisfestations like fever, lethargy, lymphadenopathy, uveitis, gingivitis, and neurologic diseases. Seroprevalence in cats varies by region but as many as 93% of cats in some geographical areas of the United States are Bartonella spp. seropositive. The organism is transmitted between cats by fleas and so prevalence is greatest in cats from states where fleas are common. Transmission to humans commonly occurs after cat bites or scratches; the disease appears to be transmitted most commonly from kittens. Humans with cat scratch disease develop a variety of clinical signs such as lymphadenopathy, fever, malaise, weight loss, myalgia, headache, conjunctivitis, skin eruptions, and arthralgia. Bacillary angiomatosis is a diffuse disease resulting in vascular cutaneous eruptions. Bacillary peliosis is a diffuse systemic vasculitis of parenchymal organs, particularly the liver. The incubation period for cat scratch disease is approximately 3 weeks. Most cases of cat scratch disease are self-limiting but may take several months to completely resolve. Blood culture, blood PCR, and serologic testing can be used to determine risk of individual cats. Cats that are culture-negative or PCR-negative and antibody-negative, and cats that are culture-negative or PCR-negative and antibody-positive are probably not shedding Bartonella into the human environment. However, bacteremia can be intermittent and false-negative culture or PCR results may occur. With PCR, false-positive results can occur and positive results do not necessarily indicate that the organism is alive. While serologic testing can be used to determine whether an individual cat has been exposed, both seropositive and seronegative cats can be bacteremic, limiting the diagnostic utility of serologic testing. Thus, testing healthy cats for Bartonella spp. infection is not currently recommended (Brunt et al, 2006). Testing should be reserved for cats with suspected clinical bartonellosis. Administration of doxycycline, tetracycline, erythromycin, amoxicillin-clavulanate, azithromycin, or enrofloxacin can limit bacteremia but does not cure infection in all cats and has not been shown to lessen the risk of cat scratch disease. Thus, antibiotic treatment of healthy bacteremic cats is controversial. Bartonella spp. infection is more common in flea-infested cats from catteries. Bartonella henselae replicates in fleas and can survive in flea feces for days. Thus, it is possible that flea feces contaminates our wounds, resulting in infection. Strict flea control should be maintained. Use of imidacloprid-moxidectin monthly was just shown to block transmission of B. henselae amongst experimental cats. Kittens should be avoided by immunodeficient people. Cat claws should be kept clipped and cats should never be teased. Cat-induced wounds should immediately be cleansed and medical advice sought.

Dogs and cats can have methicillin resistant S. aureus and S. pseudintermedius infections. Dogs and cats with infected wounds should always be cultured. Dog used for visitation can acquire methicillin resistant organisms from human patients (Lefebvre et al, 2009).

Feline plague is caused by Yersinia pestis, a gram-negative coccobacillus found most commonly in mid- and far-western states, particularly New Mexico and Colorado. Rodents are the natural hosts for this bacterium; cats are most commonly infected by ingesting bacteremic rodents or

lagomorphs or by being bitten by Yersinia infected rodent fleas. Dogs are more resistant to infection and have not been associated with zoonotic transfer. Humans are most commonly infected by rodent flea bites, but there have been many documented cases of transmission by exposure to wild animals and infected domestic cats. From 1977 to 1998, 23 cases of human plague (7.7% of the total cases) resulted from contact with infected cats. Infection can be induced by inhalation of respiratory secretions of cats with pneumonic plague, bite wounds, or by contaminating mucous membranes or abraded skin with secretions or exudates. Bubonic, septicemic, and pneumonic plague can develop in cats and humans; each form has accompanying fever, headache, weakness, and malaise. Since cats are most commonly infected by ingestion of bacteremic rodents, suppurative lymphadenitis (buboes) of the cervical and submandibular lymph nodes is the most common clinical manifestation. Exudates from cats with lymphadenopathy should be examined cytologically for the presence of large numbers of the characteristic bipolar rods. The diagnosis is confirmed by fluorescent antibody staining of exudates; culture of exudates, tonsillar area, and saliva; as well as by documenting increasing antibody titers. People that are exposed to infected cats should be urgently referred to physicians for antimicrobial therapy and public health officials alerted. Doxycycline, enrofloxacin, chloramphenicol, and aminoglycosides can be used successfully for the treatment of plague. Parenteral antibiotics should be used during the bacteremic phase. Drainage of lymph nodes may be required. Cats with suppurative lymphadenitis should be considered plague suspects, and extreme caution should be exercised when handling exudates or treating draining wounds. Suspect animals should be treated for fleas and housed in isolation. Cats are not infectious to humans after 4 days of antibiotic treatment.

Francisella tularensis is the gram-negative bacillus found throughout the continental United States that causes tularemia. Dermacenter variabilis (American dog tick), D. andersoni (American wood tick), and Amblyomma americanum (Lone Star tick) are known vectors. Human tularemia occurs most commonly following exposure to ticks and less commonly from contact with infected animals. There have been at least 51 cases of human tularemia resulting from contact with infected cats. Dogs are not considered a source of human tularemia, but may facilitate human exposure by bringing infected ticks into the environment. Cats are infected most frequently by tick bites or by ingesting infected rabbits or rodents. Most cases of feline tularemia have been documented in the mid-Western states, particularly Oklahoma. Infected cats exhibit generalized lymphadenopathy and abscess formation in organs such as the liver and spleen, which leads to fever, anorexia, icterus, and death. Ulceroglandular, oculoglandular, glandular, oropharyngeal, pneumonic, and typhoidal forms have been described in humans and develop depending on the route of exposure. Unlike plague, the organism is not often recognized in exudates or lymph node aspirates from infected cats. Cultures and documentation of increasing antibody titers can be used to confirm the diagnosis in cats and humans. Most cases of tularemia in cats have been diagnosed at necropsy and so optimal treatment is unknown. Streptomycin and gentamicin are the drugs used most commonly to treat humans. Tetracycline and chloramphenicol can be used in cases not requiring hospitalization but may be associated with relapses. The disease is prevented by avoiding exposure to lagomorphs, ticks, and infected cats. All cats dying with bacteremia should be handled carefully.

Approximately 300,000 emergency room visits per year are made by people bitten by animals in the United States. Most of the aerobic and anaerobic bacteria associated with bite or scratch

wounds only cause local infection in immunocompetent individuals. However, 28% to 80% of cat bites become infected and severe sequelae including meningitis, endocarditis, septic arthritis, osteoarthritis, and septic shock can occur. The majority of the aerobic and anaerobic bacteria associated with dog or cat bite or scratch wounds lead only to local infection in immunocompetent individuals. Immunodeficient humans or humans exposed to Pasteurella spp., Capnocytophaga canimorsus (DF-2), or Capnocytophaga cynodegmi more consistently develop systemic clinical illness. Splenectomized humans are at increased risk of developing bacteremia. Dogs and cats are subclinical carriers of multiple bacteria in the oral cavity. After a human is bitten or scratched, local cellulitis is noted initially, followed by evidence of deeper tissue infection. Bacteremia and the associated clinical signs of fever, malaise, and weakness are common, and death can occur in hours following infection with Capnocytophaga spp. in immunodeficient humans. Diagnosis is confirmed by culture. Treatment of carrier animals is not needed. Treatment of clinically affected humans includes local wound management and parenteral antibiotic therapy. Penicillin derivatives are very effective against most Pasteurella infections; penicillins and cephalosporins are effective against Capnocytophaga spp. *in vitro*. Mycoplasma spp. infections of people secondary to cat bites, one with cellulitis and one with septic arthritis, have been reported. L-form bacteria are cell-wall deficient organisms associated with chronic draining skin wounds in cats that are commonly resistant to cell-wall inhibiting antibiotics like penicillins and cephalosporins. Infection of a human after a cat bite was documented. Diagnosis can only be confirmed by histologic examination of tissue. Doxycycline has been used to successfully treat cats and people. Gloves should be worn when attending cats with draining tracts, and hands should be cleansed thoroughly.

Fungal. Of the many fungal agents that infect both humans and animal, only Sporothrix schenckii and the dermatophytes have been shown to infect humans upon direct exposure. Histoplasma, Blastomyces, Coccidioides, Aspergillus, and Cryptococcus infections of humans and animals can occur in the same household, but infection of humans generally results from a common environmental exposure rather than by direct contact with an infected animal. Sporothrix is cosmopolitan in distribution and the soil is thought to be the natural reservoir. Infection of cats and humans usually occurs after the organism contaminates broken skin. Cats are thought to be infected by scratches from contaminated claws of other cats; infection is most common in outdoor males. Humans can be infected by contaminating cutaneous wounds with exudates from infected cats. Sporothrix infection in cats can be cutaneolymphatic, cutaneous, or disseminated. Chronic draining cutaneous tracts are common. Cats commonly produce large numbers of the organism in feces, tissues, and exudates, thus, veterinary care personnel are at high risk when treating infected cats. The clinical disease in humans is similar to that in cats. Dogs generally do not produce large numbers of Sporothrix in exudates and so are less of a zoonotic risk. The organism can be demonstrated by cytologic examination of exudates or culture. Fluconazole, itraconazole, or ketoconazole are effective treatments. Gloves should be worn when attending cats with draining tracts and hands should be cleansed thoroughly.

Viral. Rabies is still the only significant small animal viral zoonosis in the United States. Since 1980, more cases of rabies have been reported in cats than in dogs in the USA. Rabies is a major, potentially lethal, occupational health hazard for those commonly working with animals with unknown vaccination status including veterinary staff as well as humane shelter and rescue group employees. Preexposure vaccination should be offered to veterinarians and others who

work with dogs and cats in rabies enzootic areas. However, in a recent survey, 85.1% of veterinary medical association members and managers of animal shelters or wildlife rehabilitation centers had been vaccinated versus only 17.5% of staff members.

Some have been concerned whether the retroviruses of cats, feline leukemia virus, feline immunodeficiency virus, and feline foamy virus, can infect people because FeLV subtypes B and C can replicate in human cell lines. However, to date, humans have not been shown to be infected with any of the feline retroviruses. In the most recent study, 204 veterinarians and others potentially exposed to feline retroviruses were assessed for antibodies against FIV and FeFV, FeLV p27 antigen, and FeLV provirus; all were negative. Since both FeLV and FIV can induce immunodeficiency, infected cats should be considered more likely than retrovirus-naive cats to be carrying other potential zoonotic agents, particularly if gastrointestinal tract signs are occurring.

Respiratory and ocular zoonoses. Bordetella bronchiseptica is a bacterium that induces respiratory tract infections in dogs and cats. The classic clinical manifestation is tracheobronchitis, but the organism can also cause pneumonia, sneezing, and nasal discharge. Humans rarely develop clinical disease due to B bronchiseptica unless they are immune compromised. Only 39 cases of B. bronchiseptica infection in people had been reported by 1998; most were immunodeficient. Amoxicillin-clavulanate, chloramphenicol, enrofloxacin, and tetracycline derivatives are effective treatments. Animals with upper or lower respiratory tract inflammatory disease should be kept away from immunodeficient people until clinically normal. However, treated animals can still shed the organism.

Chlamydophila felis (formerly Chlamydia psittaci) causes mild conjunctival disease and rhinitis in cats. In Japan, the prevalence rates of antibodies against an isolate of Chlamydophila felis were 51.1% in stray cats, 15.0% in pet cats, 3.1% in the general human population and 5.0% in small animal clinic veterinarians, suggesting that transfer between cats and people may occur. Conjunctivitis in humans following direct contact with ocular discharges from cats has been described but systemic disease is rare. Diagnosis is based on organism demonstration by culture, cytological documentation of characteristic inclusion bodies, polymerase chain reaction assay, or fluorescent antibody staining of conjunctival scrapings. Tetracycline or chloramphenicol-containing eye ointments generally are effective in the treatment of infection. Care should be taken to avoid direct conjunctival contact with discharges from the respiratory or ocular secretions of cats, especially by immunosuppressed persons. Employees should be directed to wear gloves or wash hands carefully when attending cats with conjunctivitis.

Humans are the principal natural hosts for Streptococcus group A bacteria, S. pyogenes and S. pneumoniae, which cause "strep throat" in people. Dogs and cats in close contact with infected humans can develop transient, subclinical colonization of pharyngeal tissues and can transmit the infection to other humans. However, this is poorly documented and thought to be unusual. The organism can be cultured from the tonsillar crypts. Culture-positive animals should be treated with penicillin derivatives. If animals are to be treated in a household with chronic recurrent "strep throat", all humans should also be treated since they also could be chronic subclinical carriers.

Yersinia pestis and Fransicella tularensis can be transmitted from cats to people in respiratory secretions (see Bite, scratch, or exudate zoonoses section). In endemic areas, cats with clinical signs or radiographic abnormalities consistent with pneumonia should be handled as plague or tularemia suspects. Gloves, mask, gown, and eye protection should be worn while performing transoral airway washings in suspect cats.

Genital and urinary tract zoonoses. Coxiella burnetii is a rickettsial agent found throughout the world, including North America. Many ticks, including Rhipicephalus sanguineus, are naturally infected with Coxiella burnetii. Cattle, sheep, and goats are commonly subclinically infected and pass the organism into the environment in urine, feces, milk, and parturient discharges. Seropositive dogs have been detected but zoonotic transfer to people from dogs has not been documented. Infection of cats most commonly occurs following tick exposure, ingestion of contaminated carcasses, or aerosolization from a contaminated environment. Fever, anorexia, and lethargy develop in some experimentally infected cats. Infection has been associated with abortion in cats, but the organism can also be isolated from normal parturient cats. Infection of cats appears to be common; 20% of cats from a humane society in southern California and in Maritime Canada were seropositive, and the organism was grown from the vagina of healthy cats in Japan. We have also amplified *C. burnetii* DNA from the uterus of healthy, client-owned cats. Human illness associated with direct contact with infected cats occurs after aerosol exposure to the organism passed by parturient or aborting cats; clinical signs develop 4 to 30 days after contact. Humans commonly develop acute clinical signs similar to those associated with other rickettsial diseases including fever, malaise, headache, pneumonitis, myalgia, and arthralgia. After primary infection, chronic Q fever develops in approximately 1% and can manifest as hepatic inflammation or valvular endocarditis. Tetracyclines, chloramphenicol, and quinolones are usually effective therapeutic agents in people. Gloves and masks should be worn when attending to parturient or aborting cats. People that develop fever or respiratory tract disease after exposure to parturient or aborting cats should seek medical attention.

There are at least 11 Leptospira serovars that infect dogs in the United States; cats are very resistant to infection. Leptospira spp. can be transmitted in urine from infected dogs and cats to humans, resulting in clinical disease. Host-adapted species cause subclinical infection; infection by non-host adapted species commonly results in clinical illness. Human clinical syndromes vary with the serovar, but are similar to those that occur in the dog. The organisms enter the body through abraded skin or intact mucous membranes. See recently published papers for a detailed discussion of the clinical manifestations of this disease and its treatment in dogs and cat. Leptospirosis should be suspected in dogs with acute nephritis or hepatitis. The infections also frequently cause fever; the infections can also induce chronic disease in some animals. Azotemia with pyuria but no bacteriuria are also common since the organisms are usually not seen under the light microscope. Cats generally do not develop clinical leptospirosis and the role they play in human infections is unknown but thought to be minimal. Diagnosis can be made by dark field examination of urine, culture, presence of serum antibodies, and PCR amplification of organismal DNA in urine. Intravenous administration of penicillins should be used initially for treatment followed by several weeks of doxycycline treatment to clear the tissue phases. Vaccines contain 2-4 serovars and so are not 100% protective since the serovars do not cross-protect. In addition, immunity associated with vaccination may persist less than 1 year.

Animals with suspected leptospirosis should be handled while wearing gloves. Contaminated surfaces should be cleaned with detergents and disinfected with iodine-containing products.

Brucella canis is a bacterium that preferentially infects the testicles, prostate, uterus, and vagina of dogs. The infection is maintained in dogs primarily by venereal transmission. Humans can be infected by direct contact with vaginal and preputial discharges from dogs. Clinical syndromes in dogs are diverse but commonly include abortion, stillbirth, failure to conceive, orchitis, epididymitis, vaginal discharge, uveitis, diskospondylitis, and bacteremia. Intermittent fever, depression, and malaise are common in infected people. Diagnosis is based on serologic testing or demonstration of the organism by culture. Dogs with clinical signs of brucellosis should be evaluated serologically for Brucella infection using the 2-mercapthoethanol rapid slide agglutination card test. Seronegative dogs are unlikely to be harboring Brucella unless the clinical syndrome was peracute. Seropositive dogs should have results confirmed by tube agglutination or agar gel immunodiffusion. Long term antibiotic treatment (tetracyclines, aminoglycosides, quinolones) usually does not clear the infection. Ovariohysterectomy or castration will lessen contamination of the environment. Genital tract secretions should be avoided.

SHARED VECTOR ZOONOSES

Some zoonotic agents are transmitted between animals and man by shared vectors like fleas, ticks, or mosquitoes. *Rickettsia rickettsii* (ticks), *Ehrlichia* spp. (ticks), *Anaplasma phagocytophilum* (ticks), *Borrelia burgdorferi* (ticks), *Rickettsia felis* (fleas), *Bartonella* spp. (fleas and ticks), *Dipylidium caninum* (fleas), *Dirofilaria immitis* (mosquitoes), and West Nile virus (mosquitoes) are examples of vector borne zoonoses that are common in the United States. For the flea- and tick-borne zoonoses, the pet brings the vector of the organism into the environment resulting in exposure of the human. There could be a slight increased risk of exposure to veterinary health care providers since we handle many animals infested with fleas and ticks. However, it is the vector, not direct contact with the infested animal that results with infection of the human. Flea and tick control should always be maintained animals and infested animals that are seen in the clinic should be treated immediately.

SHARED ENVIRONMENT ZOONOSES

Some agents that infect both animals and man are not commonly transmitted between the pet and the owner by direct contact but but are acquired from the same environmental source. Notable examples include *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, *Cryptococcus neoformans*, and *Aspergillus* spp..

FOOTNOTES

[a]http://www.cdc.gov/hiv/pubs/brochure/oi_pets.htm
[b]http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm
[c]http://www.aafponline.org
[d]http://www.capcvet.org

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Table 1. General guidelines for veterinarians to avoid zoonotic transfer of disease

- Veterinarians and their staff should familiarize themselves with zoonotic issues and take an active role in discussing of the health risks and benefits of pet ownership with clients so that logical decisions concerning ownership and management of individual animals can be made.
- The veterinary clinic should make it clear that the staff understands conditions associated with immune deficiency, is discreet, and is willing to help; use of signs or posters can be effective for this purpose.
- Pet owners should be provided information concerning veterinary or public health aspects of zoonoses, but veterinarians should not diagnose diseases in humans or discuss specific treatments.
- Clinically ill pet owners should always be referred to a physician for additional information and treatment.
- Veterinarians and physicians have different experiences concerning zoonoses; veterinarians should volunteer to speak to the pet owner's physician to clarify zoonotic issues when indicated.
- When public health related advice is offered, it should be documented in the medical record.
- When reportable zoonotic diseases are diagnosed, appropriate public health officials should be contacted.
- Diagnostic plans to assess for presence of organisms with zoonotic potential should be offered, particularly to owners with clinically ill pets.
- All dogs and cats should be vaccinated for rabies.
- Dogs and cats should be routinely dewormed with a drug that kills hookworms and roundworms.
- Flea and tick control should be maintained at all times.

Table 2. General guidelines for pet owners to avoid zoonotic transfer of disease

- If a new pet is to be adopted, the dog or cat least likely to be a zoonotic risk is a clinically normal, arthropod-free, adult animal from a private family.
- Once the animal to be adopted is identified, it should be quarantined from any immunocompromised person until a thorough physical examination and zoonoses risk assessment is performed by a veterinarian.
- Veterinary care should be sought for all clinically ill pets.
- Physical examination and fecal examination should be performed at least once or twice yearly.
- Fecal material produced in the home environment should be removed daily, preferably by someone other than an immunocompromised individual.
- Use litterbox liners and periodically clean the litterbox with scalding water and detergent.
- Do not allow dogs or cats to drink from the toilet.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling animals.
- Do not handle animals that you are unfamiliar with.
- Clinically ill animals should not be handled by immunocompromised people, if possible.
- Pets should be maintained within the home environment to lessen exposure to other animals that may carry zoonotic agents, exposure to excrement of other animals, and exposure to fleas and ticks.
- Pets should only be fed commercially processed food.
- People should not share food utensils with pets.
- Avoid being licked by animals.
- Claws of cats should be clipped frequently to lessen the risk of skin penetration.
- To lessen the risk of bites and scratches, do not tease or physically restrain dogs and cats.
- If bitten or scratched by a dog or cat, seek medical attention.
- Control potential transport hosts like flies and cockroaches that may bring zoonotic agents into the home.
- Cook meat for human consumption to 80 C for 15 minutes minimum (medium-well).
- Wear gloves when handling meat and wash hands thoroughly with soap and water when finished.

USE OF MOLECULAR ASSAYS FOR THE DIAGNOSIS OF FELINE INFECTIOUS DISEASES

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Clinical syndromes induced by infectious agents are common in cats. Documenting that the infectious agent is still present is the best way to make a definitive diagnosis. Commonly used techniques vary by the body system but include fecal flotation, cytology, histopathology, immunohistochemistry, culture, antigen tests, and molecular diagnostic assays. For some agents, antibody test results are also used to help make a clinical diagnosis. However, presence of antibodies may only document prior exposure, not current infection.

Sensitivity is the ability of an assay to detect a positive sample; specificity is the ability of an assay to detect a negative sample. Sensitivity and specificity vary with each assay. Positive predictive value (PPV) is the ability of a test result to predict presence of disease; negative predictive value (NPV) is the ability of a test result to predict absence of disease. Many of the infectious agents encountered in feline practice infect a large percentage of the population, resulting in positive organism detection techniques or serum antibody production. However, they only induce disease in a small number of cats in the infected group. Examples include coronaviruses, *Toxoplasma gondii*, and *Bartonella* spp.. For these examples, even though assays with good sensitivity and specificity are available, the predictive value of a positive test is actually very low.

One of the newest organism demonstration techniques used in practice is the polymerase chain reaction (PCR) assay. This reaction amplifies small quantities of DNA to detectable levels. By use of a reverse transcriptase step, RNA is converted to DNA; therefore the technique can also be used to detect RNA (RT-PCR). PCR assays are of great value for documentation of infections, particularly if the organism in question is difficult to culture (e.g., *Mycoplasma* spp.) or cannot be cultured (e.g., hemoplasmas). Specificity can be very high, depending on the primers used in the reaction. For example, primers can be designed to detect one genus but not others. Primers can also be designed to identify only one species. For example a PCR assay can be developed to detect all haemoplasmas or just one species such as *Mycoplasma hemofelis*.

Because of the inherent sensitivity of the reaction, PCR can give false-positive results if sample contamination occurs during collection or at the laboratory performing the procedure. False-negative results can occur if the sample is handled inappropriately. Results may also be affected by treatment. For example, many cats with hemoplasmosis become negative by PCR assay of blood while on doxycycline or fluoroquinolone therapy and so should be sampled prior to treatment. Other potential problems are that minimal standardization exists among commercial laboratories offering PCR assays and minimal external quality control exists.

Although PCR assays can be one of the most sensitive for documentation of infections, positive

test results do not always prove that the infection is resulting in clinical illness. For example, because the technique detects DNA of both live and dead organisms, positive test results may be achieved even if the infection has been controlled. When the organism being tested for commonly infects the background population of healthy cats, interpretation of results for a single animal can be difficult. For example, '*Candidatus* M. haemominutum' infects up to 20% of healthy cats in some environments and so detection of a positive test result in a clinically ill cat does not prove a disease association. In addition, for some agents the currently available PCR assays cannot discriminate between vaccine strains and field strains. For example, currently available PCR assays for FHV-1 also amplify modified live vaccine strains, so a positive result does not even indicate presence of a pathogenic strain. Real-time PCR can be used to determine the amount of microbial DNA in a sample. It is possible that the DNA load will correlate to the presence of disease for some agents. However, some agents are very host adapted and can have large amounts of DNA present in samples from healthy carrier cats. For example, the number of '*Candidatus* M. haemominutum' copy numbers/µl of blood does not correlate to the PCV. Based on these findings, it is very important that small animal practitioners carefully assess the predictive values of currently available PCR and the expertise and reliability of the laboratory that will be performing the assays. New PCR assays are being developed almost daily. The purpose of this lecture is to use several common infectious disease agents to emphasize important points concerning molecular assays in the diagnosis of feline infectious diseases.

Respiratory agents. Feline calicivirus (FCV) is a common differential diagnosis for cats with clinical evidence of rhinitis, stomatitis, and conjunctivitis. Less commonly, FCV is associated with polyarthritis and lower airway disease in kittens. Virus isolation can be used to document current infection but takes at least several days for results to return. Because of wide-spread exposure and vaccination, the positive predictive value of serological tests is poor. Reverse transcriptase (RT) PCR assays can be used to amplify the RNA of FCV and results can be returned quickly. However, these assays also amplify vaccine strains of FCV. FCV RNA can be amplified from samples collected from normal carrier cats as well as clinically ill cats and so have poor positive predictive value. For example, in one study in our laboratory, presence of FCV RNA failed to correlate to the presence or absence of stomatitis in cats (1). In addition, amplification of FCV RNA cannot be used to prove virulent systemic calicivirus infection. Results of FCV RT PCR can also be falsely negative and so can have poor negative predictive value.

Feline herpesvirus 1 (FHV-1) is a common differential diagnosis for cats with clinical evidence of rhinitis, stomatitis, conjunctivitis, keratitis, and facial dermatitis. Because of wide-spread exposure and vaccination, the positive predictive value of serological tests is poor. FHV-1 can be documented by direct fluorescent staining of conjunctival scrapings, virus isolation, or PCR. FHV-1 DNA can be amplified from conjunctiva, nasal discharges, and pharynx of healthy cats and so the positive predictive value of conventional PCR assays is low (2). Currently used PCR assays also detect vaccine strains of FHV-1, further lessening the positive predictive value of the assays (3). In one study in our laboratory, presence of FHV-1 RNA failed to correlate to the presence or absence of stomatitis in cats. Quantitative PCR may ultimately prove to correlate to the presence or absence of disease but failed to correlate to presence of conjunctivitis in one study (4). The negative predictive value of FHV-1 PCR assays is also in question because many cats that are likely to have FHV-1 associated disease are negative. This may relate to clearance

of FHV-1 DNA from tissues by a hypersensitivity reaction. Tissue biopsies have greater sensitivity than conjunctival swabs but do not necessarily have greater predictive value. FHV-1 DNA can be amplified from aqueous humor of some cats but whether this indicates FHV-1 associated uveitis is unknown.

Mycoplasma spp. *Chlamydophila felis*, and *Bordetella bronchiseptica* are other common respiratory pathogens in cats. As for FHV-1 and FCV, PCR positive test results for these organisms cannot be used to distinguish a carrier from a clinically ill cat. In addition, PCR assays do not provide antimicrobial drug susceptibility testing and so for cats with potential bordetellosis, culture and sensitivity is the optimal diagnostic technique, especially if an outbreak is occurring. *Toxoplasma gondii* DNA has been amplified from airway washings of some cats with lower respiratory tract disease and so PCR is an option for evaluation of samples from diseased animals from which the organism is not identified cytologically.

Gastrointestinal agents. The diagnosis of *Giardia* spp. infection is easy to make in cats with small bowel diarrhea with the combination of fecal flotation techniques and wet mount examination. Fecal antigen tests are also accurate and there are several assays available for point of care use, included one labeled for veterinary use (5). Fecal PCR assays are often falsely negative because of PCR inhibitors in stool. However, *Giardia* spp. PCR can be used to determine whether the infective species is a zoonotic assemblage which is the primary indication for this technique.

While *Cryptosporidium* spp. infection is common, it is unusual to find *C. felis* oocysts after fecal flotation in cats. Acid-fast staining of a thin fecal smear is cumbersome and insensitive. Antigen assays titrated for use with human feces are inaccurate when used with cat feces. Thus, PCR may be aid in the diagnosis of cryptosporidiosis in dogs and cats and has been shown to be more sensitive than IFA in cats (6). *Cryptosporidium* spp. PCR assays are indicated in IFA negative cats with unexplained small bowel diarrhea and when the genotype of *Cryptosporidium* is to be determined. However, *C. felis* infection in cats is common and so positive tests results do not always prove that the agent is the cause of the clinical disease. No drug is known to eliminate *Cryptosporidium* spp. infections and small animal strains are not considered significant zoonotic agents so PCR is never indicated in healthy animals.

PCR assays are also available for detection of DNA of *Tritrichomonas foetus, Salmonella* spp., *Campylobacter* spp., *Clostridium* spp., parvoviruses, and *T. gondii* and a RT-PCR assay is available for coronaviruses. Trophozoites of *T. foetus* can often be detected on wet mount examination of fresh feces which can be completed as an in clinic test. DNA of *T. foetus* can be detected in healthy carrier cats and so positive results do not always prove illness from the organism (7). Cases with suspected salmonellosis or campylobacteriosis should be cultured rather than assessed by to determine the anti-microbial susceptibility patterns. In dogs, the PPV of *Clostridium* spp. PCR assays on feces is low and if used, should be combined with enterotoxin assays. Information in cats is currently lacking. There is no current evidence that parvovirus PCR on feces is superior to currently available antigen assays. *Toxoplasma gondii* is only shed for about 7-10 days and millions of oocysts are generally shed during this time making the organism very easy to identify. Thus, PCR assays are usually not needed to diagnosis this infection. Because virus isolation is not practical clinically, RT-PCR is used most frequently to

detect coronaviruses RNA in feces. However, positive test results do not differentiate FIP inducing strains from enteric coronaviruses.

Blood borne agents. The new names for *Haemobartonella felis* are *Mycoplasma haemofelis* (Mhf), *'Candidatus* Mycoplasma haemominutum' (Mhm), and '*Candidatus* M. turicensis' (Mtc). In at least two studies of experimentally infected cats, Mhf is apparently more pathogenic than Mhm; all Mhf inoculated cats became clinical ill whereas Mhm inoculated cats were generally subclinically infected. Cats with chronic Mhm infection had more severe anemia and longer duration of anemia when experimentally infected with Mhf when compared to cats infected with Mhf alone. It appears that Mtc has intermediate pathogenicity. Diagnosis is based on demonstration of the organism on the surface of erythrocytes on examination of a thin blood film or PCR assay. Organism numbers fluctuate and so blood film examination can be falsely negative up to 50% of the time. The organism may be difficult to find cytologically, particularly in the chronic phase. Thus, PCR assays are the tests of choice due to sensitivity (8). Primers are available that can amplify all three hemoplasmas. Real time PCR assays can be used to monitor copy numbers during and after treatment but do not have greater sensitivity, specificity, or predictive value than conventional PCR assays. PCR assays should be considered in the evaluation of cats with unexplained fever or anemia that are cytologically negative. In addition, the ACVIM recommends screening cats for use as blood donors by PCR assays for haemoplasmas (9). Many cats are carriers of the relatively non-pathogenic '*Candidatus* M. haemominutum' and so positive test results may not always correlate to the presence of disease (poor PPV).

Cats can be infected by *E. canis* like organism (10) and *Anaplasma phagocytophilum* (11). Little is known about the other agents in these genera in regards to cats. As the organisms are in different genera, serological cross reactivity is variable. Thus, while the clinical syndromes can be similar, there is no one serological test to document infection and there is currently no standardized serology for cats. In addition, some cats with *E. canis* infection do not seroconvert and so PCR assay is superior to serology in cats. PCR assays can be designed to amplify each organism. Alternately, primers are available to amplify all of the organisms in a single reaction and then sequencing can be used to determine the infective species.

Cats can be infected by *Rickettsia felis* and have been shown to have antibodies against *R. rickettsii*. Fever, headache, myalgia, and macular rash in humans have been attributed to *R. felis* infection in several countries around the world. In recent study in our laboratory, we assayed 92 pairs of cat blood and flea extracts from Alabama, Maryland and Texas, using PCR assays that amplify a region of the citrate synthase gene (gltA) and the outer membrane protein B gene (ompB). Of the 92 pairs, 62 of 92 (67.4%) flea extracts and none of the cat blood samples were positive for *R. felis* DNA (12). In another study, we showed *R. felis* and *R. rickettsii* antibody prevalence rates in cats with fever to be 5.6% and 6.6%, respectively but neither organism was amplified from blood (13). These results prove that cats are sometimes exposed but further data are needed to determine significance of diseases associations. Whether *Rickettsia* spp. PCR assays are indicated for use in cats at this time is unknown.

Blood culture, PCR assay on blood, and serologic testing can be used to assess individual cats for *Bartonella* spp. infection. Serological methods include IFA, ELISA, and Western blot

immunoassay. Cats that are culture-negative or PCR-negative and antibody-negative and cats that are culture-negative or PCR-negative and antibody-positive are probably not a source of flea, cat, or human infection. However, bacteremia can be intermittent and false-negative culture or PCR results can occur, limiting the predictive value of a single battery of tests. While serologic testing can be used to determine whether an individual cat has been exposed, both seropositive and seronegative cats can be bacteremic, limiting the diagnostic utility of serologic testing. Thus, testing healthy cats for *Bartonella* species infection is not currently recommended (14). Testing should be reserved for cats with suspected clinical bartonellosis. However, because *Bartonella* spp. infection in cats is so common in healthy cats, even culture or PCR positive results does not prove clinical bartonellosis. For example, while we detected *Bartonella* spp. DNA in more cats with fever than pair matched cats without fever, the healthy cats were still commonly positive (15).

Cytauxzoon felis in clinically affected cats is usually easily identified on cytological examination of blood smears or splenic aspirates. Serologic testing is not commercially available. PCR can be used to amplify organism DNA from blood from cats that are cytologically negative (16).

Antibodies against feline immunodeficiency virus (FIV) are detected in serum in clinical practice most frequently by enzyme-linked immunosorbent assay (ELISA). Comparisons between different tests have shown the results of most assays are comparable (17). Clinical signs can occur before seroconversion in some cats, and some infected cats never seroconvert; thus false-negative reactions can occur. Results of virus isolation or PCR on blood are positive in some antibody-negative cats. False-positive reactions can occur using ELISA; hence, positive ELISA results in healthy or low-risk cats should be confirmed using Western blot immunoassay. Kittens can have detectable, colostrum-derived antibodies for several months. Kittens less than 6 months of age that are FIV seropositive should be tested every 60 days until the result is negative. If antibodies persist at 6 months of age, the kitten is likely infected. Virus isolation or RT-PCR on blood can also be performed to confirm infection. However, FIV is not present in the blood in high levels and so false negative results are common. Thus, the assay is not very accurate for distinguishing a vaccinated cat from a naturally exposed cat (18).

Most cats with feline leukemia virus infection are viremic and so molecular diagnostic assays are not usually needed in clinical practice. However, use of newer sensitive real time PCR assays have been used to accurately characterize the stages of infection (19). However, these assays are not commonly available commercially.

RNA of both FIPV and FECV can be amplified from the blood of cats and so positive test results do not always correlate with the development of FIP. Amplification of the mRNA of the M gene by RT-PCR has had mixed results in two studies performed to date. In the one study, 13 of 26 apparently normal cats were positive for FECV mRNA in blood suggesting that the positive predictive value of this assay for the diagnosis of FIP was low (20).

Ocular agents. *Toxoplasma gondii*, *Bartonella* spp., FHV-1 and coronavirus are the organisms for which DNA or RNA has been amplified most frequently from the aqueous humor of cats with endogenous uveitis. While little is know about the predictive value of these assays when used with aqueous humor, the combination of molecular assays with local antibody production

indices may aid in the diagnosis of some cases.

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Feline Obesity: Causes, Consequences & Management

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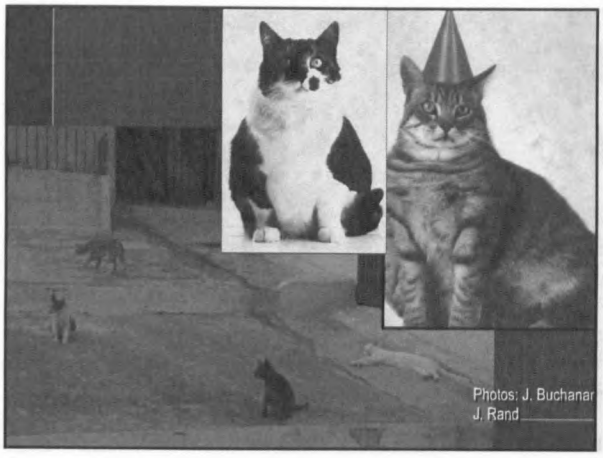
THE UNIVERSITY OF QUEENSLAND



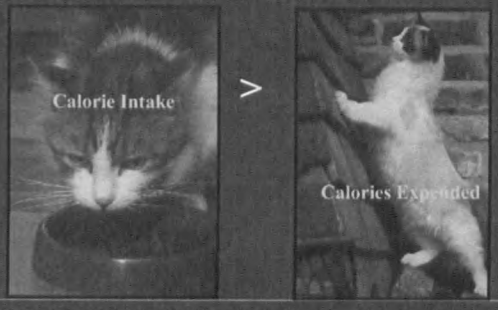
Photos: J. Buchanan
J. Rand

Prevalence

- 35-40% overweight (Sloth)
- 25% obese (>20% above ideal wt) (Scarlett et. al.)
- Overweight cats are under-diagnosed
- Incidence of obesity increasing

What Causes Obesity?

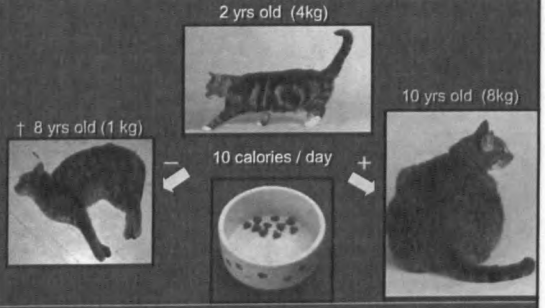
- Result of imbalance between calorie intake and expenditure
- Small imbalance life-long has marked consequences on BW



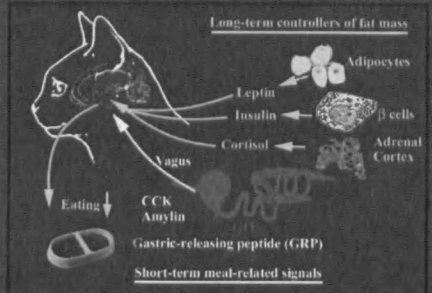
Photos: A Cat of Your Own; Publisher: Ken Fin

Excessive Calorie Intake

Calorie intake is finely controlled

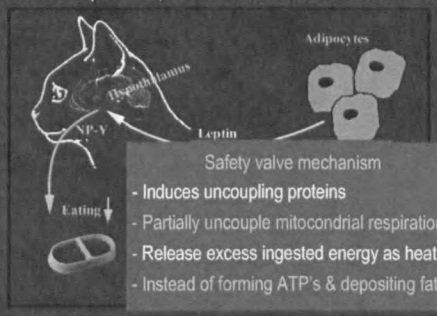


What Causes Excessive Calorie Intake?
Appetite control is complex – food intake is normally linked to energy requirements



Leptin and Obesity

- Hormone leptin = lipostat role, ie. controls amount of fat



Safety valve mechanism
- Induces uncoupling proteins
- Partially uncouple mitocondrial respiration
- Release excess ingested energy as heat
- Instead of forming ATP's & depositing fat

Current Research: Leptin

Obese cats = ↑ leptin, ∝ fat mass

Still ate excess calories & had weight gain

Leptin resistance?

Photo: A. Lister

Appleton, Rand, Sunvold *JFMS* 2001

Current Research: Insulin

Obese cats = ↑ insulin

Still ate excess calories & had weight gain

Resistance to insulin's effects on appetite control

Insulin resistance centrally & peripherally = thrifty genotype

Confers survival advantage

Other Factors Which Contribute to Excessive Food Intake

- Palatability important influence in food intake in cats
- Owners don't buy food that cat won't eat

Stimulus of highly palatable food overrides leptin signal at hypothalamus

* Environmental, behavioral & social factors influence food intake

Single & 2-cat households

> obesity

Multiple cat households

Combination of factors

- More food
- Boredom, loneliness
- Social hierarchy
- Physical activity

Photos: A Cat of Your Own; Publisher: Ken Fin

Quality of Human - Animal Bond important in predisposing to obesity

Overweight cats have:

Higher intensity relationship between owner & cat

- **Owners overhumanize relationship**
  - **"patient undemanding listener"**
- Owners play less with cat
  - **Spend more time watching it eat**

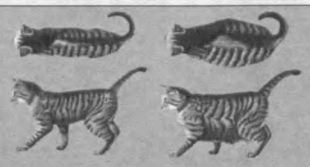
Kienzle 2000

Human - cat relationship

6 Types of cat owner based on how they perceived their cat

- playmate
- tolerated
- friend
- child substitute
- family member
- undemanding, patient listener

Lower risk of overweight



Higher risk of overweight

Kienzle 2000

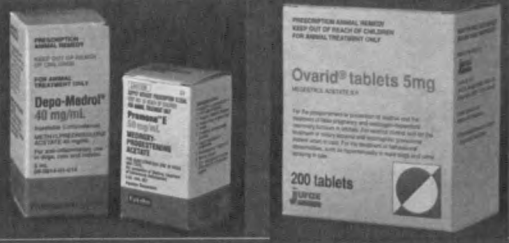
* Genetics influences risk of obesity

- Certain breeds tend to ingest excessive calories to their needs
- Domestic shorthair
  - predisposed to obesity
- Purebred cats such as Abyssinians
  - leaner
- Genetic predisposition is usually present in obese humans

Photos: A Cat of Your Own; Publisher: Ken Fin

Drugs

- Some drugs stimulate appetite centrally
- Glucocorticoids, progestins, anticonvulsants predispose to obesity



What Causes Obesity?

- Factors which influence calorie expenditure

Calorie Intake > Calories Expended

Photos: A Cat of Your Own; Publisher: Ken Fin

Physical Inactivity

- Lifestyle modern urban cat vs feral cat
- Expend less energy because physically inactive
- Urban cats often confined indoors:
  - No longer hunt for food
  - No play hunting
  - No fighting
  - No climbing trees

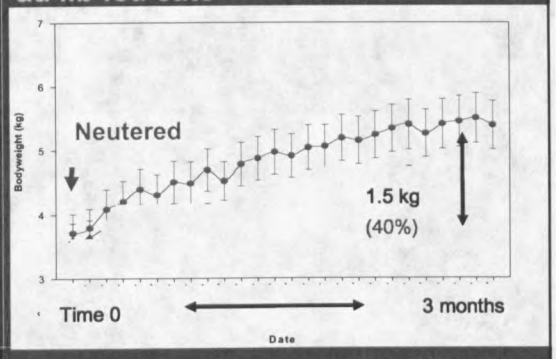
* Neutering influences body weight

Multifactorial:

- ↓'d energy requirement for maintenance
- Modifies physical activity
- Modifies appetite

→ Predisposes to obesity

Weight gain following neutering in ad lib fed cats



AGE INCREASES RISK OF OBESITY

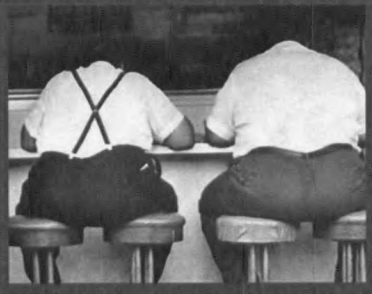
- Middle-age cats more often overweight
  - Weight peaks at 6-8 years
- Accumulative effect small excess calories
  - Older cats lower energy requirement

Photos: A Cat of Your Own; Publisher: Ken Fin

What Are the Consequences of Obesity?

Photo: A. Lister

Annual road toll in USA is 42,000 fatalities



400,000 Americans die annually from the effects of obesity, including diabetes & hypertension"

Medical Tribune News Service July 1997 (via Medscape)

Consequences of obesity in cats numerous & life-threatening

- Surgical and anaesthetic complications
- **Increased risk of infections**
- **Lameness**
- Feline Lower Urinary Tract Disease
- **Hepatic lipidosis**
- Diabetes mellitus
- **Greater risk of death**

Consequences of obesity in cats

Appleton et al 2000, 2001

Weight gain in cats

- 16 normal-weight cats
- Fed ad libitum for 10 months
  - Feline maintenance (33.0% protein, 22.3% fat)
  - Recovery / conditioning (39.8% protein, 26.6% fat)
  - Mean increase in body weight =1.9 kg, 44 %
  - Body weight 4.3 kg → 6.3 kg
  - Body condition score (5 point scale) 3 → 4.5
- All cats' weight increased by minimum of 8%
  - 6 cats classed as overweight (body condition 4/5)
  - 10 cats classed as obese (body condition 5/5)

Appleton et al 2000, 2001

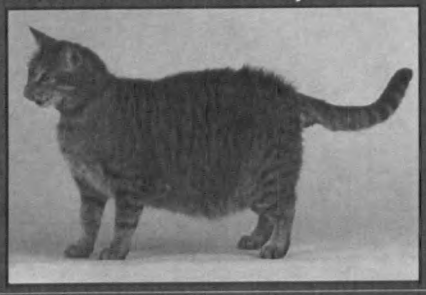
CONSEQUENCES OF OBESITY

- MUSCULOSKELETAL PROBLEMS

Appleton, Rand, Sunvold *JFMS* 2001

Consequences Of Obesity

- Unable To Groom Effectively



Appleton, Rand, Sunvold *JFMS* 2001

Consequences of Obesity

Lack of grooming:

- Fecal mats around anus
- Perianal dermatitis

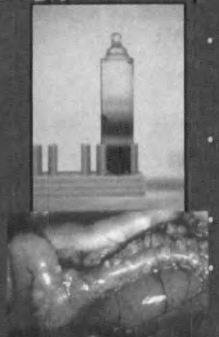
Appleton, Rand, Sunvold *JFMS* 2001

Increased susceptibility to infection

- Obese cats - ↑'d risk of bacterial skin infections (acne)
  - ↑'d susceptibility to viral & bacterial (dogs & humans)
- Decrease immuno-incompetence reported in obese humans

Photo: J. Buchanan

Triglycerides ↑'d Obese Cats (2X's)



- **Hypertriglyceridemia predisposes to pancreatitis in humans and dogs**
- Obese dogs greater risk of pancreatitis
- **Overweight cats common**
- Are ↑'d TG concs of obesity contributing to high prevalence of pancreatitis

Appleton, Rand, Sunvold *WSAVA* 2000

Biochemistry in Obesity

- Obese cats have ↑'d creatinine concs.
- Suggests increased muscle mass
- DEXA: < 50% body mass is fat & 50% supporting tissue

To support increased fat mass

- ↑ muscle mass
- ↑ blood vessels

- 1kg fat requires 28km of blood vessels!

Feline MRI

- Lean cat
- Obese cat

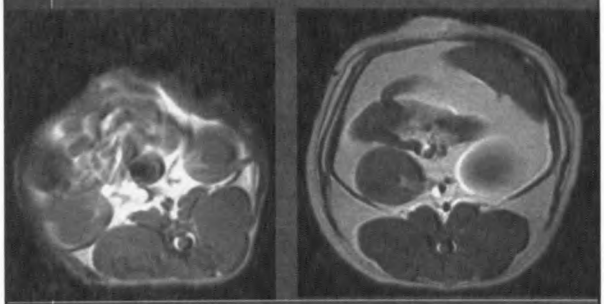
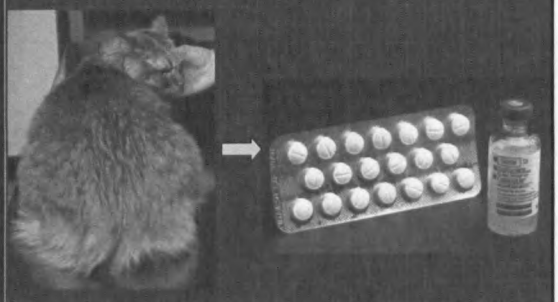


Photo: M. Coradini

Link between obesity & diabetes

- Well established link with type 2 DM (adult onset; NIDDM)



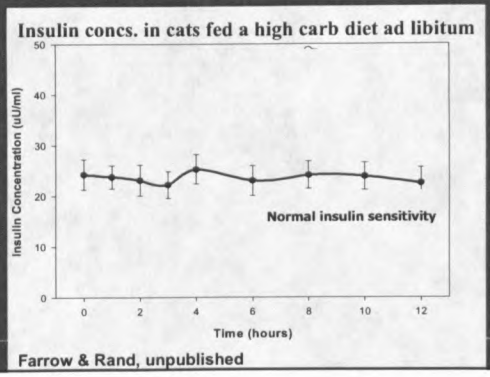
Link between obesity & diabetes

- Obese woman is 13 times more likely to develop diabetes
  - > 20% above ideal body weight
- Obese cats have 4-5 times the risk of diabetes (at diagnosis)
- Rate of type 2 diabetes closely follows rate of obesity

Picture: Times magazine

How does obesity cause diabetes?

Via insulin resistance

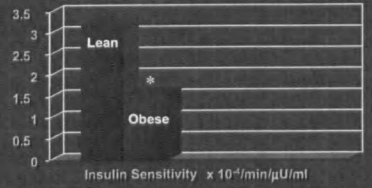


Farrow & Rand, unpublished

Insulin Sensitivity Test

Frequently sampled IV GTT & minimal model analysis (Bergman)

- Insulin sensitivity ↓ by half after weight gain of 2kg
- In some cats, insulin sensitivity markedly decreased
- 25% cats IS values ≡ diabetic cats ie. insulin resistance

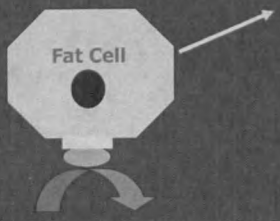


Appleton, Rand, Sunvold *JFMS* 2001

Insulin Resistance in Obesity: What is the Molecular Mechanism?

Likely multifactorial

Sympathetic Tone



Adipokines = fat secreted hormones

- Leptin
- Resistin
- Adiponectin
- Tumor-Necrosis Factor (TNFα

Other Factors

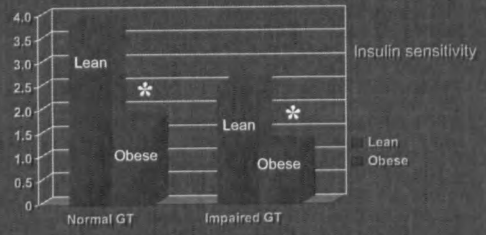
Glucose Transporter – GLUT4

How does obesity cause diabetes?

- Insulin resistance causes chronic high demand for insulin secretion
- Eventually beta cell damage & loss of insulin secretion
- Blood glucose increases → Impaired glucose tolerance & diabetes

Cats with impaired glucose tolerance in obesity:

- When lean: ↓'d insulin sensitivity & ↑'d insulin concentrations.



- IS was further decreased with weight gain

Appleton, Rand, Sunvold *JFMS* 2001

Cats with impaired glucose tolerance in obesity:

- 6/7 cats with IS values below the population median when lean

  → impaired glucose tolerance with obesity

- Some cats have underlying low insulin sensitivity

  Predisposed to impaired glucose tolerance, & probably diabetes, with obesity

Appleton, Rand, Sunvold *JFMS* 2001

Insulin Sensitivity/Resistance in Humans

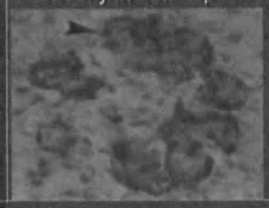
- Your underlying insulin sensitivity - genetically determined
- ↓'d by obesity
- ↓'d by physical inactivity

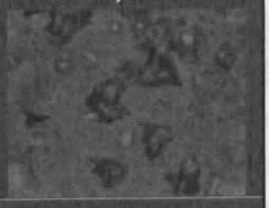
Insulin resistance, from obesity & genotype, is # 1 factor predisposing to diabetes

Other Factors in obesity → ↓'d B cells

Islet amyloid deposition

- Precipitate of amylin, secreted w. insulin from B cells
- High amylin concs. associated with ↑'d amyloid
- Obesity in other species increases amylin secretion

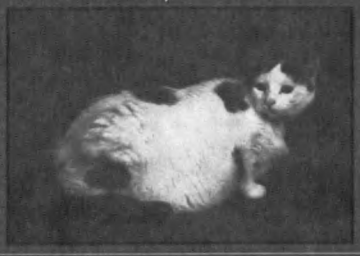




Hoenig & O'Brien 1998; Photos: Lutz *Thesis: 1995;*

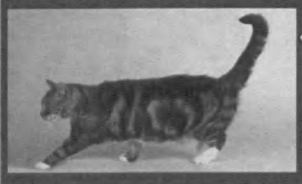
Consequences of Obesity Conclusions

- Fat cats are not healthy cats
- Fat cats need help!



Management of Obesity Consists of:

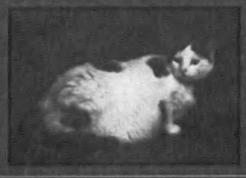
- Prevention
- Treatment:
  - Decrease body weight
  - Decrease side-effects



Management of obesity requires owner "buy in"

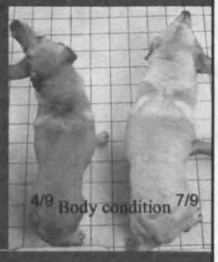
- Owner needs to understand that prevention or appropriate management of obesity

→ More active, healthier pet, with longer life



Health consequences in overweight dogs

- Body condition score of 4/9 or 7/9
- Overweight dogs had 20% reduction in life-span
- **Median age at death 11 years vs 13 years**
- What consequences of body condition score of 8/9 or 9/9?
- What about cats?



Kealy et al, JAVMA 2002

Obesity decreases lifespan of cats

- Probability for survival over 4 years = 83% for cats with optimum body condition & 53% for obese cats

- 5/10 obese cats dead
- 2/10 lean cats dead

Scarlett 1997

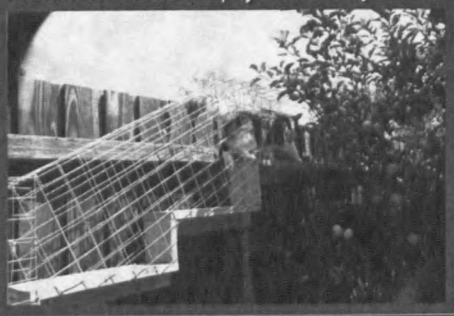
Cornerstone Management of Obesity

- Prevention & treatment

= increase physical activity

Management of Obesity

- Prevention = increase physical activity



Management of Obesity

- Prevention = increase physical activity

Prevention & treatment of obesity: Increase physical activity

- Active play for 10 min daily produced the same weight loss as calorie restriction

Giles *et al.*, 2003

Management of Obesity

- Prevention & treatment = increase physical activity

Management of Obesity

- Increase physical activity

Management of Obesity: Restrict calorie intake

Get accurate dietary history

- Look at labels of regular food & estimate amount

Management of Obesity

- Critical to monitor frequently – every 2 weeks initially
- Need evidence of success to motivate owners
  - Regular weigh-ins
  - Chart progress

Weight loss: Management of Obesity

- Restrict calories
- Begin with 80% of current intake or 60-70% of daily energy requirement (60 kcal/kg ideal weight) ie. 36 – 42 kcal/kg of ideal weight
- Adjust food fed, so not more than 2.5% BW lost per week

  ie. 8kg cat <160 gm per week = <0.5 kg/mth
- AVOID HEPATIC LIPIDOSIS
- Feed in multiple small meals not 1 large meal

Management of Obesity

- Weigh out calculated amount and mark level on measuring cup

Cornerstone Management of Obesity

- Prevention & Tx = limit energy intake & increase activity

Management of Obesity

- Prevention = increase physical activity

Management of Obesity

- Prevention = increase physical activity

Management of Obesity

- Prevention = increase physical activity

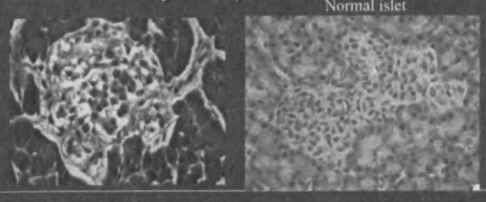
Dietary manipulations

- Minimise the side-effects of weight gain
- Facilitate loss of fat & preservation of muscle
- Help to prevent weight gain

Photos: A Cat of Your Own; Publisher: Ken Fin

One strategy: decrease postprandial insulin

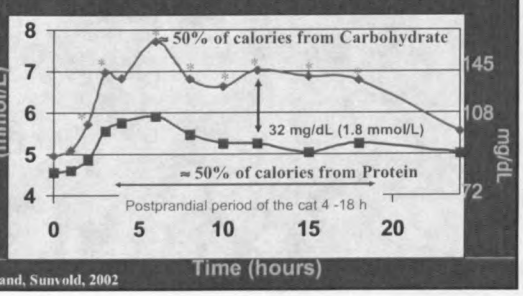
- High insulin concentrations long-term
  → promotes loss of B cells
- Lowering insulin may help to protect B cells from burnout & amyloid deposition



Photos: Link *Thesis* 2001

Blood glucose over 24h in healthy cats after eating 1/2 daily food in 30 mins (pattern if calorie restricted)

Glucose is significantly (≈ 25%) higher from 4 to 18 hr after eating high carbohydrate diet



Farrow, Rand, Sunvold, 2002

Management of Obesity: Carbohydrate versus protein

- High protein, low CHO diet
  →Lower PP insulin conc

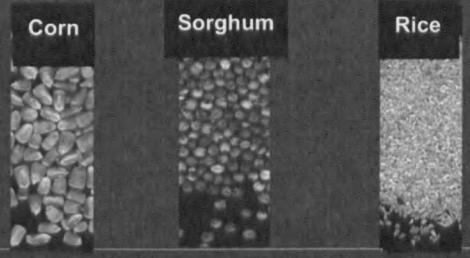
versus

- High CHO, moderate protein diet
  → ↓'d loss of B cells from burnout & amyloid; maintains muscle mass during wt loss (more fat lost)
  ≤ 15-20% ME carbohydrate, ~ 50% ME protein

(Hoenig & Alexander 2000)

Select CHO with lowest PP insulin

- Corn or sorghum ⟹ lower PP glucose & insulin than rice
- Rice commonly used in feline diets

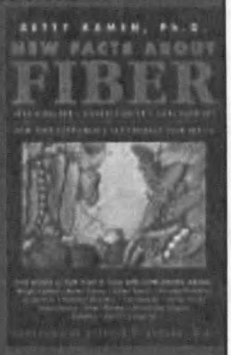


Appleton et al 2004

Increased fermentable fiber

- May improve glucose metabolism & increase satiety
- Fiber fermented by intestinal bacteria → Short chain FA →glucagon-like peptide-1

→ Decreases glucose
Suppresses appetite
Increases insulin secretion



Photos ©drugstore.com, 2001

Increased fiber?

- Controversial if increased fiber is beneficial over moderate fiber typical of maintenance diets

Photos ©drugstore.com, 2001

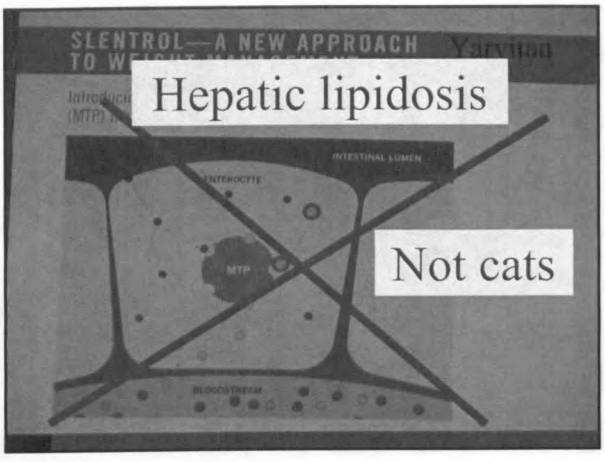
Carnitine: Management of Obesity

- Carnitinine supplementation in obese cats during weight loss

→

- Increased fatty acid oxidation
- Accelerated weight loss
- Preserved muscle mass
- Decreased biochemical & histological changes of hepatic lipidosis

Likely beneficial in weight loss diets, especially if food intake very low & protein intake may be limited



What diet?

- Important to maintain adequate nutrition when restricting calories

  Use a weight loss diet with high protein & decreased carbohydrate

- Higher conc. of essential nutrients eg. protein, essential fatty acids, vitamins, minerals

What diet?

- Use diet based owner/cat preference
  –eg. Canned/dry
- Canned food usually has lower carbohydrate
- Canned: ~ 10% cats self-restrict intake & lose weight
- Look for high protein, low carbohydrate (unless renal disease)
  ~ 50% of calories from protein (DM x 3.5)
  ~ 12 -15% carbohydrate (DM x3.5)
  ~ 25% fat (x8.5) → recalculate out of 100
- ± Carnitine

What diet?

- Palatability essential to avoid hepatic lipidosis
- Send home with samples of several foods
- Transition over 1 week – initially substitute 15% of regular food

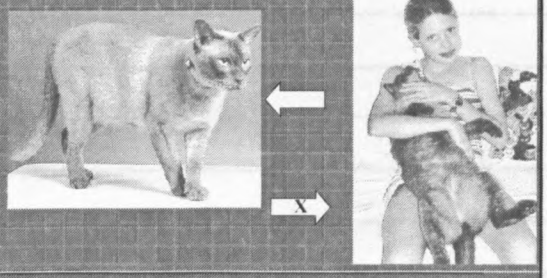
What diet?

% Met. energy:	Protein	Fat	Carb	Cr fiber %DM
Hill's w/d can	37	38	24	11
Hill's w/d dry	39	23	38	7.4
Hill's m/d can	46	40	14	6
Hill's m/d dry	43	44	13	5.5
Royal Canin DS 44 dry	46	30	24	5.3
Purina DM can	46	47	6	3.6
Purina DM dry	50	37	13	1.3

C. Kirk, Vet Clinics Nth Am 2006

Prevention & Management of Obesity

- GOOD LUCK!



Causes, Consequences & Management of Feline Obesity

- better understanding hazards
- newer strategies in feline diets

Centre for Companion Animal Health

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THE UNIVERSITY OF QUEENSLAND

CURRENT UNDERSTANDING OF THE PATHOGENESIS OF FELINE DIABETES MELLITUS & PRINCIPLES OF THERAPY

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Centre for Companion Animal Health, School of Veterinary Science,
The University of Queensland, Brisbane Australia

Classification

The current classification divides diabetes mellitus into type 1, type 2, and other specific types of diabetes.

Type 1 diabetes is an uncommon cause of diabetes in cats based on histological studies and absence of islet cell antibodies

Type 2 diabetes appears to be the most common form of diabetes in cats, based on islet histology, risk factors, and clinical behavior of the disease. Type 2 diabetes is characterized by inadequate insulin secretion and impaired insulin action, that is, insulin resistance. The relative severity of these two defects varies between patients, both feline and human. The defect in beta cell function is usually progressive, and in some cats and humans results in complete loss of insulin secretion

A substantial minority of diabetic cats have other specific types of diabetes, previously called secondary or type 3 diabetes. Diseases in this category that have been reported in cats include diseases causing insulin resistance, and those resulting from non-specific destruction of pancreatic tissue. The most frequent is pancreatic adenocarcinoma, accounting for up to 19% of feline diabetes presented to referral institutions. Pancreatitis is a common histological finding in diabetic cats, but whether it is a cause or a result of diabetes is unclear. A few cats have diabetes as a result of extensive pancreatitis, and may or may not have concurrent signs of exocrine pancreatic insufficiency. Occasional causes of naturally-occurring insulin resistance in cats include growth-hormone producing tumors resulting in acromegaly, and hyperadrenocorticism. Iatrogenic administration of megestrol acetate or long-acting steroids is commonly associated with the development of diabetes in cats.

Type 2 diabetes

Type 2 diabetes is characterized by insulin resistance and decreased insulin secretion. In humans it has been debated whether reduced insulin secretion or insulin resistance is the predominant initial defect in type 2 diabetes, and it appears that the initial defect varies between individuals. Insulin's ability to control blood glucose is dependent on both adequate insulin concentrations and adequate tissue sensitivity, and decreases in either interact to reduce the capacity to maintain blood glucose. Both insulin resistance and decreased insulin secretion are present once clinical signs of diabetes occur. Genotype, obesity, physical inactivity, and some drugs are all associated with insulin resistance.

Insulin resistance

Insulin resistance is the second major abnormality in type 2 diabetes. Diabetic cats are approximately 6 times less sensitive to insulin than normal cats, and humans with type 2 diabetes have similar magnitudes of insulin resistance.

Insulin resistance and obesity

Obesity is a recognized risk factor for the development of diabetes in cats and humans, although not all cats or humans with type 2 diabetes are overweight. In cats and humans, obesity causes insulin resistance.

Genetics of type 2 diabetes

In humans with type 2 diabetes and in some cats, there is strong evidence for a genetic basis for the disease. Population studies have demonstrated a higher incidence of diabetes within some families of cats and ethnic groups of people.
In humans, it is considered likely that the multiple genes involved in predisposition to type 2 diabetes are both primary genes controlling insulin secretion and action, as well as secondary genes, influencing factors such as propensity to obesity.

Breed is a recognised as a risk factor in cats. The incidence of diabetes is over-represented in Burmese cats in Australia, New Zealand, and the United Kingdom. The frequency of diabetes in Burmese cats is approximately 4 times higher than that of Domestic cats in Australia, with 1 in 50 Burmese affected compared to less than 1 in 200 Domestic long- and short-hair cats. In some Burmese families, more than 10% of the offspring are affected.

Age

Increasing age is also a risk factor for type 2 diabetes, and most cats are older than 8 years of age when diagnosed, with a peak incidence between 10 and 13 years of age. Although 1 in 50 Burmese cats have diabetes, the incidence increases to 1 in 10 for Burmese cats 8 years or older.

Obesity and physical inactivity

Environmental influences interact with genetic influences, and play an important role in the development of diabetes in humans, and most likely in cats. Environmental or lifestyle factors shown to be important in humans and probably in cats, include obesity, physical inactivity, dietary factors, and urban rather than rural residence. The lifestyle of many domestic cats has changed similarly to humans, with inactivity and obesity increasing in urban cats. Exclusively indoor cats are usually less active than outdoor domestic cats that hunt and defend territory, and significantly less active than feral cats, which have to hunt to obtain all their

nutrition. In humans and rats, exercise has been shown to increase insulin sensitivity. Lack of exercise impairs insulin action, and adds to the underlying level of genetically-determined insulin resistance. Less physically active cats and exclusively indoor cats are at increased risk of diabetes.

Obesity associated with insulin resistance is an important risk factor in the development of type 2 diabetes in humans, and even small increases in body mass index are associated with an increased risk of diabetes. Obesity has also been identified as a significant risk factor for diabetes in cats. In a study where cats were allowed free-access to a highly palatable energy dense diet over 10 months and increased their bodyweight by 44%, their insulin sensitivity decreased by more than half. Following weight gain 25% of the cats in the study had insulin sensitivity values within the range reported for diabetic cats.

Diet and type 2 diabetes

In both cats and humans, obesity has been shown to be a major risk factor for diabetes. Overfeeding of highly palatable, calorie-dense food in cats with reduced physical activity, likely contributes to obesity, and hence diabetes. Recent evidence in cats suggests that a high carbohydrate diet increases the demand for insulin secretion when compared to a low carbohydrate, high protein diet. In susceptible cats, this long-term demand for increased insulin secretion may lead to beta cell apoptosis and a decline is insulin secretory capacity, precipitating impaired glucose tolerance and diabetes, as hypothesized by the Carnivore Connection Theory. *Ad libitum* feeding of cats is not recommended except in cats which self-regulate food intake and maintain an ideal body condition. Most cats fed commercial food *ad libitum* ingest excess energy, resulting in obesity and increased risk of diabetes.

Amyloid

Many, but not all cats and humans with diabetes, have amyloid deposition replacing islets cells. Amyloid deposition does not appear to be an essential component of type 2 diabetes in cats or humans, but contributes to beta cell loss and failure of insulin. In a model of induced diabetes in cats, cats with high amylin concentrations tended to have more profound amyloid deposition. Obesity likely contributes to amyloid deposition in susceptible cats by stimulating hyperamylinemia and hyperinsulinemia, secondary to insulin resistance.

Glucose and lipid toxicity

Once persistent hyperglycemia occurs, insulin secretion is reduced through a phenomenon termed glucose toxicity. There is evidence that initially, suppression of insulin secretion is functional and reversible, and is not associated with visible lesions in beta cells. With hyperglycemia of longer than 2 weeks duration, histological abnormalities are evident, including glycogen deposition and cell death. The severity of the glucose toxicity effect is dependent on the degree of hyperglycemia and the duration.

Increased fatty acids produce a similar effect to glucose toxicity, called lipotoxicity. The clinical implications of glucose and lipid toxicity are very important. It is vital that effective therapy be instituted as soon as possible to reduce hyperglycemia in diabetic cats, if beta cell function is to be preserved. This is important, because data in humans indicates that patients with residual beta cell function have better glycemic control when treated with insulin, than patients with no significant endogenous insulin secretion. Secondly, it is important because the majority of cats will undergo remission of their diabetes, if the effects of glucose toxicity are minimized.

Insulin resistance and chronic hyperglycemia

Chronically elevated blood glucose also causes insulin resistance. Once overt diabetes mellitus with persistent hyperglycemia occurs, the added insulin resistance further compounds the problem of inadequate insulin secretion. This has implications for therapy, because once glucose concentrations are decreased with treatment, insulin sensitivity may improve.

Diabetic remission or transient diabetes

Diabetic remission occurs in up to 90% of newly diagnosed cats if treated appropriately. Remission occurs most commonly after 1 to 4 months of insulin therapy, and in some cats, glucose tolerance is normal in remission. Based on experience, remission is more likely if glycemic control is optimum, so beta cells can recover from glucose toxicity. Therefore insulin therapy is recommended as the initial therapy to maximize control of blood glucose and increase the probability of remission.

Clinical Signs and Diagnosis

There are no internationally agreed criteria for diagnosis of diabetes mellitus in cats. Clinical signs such as polydipsia/polyuria, weight loss, or polyphagia are non-specific, and diagnosis cannot be confirmed by clinical examination. Diagnosis in cats is often complicated by stress hyperglycemia, which in sick non-diabetic cats may lead to glycosuria or blood glucose levels in excess of 360 mg/dL (20 mmol/L). Blood glucose in non-diabetic unstressed client-owned cats is usually less than 171 mg/dL (9.5 mmol/L). When sampling blood, it is very important to avoid struggling, as this has been shown to be associated with transient hyperglycemia as high as 288 mg/dL (16 mmol/L) in normal cats. Blood glucose should be measured several hours after the first sample to confirm persistent hyperglycemia, especially if the blood glucose is less than 360 mg/dL (20 mmol/L). Signs of diabetes occur once blood glucose concentration exceeds the renal threshold, which is approximately 250-288 mg/dL (14-16 mmol/L) for normal cats.

Fructosamine may be useful in assisting diagnosis, especially when typical clinical signs of diabetes have not been observed or reported. However, some cats that do not have diabetes have elevated fructosamine levels similar to those of diabetic cats (false

positive), and occasionally untreated diabetic cats may have fructosamine levels similar to that of normal cats (false negative). A fructosamine level of greater than 400 µmol/L in a cat strongly supports a diagnosis of diabetes. In experimentally-induced hyperglycemia in cats, although fructosamine concentration increased significantly from baseline within 3 days when blood glucose was maintained at 306 or 540 mg/dL (17 or 30 mmol/L), mean fructosamine did not increase above 350µmol/L when glucose was 306 mg/dL (17 mmol/L) for 6 weeks.

Measurement of water intake is inexpensive and useful for confirming polydipsia once blood glucose is above the renal threshold. In normal cats, total water intake including water in food ranges from 60 to 100 mL/kg/24h, but water drunk is much less, especially if the cat is consuming canned food, with average values of approximately 20 mL/kg or less. Measurement of water intake to document polydipsia may only be practical in a cat which is clinically healthy, and the decision to treat can be delayed by a few days.

If there is doubt whether the hyperglycemia is transient and associated with stress or is from diabetes, in sick cats it is prudent to begin insulin therapy and monitor glucose concentrations carefully for the next few days. Reducing glucose concentrations with exogenous insulin reduces the suppressive effect of glucose toxicity and makes recovery of beta cells more likely. Because glucose toxicity can reduce insulin secretion in normal cats to levels of insulin-dependent diabetic cats within 3 to 7 days, do not wait to begin insulin therapy if blood glucose concentration is 270 mg/dL (15 mmol/L) or higher. Likewise, in cats with iatrogenic or spontaneous hyperadrenocorticism or acromegaly, begin insulin therapy immediately to preserve remaining beta cells. Therapy for the underlying disease can then be instituted and glucose concentrations monitored to adjust insulin dose. Do not wait to see if the diabetes resolves once the underlying disease process is treated or the exogenous hormone eliminated, because this makes permanent diabetes more likely.

Ketoacidosis

Ketoacidosis occurs in approximately 12 – 37% of diabetic cats at the time of diagnosis, and a smaller percent are ketotic without acidosis. Ketoacidosis results in depression, vomiting and anorexia. Ketoacidosis can be precipitated by concomitant disease, especially infection. It is also important to realize that once cats become markedly insulinopenic, even previously normal cats progress to ketosis within 10 – 30 days, without evidence of precipitating disease. If untreated, acidosis quickly ensues. Small doses of insulin will usually correct ketonemia and prevent life-threatening acidosis, even if marked hyperglycemia persists. In experimentally induced diabetes, ketonemia occurred on average 5 days before ketonuria was detected using a urine test strip, and acetone odor to the breath was also detected before ketonuria. Although ketotic cats usually have low insulin concentrations, with appropriate therapy to overcome glucose and lipotoxicity, some beta cell function may return, and many of these cats achieve remission.

Principles of therapy

Therapy for diabetes should be instituted as soon as possible after diagnosis. The main aim of therapy is to achieve exemplary glycemic control to facilitate remission. In cats, in which remission is not possible, resolution of clinical signs and avoidance of clinical hypoglycemia are the goals. Administration of insulin and dietary modification are the principal therapies used for management of diabetic cats. Oral hypoglycemic drugs may be useful in some cats depending on the loss of function from glucose toxicity, residual beta cell mass, and other concurrent therapy. A recent study has shown that if good glycemic control is achieved early in newly diagnosed diabetic cats, very high remission rates occur within 4 weeks of treatment. Good glycemic control reverses the glucose toxicity suppressing beta cells, and maximizes the chance of preserving beta cell function and achieving diabetic remission.

Summary

Understanding the features of feline diabetes is important for good patient management, and may help to decrease the incidence of diabetes.

KEYWORDS, feline diabetes, diabetic remission, glucose toxicity

Recommended reading

Selected articles are available our website: www.uq.edu.au/vetschool/centrecah

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MANAGEMENT OF FELINE DIABETES MELLITUS: PART 1. WHICH INSULIN DO I CHOOSE & HOW DO I ADJUST THE DOSE?

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MANAGEMENT OF FELINE DIABETES

Therapy for diabetes should be instituted as soon as possible after diagnosis. The main goal of therapy is to achieve euglycemia without the need for insulin therapy, commonly termed diabetic remission. For those cats not achieving remission the goals are to resolve clinical signs and avoid hypoglycemia. Administration of insulin and dietary modification are the principal therapies used for management of diabetic cats. Oral hypoglycemic drugs have limited usefulness in the initial management of diabetic cats, and if used as a sole agent without insulin, will substantially decrease the probability of remission.

Cats that are not substantially dehydrated and are still eating can be treated with subcutaneous insulin. Cats initially presented with diabetic ketoacidosis can be treated with subcutaneous insulin after stabilization. When used intramuscularly or intravenously, glargine acts like regular insulin and can be used instead of regular insulin for initial stabilization of diabetic cats. The use of long-acting insulins, particularly glargine and detemir, and low carbohydrate diets facilitates achieving better glycemic control and increases the probability of remission, while minimizing the chance of hypoglycemia. If using lente insulin, because clinical hypoglycemia is more common and can be life-threatening, avoid aiming for perfect glycemic control.

Insulin therapy

Long-acting insulin therapy remains the preferred initial and long-term treatment of choice for diabetes mellitus in cats. Its effectiveness and safety is be enhanced when combined with a low carbohydrate diet. Oral hypoglycemic agents such as acarbose may be effective as an additional therapy in cats which require a high carbohydrate diet, provided they are not *ad libitum* feeding. Many types of insulin are available and have been used in cats. Achieving good glycemic control with intermediate acting potent insulins such as NPH and lente is often difficult, and increases the risk of clinical hypoglycemia. Recent data suggests that the long-acting insulins glargine and detemir provide better glycemic control and reduced risk of clinical hypoglycemia when given twice daily and combined with a low carbohydrate diet. More importantly, their use results in a significantly higher probability for remission.

Oral hypoglycemic drugs

The use of oral hypoglycemic drugs to treat feline diabetes has been limited for a number of reasons. Many owners find administering tablets more difficult than injecting with insulin. Drugs which stimulate insulin secretion (eg. sulphonylureas) require adequate beta cell function to be effective, and if there is inadequate glucose-lowering effect, persistent hyperglycemia can lead to continued beta cell loss through glucose and lipid toxicity. These drugs may also stimulate accelerated islet amyloid deposition exacerbating beta cell loss. Acarbose acts by reducing glucose absorption from the gastrointestinal tract and is indicated as an adjunct to insulin therapy in cats which are meal fed a high carbohydrate diet. The greatest indication for using them is in cats with advanced renal failure which require a restricted protein diet. However, these cats usually have a reduced appetite and need to be fed *ad libitum*, which greatly reduces the efficacy of acarbose.

Monitoring therapeutic efficacy

Response to treatment can be evaluated in a number of ways, and no individual modality should be used as the sole parameter for adjusting therapy. A combination of owner assessment, clinical signs, and changes in body weight and water intake are often the best indicators of glycemic control. Dosage changes can be made based on a number of different blood glucose parameters, and optimally should include more than one parameter. The pre-insulin glucose concentration is important when using glargine, detemir and PZI, as there is often a persisting effect from the previous injection. Nadir (lowest) glucose concentration is important for dosage adjustment. It limits the dose increase that can be made when nadir glucose concentration is in the lower end of the normal reference range. Water drunk and urine glucose concentration are probably more important when using glargine than for other types of insulin, and is discussed below.

When using other insulins (eg lente or NPH), dosage changes are usually based on nadir blood glucose. Pre-insulin glucose, time to nadir and the time to return to baseline are also used where appropriate, and recommendations for their use are listed in table 2. Water drunk, urine glucose and clinical assessment may be less important for making dosage changes with lente and NPH insulins, but should still receive consideration when adjusting dosage.

Table 1: Parameters for changing insulin dosage and frequency based on blood glucose measurements when using lente or NPH insulin in diabetic cats.

Blood Glucose Variable	Recommendation
Use an initial dose 0.5 U/kg of lean body weight BID if blood glucose is $\geq$ 360 mg/dL (> 20 mmol/L) and 0.25 U/Kg BID if glucose < 360	

mg/dL (> 20 mmol/L).	
If pre-insulin blood glucose concentration is <210mg/dL (< 12mmol/L)	With-hold insulin and check for diabetic remission provided cat treated for a minimum of 2 weeks; otherwise reduce dose
If pre-insulin blood glucose concentration is 211-250mg/dL (13 - 16mmol/L)	Total dose should be no more than 1U/cat bid
If nadir blood glucose concentration is < 54mg/dL (<3mmol/L)	Dose should be reduced by 50 %
If nadir blood glucose concentration is 54-90mg/dL (3 – 5mmol/L)	Dose should be reduced by 1U if poor control of clinical signs of diabetes; dose should remain the same if exemplary control of clinical signs
If nadir blood glucose concentration is 91-180mg/dL(6 – 9mmol/L)	Dose should remain the same
If nadir blood glucose concentration is >180mg/dL(> 10mmol/L)	Dose should be increased by 1U
If nadir blood glucose concentration occurs within 3 hours of insulin administration, or blood glucose returns to baseline within 8 hours	Change to longer acting insulin (ie. Glargine, detemir or PZI)
If the nadir blood glucose concentration occurs at 8 hours or later	Once daily administration may be used, although twice daily administration at a reduced dose is preferred

Glargine

Glargine is a new human synthetic insulin analogue produced by recombinant DNA technology utilizing *E.Coli.* It differs from human insulin in that the amino acid asparagine at position A21 is replaced by glycine and two arginines are added to the B-chain terminus. Glargine is a clear aqueous solution in 100U/ml vials with pH=4 until injected subcutaneously. The interaction of the acidic insulin and the relatively neutral pH of the subcutaneous tissues forms micro-precipitates, and has a relatively constant systemic absorption profile. The formation of micro-precipitates and slow absorption are dependant on the acidity of glargine, hence glargine cannot be mixed or diluted.

Glargine is marketed for human patients as a very long-acting "peak less" insulin, with regard to its glucose lowering effects. It is designed to provide a basal or background insulin concentration, with the intention that a shorter-acting insulin be administered at meal times to achieve optimal glycemic control. Insulin glargine gained approval from the United States Food and Drug Administration in June 2000, for use in treating type 1 and type 2 diabetes in humans. The expected benefits in diabetic cats of an insulin preparation with a longer duration of action include improved glycemic control resulting in increased rates of diabetic remission, reduced rates of euthanasia, and decreased cost to clients.

The pharmacokinetics and pharmacodynamics of once daily administration of glargine compared with two of the most commonly used insulin preparations, porcine lente and protamine zinc insulin (PZI), has been reported in healthy cats. Once daily administration of glargine was found to have a similar mean daily glucose concentration and area under the 24hr glucose curve to PZI, and both were significantly lower than lente insulin. Glargine produced a glucose nadir later than PZI or lente, and had longer duration of action than lente. The duration of action for glargine was 22hrs, and 5 of the 9 cats had significantly decreased blood glucose concentration at 24hrs.

The administration of glargine once daily versus twice daily has been compared in healthy cats. A longer effect was achieved by administering glargine BID compared to once daily. Once daily administration of glargine has been shown to produce similar remission rates to twice daily dosing of lente insulin. Because excellent glycemic control facilitates remission and superior glycemic control is achieved if glargine is injected twice daily, twice daily dosing should be used for at least the first 4 months of treatment after diagnosis.

The usefulness of glargine for treating newly diagnosed diabetic cats has been evaluated. Twenty-four newly diagnosed diabetic cats (17m,7f) were treated with either glargine, PZI or lente (n=8 for each group) and fed a very low carbohydrate-high protein diet (Purina DM canned). Insulin was initially given at 0.5U/kg BID S/C if blood glucose was >360mg/dl, and 0.25U/kg BID S/C if blood glucose was <360mg/dl. Insulin dose was then adjusted based on serial blood glucose curves and water intake. Cats were defined as achieving diabetic remission if normoglycemia was maintained without insulin therapy for more than 2 weeks.

At diagnosis, there was no statistical difference between treatment groups for age, body weight, body condition score, or concentrations of fructosamine, blood glucose, B-hydroxybutyrate or bicarbonate.

There was a non-significant trend for glargine treated cats to have lower 12hr glucose concentrations after 10 and 17 days, than those treated with PZI or lente. Mean 12hr blood glucose at 4 weeks was significantly lower for glargine than PZI and lente treated cats. Fructosamine concentration after 4 weeks of treatment was significantly lower than at diagnosis for glargine treated cats but not for PZI or lente.

All 8 cats treated with glargine went into diabetic remission within 4 months of beginning treatment, while 3 cats treated with PZI and 2 cats treated with lente achieved diabetic remission.

Only 1 cat treated with glargine required an increase in insulin dose above 0.5U/kg BID, and 7 of 8 cats had their insulin dose reduced in the first 3 days of treatment. This is an important factor when initiating treatment with glargine, as there is usually a carry-over effect from the previous dose that may take several days to become apparent.

A significant finding in this trial was that no cat treated with glargine showed clinical hypoglycemia despite having biochemical hypoglycemia, while 2 cats treated with lente and 1 cat treated with PZI insulin exhibited signs of clinical hypoglycemia.

Glargine can be safely instituted at 0.5U/kg bid and serial blood glucose curves should be obtained daily for 3 days either in hospital or at home. When evaluating the blood glucose curve using glargine, it is often more useful to assess pre-insulin glucose concentration rather than the nadir glucose. We have found it often takes 3-5 days for a good glucose-lowering effect to be seen in the glucose curves, possibly because of the long duration of action and carry-over effect of glargine. Almost all cats will need to have their initial dose reduced within 2 weeks and many will achieve remission within 4 weeks.

Detemir is a newer synthetic insulin analogue with long duration of action that is produced using recombinant DNA technology in yeast (*Saccharomyces cerevisiae*). The insulin molecule is modified by the addition of an acylated fatty acid chain that enables reversible binding to plasma proteins, especially albumin, from where it is released slowly into plasma. This modification leads not only to a prolonged absorption from the subcutaneous tissue, but slow release from plasma proteins. Detemir results in similar remission rates and time to remission as glargine, but the median maximum dose used (1.75 IU/cat BID) is about 30% less than with glargine (2.5 IU/cat BID)

Monitoring and adjusting insulin dose when using glargine or detemir should be based on a number of parameters including; pre-insulin and nadir glucose concentration, water intake, urine glucose concentration and clinical assessment as shown in Table 2. We have found pre-insulin glucose concentrations measured at home an excellent tool for well-educated owners to safely modify daily doses of glargine or detemir. Cats treated with glargine should have a negative, 1+ or 2+ urine glucose (scale 0-4+) and a value of 3+ or 4+ likely indicates that a dose increase is required.

The good glycemic control achieved when using glargine or detemir likely reverses glucose toxicity of the B-cells, which facilitates endogenous insulin production and a reduced requirement for exogenous administration. Insulin dose may be reduced sequentially as indicated by blood glucose concentration, urine glucose and water intake until the dose is ½-1U/cat SID. Even if normoglycemic, it is recommended that insulin is not withdrawn within 2 weeks of commencement of therapy. Sequential deduction of insulin dose to ½-1 U/cat SID is recommended before insulin is withdrawn, and the cat carefully monitored afterwards to ensure remission has continued. It is also imperative that cats remain on a low-carbohydrate diet with calorie control to prolong the remission period. Newly diagnosed diabetic cats that have good glycemic control within the first few weeks of therapy, are very likely to go into diabetic remission. Cats that have been long-term diabetics are less likely to go into remission probably because of progressive B-cell loss associated with glucose toxicity. Remission rates are very significantly reduced if good glycemic control is instituted longer than 6 months after diagnosis.

In conclusion, glargine and determir are safe and effective in treating feline diabetes and are the preferred insulins in newly diagnosed diabetic cats. Long-term diabetic cats should be changed to glargine or detemir if there is poor glycemic control or owners wish to pursue once daily injections. High remission rates are expected in newly diagnosed cats when combined with a low-carbohydrate diet and twice daily injections.

Table 2. Parameters for changing insulin dosage when using insulin glargine or detemir in diabetic cats.

Parameter used for dosage adjustment	**Change in dose**
Begin with 0.5 U/kg if blood glucose (≥360 mg/dL (≥ 20 mmol/L) or 0.25/kg of ideal weight if blood glucose is lower. Do not increase in first week unless minimum response to insulin occurs, but decrease if necessary. Monitor response to therapy for first 3 days If no monitoring is occurring in first week, begin with 1 U/cat BID	
If pre-insulin blood glucose concentration >216mg/dL (>12mmol/L) provided nadir is not in hypoglycemic range ***or*** If nadir blood glucose concentration >180mg/dL (>10mmol/L)	Increase by 0.25-1U
If pre-insulin blood glucose concentration 180<216mg/dL (≥ 10 - ≤12mmol/L) ***or*** Nadir blood glucose concentration is 90-160mg/dL (5-9mmol/L)	Same dose
If pre-insulin blood glucose concentration is 198-252mg/dL (11-14mmol/L). ***or*** If nadir glucose concentration is 54-72 mg/dL (3-4 mmol/L).	Use nadir glucose, water drunk, urine glucose and next pre-insulin glucose concentration to determine if insulin dose is decreased or maintained.
If pre-insulin blood glucose concentration <180mg/dL (10 mmol/l) ***or*** If nadir blood glucose concentration < 54mg/dL (<3 mmol/l)	Reduce by 0.5- 1UU ***or*** if total dose is 0.5-1U SID, stop insulin and check for diabetic remission
If clinical signs of hypoglycemia are observed	Reduce by 50%
If blood glucose measurements are not available:	
If water intake is ≤20mls/kg on wet food or ≤60mls/kg on dry food	Same dose

If water intake is >20mls/kg on wet food or >60mls/kg on dry food	Increase dose by 0.5-1U
If urine glucose is > 3+ (scale 0 - 4+)	Increase dose by 0.5-1U
If urine glucose is negative	Decrease dose until 0.5-1 U SID and then check for diabetic remission

KEYWORDS, feline diabetes, diabetic remission, insulin, glargine

Suggested reading:

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MANAGEMENT OF FELINE DIABETES MELLITUS: PART 2.: WHAT DIET SHOULD I CHOOSE & HOW DO I MANAGE PROBLEM CATS

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Feeding

While the ideal combination of macronutrients (protein, fat and carbohydrate) to feed diabetic cats is not known, diets low in carbohydrates and high in protein reduce post-prandial hyperglycemia and insulin concentrations in healthy cats. Initial data from diabetic cats also suggest that low carbohydrate-high protein diets result in better clinical control, reduced insulin requirements and increased rates of diabetic remission. Thus a commercial low carbohydrate should be used in diabetic cats, unless contraindicated by other disease. During the first few weeks of treatment, diabetic cats may have a reduced appetite, and if they refuse these low carbohydrate diets, they should be offered any palatable food.

Care should be taken with cats diagnosed with advanced renal disease, as diets high in protein may have a deleterious effect. For these cats, dietary management of renal disease using a restricted protein diet should take precedence over dietary management of diabetes, and acarbose used to reduce glucose absorption from the GIT.

Obesity in cats markedly reduces insulin sensitivity and hence energy fed should be restricted so weight loss occurs in obese cats at a rate of 1-2% loss of body weight per week. Because of the decreased postprandial hyperglycemia with a low carbohydrate diet, it is suggested that diets with less than 20% of energy from carbohydrate (eg.Hills m/d, Purina dm) should be used for obese diabetic cats during the calorie restriction phase. Currently, most feline weight loss diets are low fat, high carbohydrate diets. Weight loss improves insulin sensitivity, and may reduce insulin requirements. In some cats, diabetic remission is obtained after weight loss and short-term insulin or oral hypoglycemic therapy.

Acarbose

The α-glucosidase inhibitors (eg acarbose) reduce intestinal glucose absorption (Greco 1999) and are generally not effective in the treatment of feline diabetes alone, but can be used in conjunction with insulin and/or other oral agents to gain better glycaemic control. Cats given acarbose and meal fed a high carbohydrate diet have significantly reduced blood glucose concentrations but the same effect can be achieved by using a low carbohydrate diet.

Problem cats

When cats treated with insulin fail to stabilise, a number of underlying causes and approaches to treatment should be considered. It is important to remember that some cats take 1 to 4 months to stabilize. Lente and NPH insulins provide inferior control of blood glucose and are more difficult to adjust to get good glycemic control, and are more likely to be associated with problem cats. These insulins are more often associated with marked changes in blood glucose concentration and clinical hypoglycemia than longer acting insulin such as glargine, detemir and PZI,.

The most common problems resulting in poor control are excessive dose, miscalculation of dose, too short duration of insulin action, or poor absorption of insulin. When using lente, NPH or ultralente, some cats are mistakenly labelled problem cats when the clinical signs are well controlled, but blood glucose measurements are less than ideal. This usually occurs when there are unrealistic goals for glycemic control using these insulins and lack of understanding that for 4 hours twice daily, cats treated with these insulins have negligible blood glucose lowering effect from the insulin. If the glucose nadir is below 10 mmol/L (182 mg/dL) after each insulin injection, peak action occurs >3 hours after administration, and hypoglycaemia is not occurring, glycemic control is usually adequate. These cats usually have good clinical control (stable body weight, good coat condition, active, alert, water drunk <100ml/kg/24h). Swapping to a longer acting insulin such as glargine and detemir will usually improve glycemic control and improve the probability of remission.

Problem cats have persistent clinical signs including polydipsia (water drunk > 100 mL/kg/24h), low body condition score, polyphagia, lethargy, and a poor hair coat; an insulin dose higher than normal (1.5 – 2 or more IU/kg/injection); and either a nadir glucose> 180 mg/dL (10 mmol/L) or hypoglycemia. For problem-solving in problem cats, it is important to first rule-out administration problems. Expired insulin, heat affected insulin (eg. left in a car in summer), poor mixing of suspensions (eg. lente insulin), failure of administration (eg. injecting through the skin pinch onto the hair-coat), and the presence of air bubbles in the syringe causing a lower administered dose, all occur regularly in practice. Insulin syringes can be difficult to manage for elderly owners with arthritic hands and poor vision. These owners are often better able to cope with insulin pens. Misunderstandings between the owner and veterinarian regarding the number of units to be administered can occur when using 40-IU/mL insulin in a 100-IU/mL syringe, because the cat is only getting 40% of the dose indicated by the markings on the syringe. Watch the owner administer the insulin. If it is an old bottle of insulin, change to a new one. If the cat has been treated for at least 8 to 12 weeks and insulin is being correctly administered but poor control is still evident, measure water intake over consecutive days at home (measure fructosamine concentration if water intake cannot be measured), and obtain a blood glucose curve.

Poor control may result from an excessive dose of intermediate acting insulin, which may cause apparent insulin resistance (dose >1.5 – 2 IU/injection with persistent hyperglycaemia), or short duration of insulin action. In many cats treated with

the intermediate-acting insulins such as lente and NPH (isophane), these potent insulins rapidly lower blood glucose. This stimulates counter-regulatory responses, even when blood glucose concentration is not in the hypoglycemic range. The resulting counter-regulatory response increases blood glucose concentration, and causes an apparent short duration of insulin action and insulin resistance. This can be very frustrating for veterinarians when managing diabetic cats. This response happens because of the action of the hypothalamic neurons that sense blood glucose concentration and initiate counter-regulation. The hypothalamic neurons control entry of glucose into their cytoplasm, and actively maintain a large concentration gradient with plasma glucose when blood glucose concentrations are high. When potent insulin such as lente insulin is given and blood glucose concentration decreases rapidly, the intracellular glucose concentration of the hypothalamic neurons decreases more quickly into the range perceived by the neurons as hypoglycemic and a counter-regulatory response is triggered, even before hypoglycemia develops. The resultant secretion of glucagon, epinephrine, cortisol and growth hormone increases blood glucose concentration, and causes an apparent short duration of insulin action. Because the glucose lowering effect of lente and NPH in cats is less than 8 hours, most diabetic cats have blood glucose concentrations of 360 to 430 mg/dl (20 to 24 mmol/l) at the time of the next insulin dose, predisposing them to premature counter-regulation. The result is that in some cats, lente and NPH insulins may only lower blood glucose for 2 to 3 hours. This inherent short duration of action of lente, NPH and ultralente insulins, coupled with the response of the hypothalamic neurons can be very frustrating for practitioners. It also is dangerous for diabetic cats, because their insulin dosage often is wrongly increased. The end result is that the effect of lente, NPH and ultralente is often too short to achieve good glycemic control, and insulin resistance and signs of hyperglycemia and hypoglycemia ensue.

For cats on potent insulins such as lente or NPH, if the cat is polydipsic and insulin seems to have little effect, especially when previously it caused substantial lowering of glucose, or the duration of action seems to be short, there are two options. The preferred option is to swap to glargine or detemir. Alternatively try lowering the dose of insulin to 0.3 to 0.5 IU/kg for 10-14 days to see if blood glucose or water intake improve towards the end of the period. If clinical control is not improved with a lower dose, check the glucose response to a standard dose of 0.5 IU/kg of insulin, to determine the duration of effect. If the glucose nadir occurs 2 – 3 hours after injection, switch to a longer acting insulin (glargine or detemir), or increase the frequency of administration to TID. With PZI or ultralente, if there is little response to insulin, try swapping to glargine or detemir and slowly increasing the dose until glycemic control is achieved, which may require a dose of 5-10U/cat twice daily in some problem cats. If there is still polydipsia (water drunk>100ml/kg/24 h) and little glycemic response after 1-2 months at a dose of 5-6U/cat twice daily, check the cat for hyperthyroidism, hyperadrenocorticism, acromegaly or other systemic disease such as renal failure. We have seen improved glycemic control in cats with periodontal disease, following dental surgery in combination with short-term antibiotics. In the meantime, increase the dose by 1 IU every 1-2 weeks until some glycemic response is achieved. Control is achieved in most difficult cats, with the exception of cats with acromegaly, once glargine dose is 5-10 U/cat twice daily (4-5 U/cat with detemir). Warn the owner that a severe hypoglycemic episode can occur with this protocol, and to be particularly vigilant regarding the early signs of hypoglycaemia (lethargy, mental dullness, wobbliness, trembling and dilated pupils). In some cats which appear insulin resistant, but no cause can be found, admitting them to hospital for carefully observed intensive insulin therapy to normalize blood glucose for several days, may substantially reduce the subsequent insulin doses that achieve control. Most cats are eventually controlled on 1-3 U/cat BID of glargine or 1-2 U/cat BID of detemir, even if they required a dose as high as 5-6 U/cat BID in the first 1-3 months to control blood glucose.

KEYWORDS, feline diabetes, diabetic remission, insulin, glargine

Suggested reading:

Selected articles are available our website: www.uq.edu.au/vetschool/centrecah

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Feline Nutrition: Clinical management of a carnivore

J. Wakshlag

Over the past 40 years we have learned a tremendous amount about nutrition in cats and have shown a number of idiosyncracies that will be discussed in some depth, as well as newer ideas of nutritional management of lower urinary tract disorders, renal insufficiency, inflammatory bowel disease and anorexia.

As we know cats are carnivores and have multiple idiosyncracies regarding metabolism that make them unique resulting in a "top 10 list" of why cats are carnivores.

1) Dentition pattern and absence of salivary amylase. Cats cannot start carbohydrate digestion in the mouth and stomach through the actions of salivary amylase, and the dentition pattern is ideal for ripping and tearing rather than crushing and grinding.
2) Lack hepatic glucokinase activity. Cats only have hexokinase and do not up regulate glucokinase activity during episodes of hyperglycemia. Additionally cats cannot tolerate oral sucrose like omnivores can.
3) Cannot down regulate amino acid deaminase activity. Unlike other primarily carnivorous omnivores, cats cannot turn off the hepatic machinery that results in deamination and synthesis of glucose precursors from amino acids.
4) Cats require arginine in the diet. Cats cannot synthesis citrulline in the intestinal cells efficiently, which is a precursor to arginine formation. If arginine is absent from the diet, then ammonia conjugation into urea is lacking causing hyperammonemia resulting in coma and death.
5) Taurine is required in the diet. Not only do cats use taurine exclusively to make bile salts causign rapid depletion of taurine, but the precursor amino acid for taurine synthesis cysteine is more readily converted to pyruvate for energy resulting in a dietary need for taurine
6) High tyrosine and phenylalanine requirements. Tyrosine is an important amino acid for melanin formation in the skin and hair. If tyrosine/phenylalanine concentration in the diet are insufficient black coated cats can become rust colored. The requirements are over twice the requirement for growth.
7) Arachidonic acid is required in the diet. Cats have very lower delta 6 desaturase activity, therefore cannot form sufficient arachidonic acid from the plant based fatty acid linoleic acid. Arachidonic acid deficiency has been associated with poor fertility in queens.
8) Inability to form sufficient vitamin A from B-carotene. Lack of the enzyme 15,15-dioxygenase at the intestinal mucosa means they require preformed vitamin A from animal sources. Regardless of common misperception cats are very resistant to vitamin A toxicity.
9) Inability to form vitamin D from sun exposure. The precursor to vitamin D called 7-dehydrocholesterol is rapidly metabolized, thereby not allowing sufficient quantities to get to the skin for conversion to previtamin D3.
10) High niacin requirement. Cats do not have the same capability to convert tryptophan into niacin like many other species, resulting in a higher requirement of dietary niacin.

The evidence is clear that a meat based diet is an evolutionary adaptation resulting in recent recommendations to feed higher protein, higher fat foods often resulting in a preference of canned over dry foods. However one should not make this a global recommendation since there are many cats that refuse one form of food due to cats being neophobic in nature. It may be best to have cats adapted to eating both dry and canned foods so that depending on the health needs of each individual cat, either form of food can be used when needed.

Global recommendations of canned foods have become preferred due to the high predisposition of cats to urinary tract disorders and an important part of management of FLUTD is water consumption. Evidence suggests that cats eating canned products resulting in higher overall water intake than cats offered dry food and water ad lib. Various techniques to increase water consumption from free flowing water systems (fountains etc) and addition of water to foods are advocated techniques. However, recent evidence suggests that free flowing water systems may not be effective, therefore each cat needs to be monitored for effectiveness of the intervention, and routine specific gravity monitoring is advised (less than 1.025).

Dietary strategies differ among various therapeutic food distributors from use of salt to restriction of minerals based on the potential for specific urolithiasis issues. The high versus low salt debate continues, and practical recommendations suggest a full work up before beginning a higher salt diet since concurrent renal compromise or renal calcification may be determining factors in choosing a FLUTD diet.

Of course, as renal disease progresses there are multiple dietary principles that play a role in longevity in cats and recent evidence suggests that dietary therapy is a major factor in morbidity and mortality. As renal disease progresses the principles in maintaining appropriate body condition and calorie intake often take precedence over the "perfect diet" as lean body mass loss plays a significant role in quality of life issues. In many cases it may be best to consider placement of esophagostomy or g-tubes to enhance quality of life and to deliver the appropriate diet long term.

Anorexia in renal failure and other diseases, such as gastrointestinal disorders, plays a significant role in disease progression and using not only appropriate foods, but also enough energy are underlying principles in successful management of these conditions. Although scientifically unproven, the use of mirtazapine is gaining popularity by clinicians, but appropriate dosing is important as the side effects seem to include agitation, and hyperactivity.

Too often our clients revert to non-traditional feeding practices which can be detrimental to the health of our feline companions due to specialized nutrient requirements, particularly during gastrointestinal maladies, where food sensitivity may be an issue. In many cats with gastrointestinal disorders there are inherent deficiencies that can develop even when novel protein and/or hydrolyzed diets are used including cobalamin, due to poor caloric intake or malabsorption. These deficiencies can be exacerbated if non-traditional feeding practices are instituted. Typical protein sources (poultry and fish) often lack enough of certain amino acids (i.e. taurine), and a lack of fat in the diet lead to poor calorie intake, as well as deficiencies in various minerals, fat soluble vitamins and other water soluble vitamins.

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FELINE PANCREATITIS: WHERE ARE WE?

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Since its initial description in 1989 feline pancreatitis has emerged as an important and potentially life threatening disease. Despite increased awareness its etiology remains unknown, diagnosis is challenging, and surgical biopsy is often required to confirm a diagnosis, and facilitate detection of intercurrent disease. Treatment is generally symptomatic and typically involves aggressive nutritional support. This article reviews the current state of play in the diagnosis and treatment of acute pancreatitis in cats.

Clinical findings

Signalment and History:

Acute pancreatitis has been reported in cats aged from 4wks to eighteen years old. Domestic Short- and Long-hair cats are most commonly affected. Siamese cats have been over-represented in some series. No sex bias has been demonstrated.

A small number of cases have been associated with trauma, *Toxoplasma gondii*, pancreatic and liver flukes, FIP, calicivirus (virulent variant) and lypodystrophy. Usually there are no obvious associated factors.

The most common clinical findings in cats with acute pancreatitis are lethargy, anorexia, and weight loss. Vomiting diarrhea, constipation, icterus, dehydration, ascites and dsypnea are more variably present. Polyuria and polydipsia have been encountered in some cats with diabetes mellitus and pancreatitis. The duration of clinical signs until presentation varies from less than 3 days to 12 wks.

Physical Examination:

Dehydration, and hypothermia are commonly reported. Icterus may also be present. Abdominal pain is infrequently elicited. The presence of a palpable cranial abdominal mass or abdominal pain has been reported in a quarter to a third of cats in some clinical series and cats with experimental and trauma - induced pancreatitis.

Diagnostic approach and differential diagnosis

Lethargy anorexia and weight loss are the most common presenting complaints.Localizing signs or findings such as vomiting, icterus, diarrhea, abdominal pain, abdominal mass, polyuria or polydipsia should be pursued if present.

Where vomiting is present it is approached by pursuing localizing findings such as abdominal pain or masses and by ruling out infectious, parasitic, metabolic and gastrointestinal causes. Hyperthyroidism should be ruled out in cats >5yrs old by determination of serum total T_4 concentration. Elevated hepatic enzymes, hyperbilirubinemia, hyperglycemia, and glucosuria are frequently encountered in cats with acute pancreatitis so pancreatitis should be strongly considered in these cats.

The diagnostic approach to feline icterus is to first rule out pre-hepatic causes i.e hemolysis, and then to pursue hepatic or post-hepatic causes. The association of acute pancreatitis and hepatic lipidosis of increased mortality, cholangiohepatitis and inflammatory bowel disease has been shown in some studies. A high index of suspicion should be adopted for pancreatitis in cats with hepatic, biliary or intestinal disease. Cats with a confirmed diagnosis of hepatic lipidosis who have a peritoneal effusion should also be strongly suspected of having pancreatitis.

Pancreatitis may be the cause of diabetes mellitus in some cats, but the true association between these diseases is unclear. One study suggests that cats with pancreatitis and diabetes mellitus are very sensitive to insulin. Transient euglycemia and reduced insulin requirements after removal of a pancreatic abscess suggest that pancreatic inflammation or infection can exacerbate diabetes mellitus in cats. Transient diabetes mellitus has also been reported in a cat that was suspected of having pancreatitis.

Where a high index of suspicion for pancreatitis is present ultrasonography and determination of pancreatic markers (e.g. pancreas specific lipase) should initially be employed to help to detect pancreatitic

inflammation. However, given the spectrum of inter-current disease in cats with pancreatitis a well performed exploratory laparotomy with biopsy of the pancreas, liver, intestines and mesenteric lymph nodes is often required to generate an accurate diagnosis and enable feeding tube placement.

LABORATORY FINDINGS

Hematology: A mild anemia that may be non-regenerative, and leukocytosis, often without a left-shift, are common in cats with pancreatitis. Leukopenia is present in some cats and carries a poorer prognosis.

Serum biochemistry : Increased ALT, SAP, bilirubin, cholesterol and glucose, and hypokalemia and hypocalcemia (total and ionized) are most frequently observed. Azotemia is variably present. Hypocalcemia, present in about 50% of cases, is perhaps the most helpful finding for raising the probablility of a diagnosis of pancreatitis. Pancreatitis associated hypocalcemia may be caused by a variety of reasons, such as saponifcation of fat , soft tissue accumulation and changes in PTH homeostasis. The presence of ionized hypocalcemia (<1mmol/l) carries a poor prognosis. Hypocobalaminemia is present in some cats with pancreatitis and is thought to reflect concurrent intestinal disease, rather than exocrine pancreatic insufficiency.

Urinalysis: Enables azotemia to be characterized as renal or pre-renal. The presence of glucose or ketonuria should prompt consideration of diabetes mellitus.

Pancreas specific enzymes: Classically, elevations in serum amylase and lipase activity have been used as indicators of pancreatic inflammation in dogs. In cats it seems fair to state that total serum amylase and lipase are of no utility for diagnosing acute pancreatitis.

These limitations have stimulated the development of assays for enzymes or "markers"considered pancreatic in origin. Tests for trypsin-like immunoreactivity (TLI), trypsinogen activation peptide (TAP) and pancreas specific lipase have been evaluated in cats.

Feline Trypsin like immunoreactivity (fTLI). Immunoreactive trypsin has been shown to be a reliable indicator of pancreatic mass, enabling the reliable detection of feline and canine exocrine pancreatic insufficiency. It is much less useful as an indicator of pancreatic inflammation. It's sensitivity has been reported to be as low as 28%, and cats with fatal acute pancreatitis frequently have values within the normal range. Specificty is better, @ 66-75%. The poor sensitivity, particularly in cats with severe acute pancreatitis strongly suggests down regulation of TLI in the inflamed pancreas, similar to that observed in dogs with pancreatitis. Altered renal clearance in cats with renal failure can impact the specificity, as can the finding of normal pancreatic histology in cats with high TLI and intestinal disease.

Pancreas specific lipase immunoreactivity (fPLI).
Given the limitations of fTLI a test to measure feline pancreas specific immunoractive lipase has recently been developed. It's clinical utility is still being ascertained. However the initial results for fPLI are a lot more promising than fTLI, with sensitivity for pancreatitis reported as 67%, and specificity at 91%.

Trypsinogen activation peptide (TAP), is a peptide generated by the activation of trypsiongen. In health TAP is not detected in the circulation or urine. However the intrapancreatic acticvationof trypisnogen liberates Tap that can be measured in EDT plasma and urine. Experimental studies have shown that TAP generation can be detected in cats with edematous and hemorrhagic pancreatitis, with higher levels generated in those with hemorrhagic pancreatitis. Unfortuantely, clinical application is unlikely as the assay is generally unavailable.

DIAGNOSTIC IMAGING

Radiography:
Radiographic findings in cats with acute pancreatitis may include loss of serosal detail, increased opacity in the right cranial quadrant of the abdomen, displacement of the duodenum ventrally and/or to the right, dilated hypomotile duodenum and caudal displacement of the transverse large intestine. Although radiographic signs often are absent and non-specific radiography is a logical first choice imaging modality for animals with gastrointestinal signs. Negative or equivocal radiographic findings may be followed up with ultrasonography or an upper gastrointestinal contrast study. Thoracic radiographs may enable the detection of pleural fluid, edema or pnemonia which has been associated with pancreatitis in dogs and cats.

The high rate of pulmonary thromboembolism associated with feline pancreatitis may explain some of the throracic radiographic abnormalities.

Ultrasonography: Ultrasonographic findings include enlarged, hypoechoic pancreas, cavitary lesions such as abscess or pseudocyst, dilated pancreatic duct, swollen hypomotile duodenum, biliary dilatation and peritoneal fluid. Findings in cats indicate that ultrasound will detect from 35 to 67 % of cats with pancreatitis, with a specificity of @ 73%. This clearly means that a normal ultrasound does not rule out pancreatitis, and that diseases other than pancreatitis (e.g. pancreatic hyperplasia,pancreatic neoplasia) should be considered when an abnormal pancreas is visualized
The clinician should also be careful to consider differential diagnoses of enlarged peri-pancreatic structures, which can have an identical ultrasonographic appearance to pancreatitis. Fine needle aspirates of cavitary lesions may be useful to distinguish abscess from pseudocyst, neoplasia from inflammation etc.

Computed tomography
Contrast enhanced computed tomography (CE-CT) is the diagnostic test of choice for diagnosisng pancreatitis in people. Studies in cats have been disappointing, ranging from a failure to detect the pancreas to no diffrenecs visualized in cats with pancreatitis.

Abdominal paracentesis: Examination of peritoneal fluid may aid the detection of various causes of acute abdominal signs such as pancreatitis, gastrointestinal perforation or ruptured bile duct. The accumulation of fluid in the abdomen or the pleural cavity has been variably encountered in cats with acute pancreatitis. Effusion in the abdomen or chest was present in 17/40 cats in one study, in the abdomen of 5/5 cats with hepatic lipidosis and pancreatitis, and the abdomen of 2/8 cats another.

PROGNOSTIC INDICATORS:
Stratifying the severity of pancreatitis is useful when deciding how aggressive to be with medical and nutritional support, and in offering a prognosis. Severe pancreatitis requires aggressive support and carries a guarded prognosis, whereas mild pancreatitis may respond to short-term symptomatic therapy. Clinical and clinicopathological criteria can be used to predict the severity of acute pancreatitis. The presence of shock or abnormalities such as oliguria, azotaemia, icterus, markedly elevated transaminases, ionized hypocalcaemia (<1mmol/l), hypoglycaemia, hypoproteinaemia, acidosis, leukopenia, falling haematocrit, thrombocytopaenia and DIC should be considered likely indicators of severe pancreatitis in the cat.

The measurement of components of the systemic inflammatory response such as TNF-α, alpha-1acid glycoprotein, and IL-6 may also yield information about the severity of pancreatitis in cats, and in the future might lead to the administration of specific antagonists of this response. Indicators which are potentially useful in both the diagnosis and prognosis of pancreatitis include trypsinogen activation peptide (TAP), trypsin complexed with inhibitors and phospholipase A_2. Further validation of these markers is required before clinical application.

Pancreatic Biopsy and Histology
The pancreas can be biopsied surgically or laparoscopically. Current recommendations, based on the patchy distibutionof pancreatic inflammation, suggest taking biopsies from parts that look or feel abnormal,and from the left and right limbs and the body. Histological findings are variable and there is not yet a consensus on their interpretation. In general histopathology is reported according to the predominant features as acute necrotizing (necrosis predominates), acute suppurative (neutrophils predominate) or non-supputative (lymphocytic/plasmacytic inflammation and fibrosis). Whether these histologic types indicate a distinct etiology or some form of progression is unclear. The prognosis for suppurative pancreatitis is poor.

MEDICAL MANAGEMENT:
Medical treatment is based on maintaining or restoring adequate tissue perfusion, limiting bacterial translocation and inhibiting inflammatory mediators and pancreatic enzymes; surgical treatment consists principally of restoring biliary outflow, removing infected necrotic pancreatic tissue, or coping with sequela such as pseudocysts. No studies have critically evaluated treatment modalities in cats with naturally occurring pancreatitis.
The initial medical management is usually initiated before a diagnosis is confirmed, and is based on the presenting clinical findings and initial laboratory data. Dehydration or hypovolemia are supported with intravenous fluid therapy. Lactated Ringers solution or 0.9% NaCl are common first choices. Potassium

and glucose should be supplemented where necessary. The type of fluid should be tailored on the basis of electrolyte and pH measurements to restore normal electrolytes and acid-base balance. Inonized hypocalcemia is a common finding in cats with acute pancreatitis and impacts prognosis. However, it is not clear if treatment of hypocalcemia, which is not usually associated with fasiculations, teatny or seizures, will impact outcome.

Plasma (20ml/kg i.v.) or colloids (10-20ml/kg/day i.v.). may be indicated in the presence of hypoproteinemia or shock. Colloids such as dextran 70 and hetastarch may also have antithrombotic effects that help maintain the microcirculation.

Insulin therapy is initiated in diabetic patients. Stress hyperglycemia has to be diffrentiated from diabetes mellitus.

Where vomiting is a persistent problem antiemetics (chlorpromazine .2-0.4 mg/kg administered subcutaneously or intramuscularly every 8 hours,) and antacids (e.g. famotidine 0.5-1mg/kg) may be beneficial.

Prophylactic broad-spectrum antibiotics (e.g. amoxicillin ± enrofloxacin depending on severity) may be warranted in patients with shock, fever, diabetes mellitus or evidence of breakdowm of the GI barrier. Bacterial translocation has been demonstrated in experimental feline pancreatitis using distinct E.coli placed in the colon, and other sites e.g. bile, and colonization was prevented with cefotaxime (50mg/kg TID).

Analgesia is an important aspect of caring for animals with pancreatitis. It can be provided using injectable opioids such as buprenorphine (0.005-0.01mg/kg SC q6-12hrs) or oxymorphone (0.05-0.1mg/kg cats IM, SC Q 1-3hrs). It may be necessary to administer low dose sedation with acepromazine (0.01mg/kg IM) to patients who become dysphoric after opioids. Buprenorphine is a partial agonist and may antagonise the administarion of more potent analgesics in animals with severe pain. A transdermal fentanyl patch (Duragesic, Janssen) applied to a clipped clean area of skin provides longer duration of analgesia (25µg/hr patch q118hrs). Adequate fentanyl levels are not attained for between 6-48 hrs after application, so another analgesic should be administered in the short term. This author does not use non-steroidal antiinflammtory drugs to provide analgesia to cats with suspected pancreatitis.

Once a diagnosis of pancreatitis is confirmed potentially more specific therapy may be employed.
The specific treatment of pancreatitis has evolved along two lines: 1. Stopping further pancreatitis from occurring. 2. Limiting the local and systemic consequences of pancreatitis.
The lack of success with inhibiting the progression of spontaneous pancreatitis has led to increased emphasis on damage limitation; ameliorating the effects of inflammatory mediators or pancreatic enzymes on the patient and maintaining pancreatic perfusion.
Coagulation abnormalities should be pursued and treatment with parenteral vitamin K can be assessed.
Where a coagulopathy e.g. DIC, or hypoproteinemia are present, or the patient with pancreatitis is deteriorating, fresh frozen plasma (10-20ml/kg) may be beneficial in alleviating the coagulopathy, hypoproteinemia and restoring a more normal protease-antiprotease balanvce. The administration of heparin (75-150IU/kg TID) may be potentially useful in ameliorating DIC, promoting adequate microcirculation in the pancreas and clearing lipemic serum. In experimental pancreatitis isovolemic rehydration with dextran has also been shown to promote pancreatic microcirculation in dogs. A dopamine infusion (5µg/kg/min) had a protective effect when admisintered to cats within 12hrs of induction of experimental pancreatitis. H_1 and H_2- antagonists blocked the progression of edematous to hemorrhagic pancreatitis in experimental cats and may be beneficial in patients.
In the future therapy to directly abrogate the systemic inflammatory response e.g.antagonists of PAF (e.g lexipafant), IL-1 and TNF-α may prove to be beneficial.
Oral pancreatic enzyme extracts have been reported to reduce pain in humans with chronic pancreatitis, though this is controversial. The presence of a protease mediated negative feedback system. Has not been described in cats.

DIETARY MANAGEMENT:_
In contrast to dogs, where vomiting and abdominal pain predominate, pancreatitis in cats is usually associated with anorexia and weight loss. The presence of anorexia and weight loss in cats with pancreatitis

may be a significant contributing factor to their poor prognosis. Prolonged fasting (>3 days) to avoid pancreatic stimulation may only serve to compound malnutrition. The clinician is faced with the dilemma of having to provide nutritional support to prevent or reverse malnutrition and hepatic lipidosis, and fasting the patient to prevent "pancreatic stimulation". Current dogma suggests that oral intake be avoided in patients with pancreatits who are vomiting or have abdominal pain, and that enteral nutrition should avoid nutrients that stimulate the pancreas (though the protein requirements of cats makes this unachievable).

However, there is growing evidence in people, and animals, that enteral nutrition is superior to parenteral nutrition in the treatment of acute pancreatitis. Jejunal feeding (distal to the site of pancreatic stimulation) does not exacerbate acute pancreatitis in people or experimental animals. People with acute pancreatitis fed via jejunostomy tubes (these can be oral transpyloric tubes), have lower morbidity, shorter hospital stay, and less cost than those treated with TPN (total parenteral nutrition). As it is now feasible to place jejunostomy tubes non-surgically in cats and dogs, through the nose, esophagus or stomach, clinical application of this feeding strategy is not restricted by a surgical procedure. It remains open whether cats with acute pancreatitis really require jejunal delivery of nutrients. Good responses (approximately 70% discharge rate) have been observed at referral centers employing esophagostomy or gastrostomy tube feeding of enteral diets (e.g. clinicare) containing approximately 50% calories as fat. These results seem consistent with findings in people and experimental dogs that show the major benefits of enteral support in acute pancreatitis are due to reductions in the systemic inflammatory response and the translocation of enteric bacteria rather than a reduction in pancreatic stimulation.

The author does not mean to imply that parenteral nutrition should be discarded, but its use should be restricted to patients that really need it, for instance those in whom caloric intake is severely and persistently impaired by persistent vomiting.

When parenteral nutrition is indicated a choice has to be made between total and partial parenteral nutrition. Partial parenteral nutrition (PPN) is a more practical and manageable procedure than TPN in most settings and has been shown to be a safe and effective way of providing nutrition to dogs with pancreatitis and gastrointestinal disease. Interestingly dogs that received a combination of enteral and PPN survived more often than those receiving PPN exclusively.

PATIENT MONITORING:

Patients with suspected or confirmed pancreatitis should be monitored to enable early detection of shock or other systemic abnormalities. Minimal monitoring for stable patients includes regular assessment of vital signs and fluid and electrolyte balance. In those with systemic abnormalities, monitoring should be more aggressive and may include vital signs, weight, haematocrit, total protein, fluid intake and output, blood pressure (central venous and arterial), electrolytes and glucose, acid-base status, platelets and coagulation status. Ultrasound-guided fine needle aspiration of the pancreas may enable infected pancreatic necrosis to be detected. Ultrasonography may also enable detection of delayed consequences of acute pancreatitis such as pancreatic abscessation, pseudocyst formation and biliary obstruction.

SURGERY:

Surgery is often necessary to confirm a diagnosis of acute pancreatitis in cats and also enable feeding tube placement. The increased utility of ultrasonography and measurement of markers of pancreatic inflammation (e.g. fPLI) may lead to a reduced dependency on surgery in cats with high fPLI and sonographic abnormalities. However it should be stressed that cats with pancreatitis often have concurrent abnormalities in other organ systems e.g. liver and gut, and biopsy of these organs and the pancreas may be indicated to optimize diagnosis and treatment. Transient euglycemia and reduced insulin requirements were noted after the removal of a pancreatic abscess in one cat suggest that surgical intervention may be beneficial in these cases. Surgery is potentially indicated for infected pancreatic necrosis, abscess drainage, and to investigate and to relieve persistent biliary obstruction. Resection or surgical drainage of pancreatic pseudocysts is not always necessary as these can resolve spontaneously or following percutaneous drainage.

PROGNOSIS:
The prognosis for acute pancreatitis in cats must always be considered guarded. Extensive hepatic lipidosis, suppurative pancreatitis, leucopenia and ionized hypocalcemia <1mmol/l are associated with a poor prognosis.

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Inflammatory
Liver Disease

What's New: Feline Inflammatory Liver Disease

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Feline *Inflammatory Liver Disease*

Feline liver disease usually involves Zone 1 (portal triad) and focuses on components of the biliary system (bile ductules, bile ducts, common bile duct, pancreatic ducts, gallbladder). Inflammatory effacement of the limiting plate (hepatocytes surrounding the portal triad) and associated apoptotic or necrolytic hepatocyte death (as recognized in chronic canine hepatitis) is uncommon without involvement of biliary structures. Thus, it appears that the cholangitis/cholangiohepatitis syndrome (CCHS) is the feline equivalent to canine chronic hepatitis. The CCHS syndrome can affect cats of any age (3 mths-19 yrs). However, the most common form of CCHS (nonsuppurative) is usually diagnosed in middle aged or older cats. Despite early suggestion of a Siamese predisposition, there is no apparent breed predilection.

While a syndrome of "portal hepatitis" has been described in cats, this is an uncommon diagnosis and may be an artifact of uneven CCHS lobe involvement, sampling of a single liver lobe, or slender needle biopsies. The confusing designation of "reactive hepatitis" must not be interpreted as CCHS. This terminology does not implicate hepatitis but rather describes random foci of ceroid-lipofuscin filled macrophages, hemosiderophages, iron laden Kupffer cells, and inflammatory cells reflecting the sentinel role of the liver.

Subcategorization of CCHS: Suppurative vs Non-Suppurative

Suppurative CCHS does not appear to be antecedent to nonsuppurative CCHS based on studies conducted at Cornell. Rather, primary disorders promoting bile stasis are often discovered in cats with suppurative CCHS, examples include: extrahepatic bile duct occlusion (EHBDO), choledochitis/cholecystitis, cholelithiasis, acute severe inflammatory bowel disease (IBD, duodenitis), and pancreatitis (causing distal bile duct occlusion). Choleliths may play a causal role or develop consequent to cholestasis, cholechochitis, or hemobilia. Suppurative CCHS may be more common in young, male cats. Affected cats usually present with acute clinical signs including variable lethargy, fever, inappetence, painful abdomen, acute onset vomiting and/or diarrhea, dehydration, +/- jaundice. Less than <50% of cats have a large liver on palpation.

Diagnosis of Suppurative CCHS: Typical clinicopathologic features include a leukocytosis, often with a left shift and toxic neutrophils, and increased but highly variable ALT, AST, GGT +/- ALP activities. Variable bilirubin concentrations (some normal) may reflect the acute presentation associated with suppurative CCHS. Bilirubinuria is found in the absence of overt hyperbilirubinemia. In some individuals, jaundice may reflect "sepsis" rather than mechanical disturbance of bile flow. Acutely ill cats often present dehydrated and have pre-renal azotemia. Some cats present with classic features of hepatic lipidosis (HL) consequent to inappetence, vomiting, and diarrhea. Discovery of high GGT activity helps identify an underlying necroinflammatory process involving hepatobiliary structures or pancreas. We have managed some cats with suppurative CCHS that have been infected secondary to therapeutic immunosuppression (e.g. treatment if nonsuppurative CCHS or lymphoma). In these, infections have commonly been derived from feeding appliances (esophagostomy or gastrostomy tubes).

Histologic Characterization of Suppurative CCHS: Histologically, suppurative CCHS is characterized by neutrophilic infiltrates around and within intrahepatic bile ducts, periductal edema, and in many, hepatocellular cholestasis (canalicular bile plugs). With chronicity (> several weeks), a circumferential periportal fibrolamellar mantel surrounds and bridges between ducts and biliary epithelium undergoes rampant replication (oval cell hyperplasia). There is no distinct ultrasonographic (US) appearance aside from recognition of abnormalities involving large bile ducts, gallbladder, or pancreas; coexistent HL complicates US interrogation owing to diffuse hepatic parenchymal hyperechogenicity.
Differentiation of "acute" and "chronic" subsets of suppurative CCHS based on cellular infiltrates has confused syndrome characterization. A mixed lymphoplasmacytic infiltrate combined with a neutrophilic or eosinophilic infiltrate develops in some cats. By itself, cellular infiltrates do not discriminate acute from chronic. Differentiation of acute and chronic subsets should consider the duration of clinical illness and the extent of tissue remodeling including alterations in biliary structures,

the extent of oval cell hyperplasia, and development of periductal fibrosis. While histology confirms a diagnosis of suppurative CCHS, not all cats with this syndrome should be taken to surgery as liver and bile aspirates can confirm infection and direct initial therapy. Surgical intervention is warranted for biliary tree decompression in cats with major bile duct occlusion, removal of choleliths likely perpetuating bile duct occlusion or infection, or removal of focal infections (e.g. abscesses) that may be identified during US evaluation.

Cultured Organisms: Culture of liver, bile, or choleliths are positive in 18-25% of feline submissions. One report described positive cultures in 7/49 (14%) liver and 5/14 (36%) bile samples.[2] Single bacterial (75%-90%) and polymicrobial infections (10%-15%) may be encountered. Gram negative aerobes (E. coli, Enterococcus, Streptococcus) are most common; most common anaerobes include Bacteroides spp and Clostridium spp. Finding bacteria does not confirm a causal relationship to CCHS because any form of cholestasis predisposes to infection by virtue of obstruction of the normal egress pathway for translocating enteric opportunists. In addition to intestinal translocation (fostered by IBD), bacteria may ascend the biliary tree secondary to duodenitis or as a result of pressure changes during the act of vomiting that propel duodenal bacteria into the common bile duct ampulla. Alternatively, organisms may be hematogenously dispersed from infections located elsewhere in the body. Vomiting and diarrhea common to CCHS may coincide with portal bacteremia or reflux of enteric flora into biliary or pancreatic ducts.

Treatment Suppurative CCHS: Elimination of cholestatic factors and systemic infection is imperative. Antimicrobials (4-6 wks) are initially select based on the morphologic and gram staining characteristics of bacteria identified on cytologic preps (aspiration samples or liver biopsy imprints). Initial recommendations are refined if on the basis of tissue / bile cultures. If cultures are negative, a lack of cytologic samples compromises optimal case management. Hydrocholeresis with ursodeoxycholate (UDCA) and s-adenosylmethionine (SAMe, Denosyl®) provide hepatoprotective and antioxidant benefits in addition to a mechanical cleansing effect. Vitamin supplementation (water soluble, ensure B_{12} repletion,Vitamin E [alpha-tocopherol acetate, 10 U/kg/day PO]) are recommended along with a balanced protein replete feline diet. Adequate nutritional support is the cornerstone to recovery. The role of silibinin (milk thistle) is unclear. Recent work has confirmed that cats can acquire systemically measurable silibinin from milk thistle derivatives combined with polyunsaturated phosphatidylcholine (Marin™, silibinin with PPC). Lipoic acid as a thiol donor is not recommended as this has been shown to be lethally toxic to cats in doses easily handled by dogs and humans.[3] Vitamin K_1 (0.5 mg/kg) is usually provided independent of PIVKA analysis based on data previously published by the author.[4] Three doses given at 12-hr intervals are recommended.

Follow-up hematologic, biochemical, and urinalysis monitoring are essential to confirm resolution of abnormal findings before antimicrobials are discontinued. For cats with clinical signs or laboratory features that fail to resolve, considerations should include lack of eradication of bacterial organism(s) (e.g. hepatic or non-hepatic associated abscess: pyelonephritis, splenic abscess, infected choledochal cyst; or development of bacterial resistance), failure to identify or resolve mechanical obstruction of bile flow, failure to identify primary sclerosing CCHS (see below) that was secondarily infected, presence of choleliths compromising bile flow or perpetuating infection, transformation of suppurative to non-suppurative inflammation, presence of underlying hepatic lymphoma, development of hepatic lipidosis, "smouldering pancreatic inflammation, or unrecognized IBD. Follow-up US guided hepatic parenchymal, gallbladder bile, or pancreatic aspiration, bowel biopsy, or re-biopsy of the liver may be necessary.

Non-Suppurative CCHS: Cats with nonsuppurative CCHS show few clinical signs in the early stages (months to years). Even with chronicity, clinical signs may remain vague and cyclic, including: lethargy, weight loss, anorexia or polyphagia (sclerosing cholangitis induces malassimilation), vomiting, diarrhea, and polydipsia. Since CCHS often coexists with IBD, gastrointestinal signs may dominate. Jaundice may be absent, intermittent, or marked. Rarely, in advanced disease, cats may display signs of hepatic encephalopathy (ptyalism, aggression, somnolence). These individuals are usually jaundiced and may develop abdominal effusion. Most cats with nonsuppurative CCHS have a palpable "normal to large" liver. Typically, inappetence and illness are followed by spontaneous remissions leading owners to question the gravity of their cats illness. Cyclic disease is apparent on sequential liver enzyme and

total bilirubin assessments. Some cats initially present for hepatic lipidosis (HL) during cyclic illness. In these cases, underlying CCHS is often recognized by finding a high GGT activity which reflects involvement of biliary or pancreatic ductal components. Some cats present primarily for pancreatitis seemingly associated with periductal inflammation. The unique feline anatomy in which a common ampulla unites the common bile duct and major pancreatic ducts, provides a conduit for direct sharing of infectious agents, inflammatory mediators, and obstructing debris between organ systems. Common epithelial antigenic epitopes (ductal epithelium) may be a critical target in the most severe form of nonsuppurative CCHS (so called sclerosing CCHS). In these, small- and medium- sized bile ducts are gradually eliminated by persistent immune-mediated inflammation in which T-cell targeting leads to diffuse "ductopenia". Some of these cats present for signs consistent with major bile duct occlusion, including acholic feces.

Diagnosis of Nonsuppurative CCHS: Recent work at Cornell[1] has advanced the classification of CCHS based on histologic features, lymphocyte immunophenotyping, cytokeratin confirmation of small duct status, interrogation of lymphocyte clonality, and investigation for associated eubacterial pathogens.

While cytologic assessment of liver aspirates can deduce septic inflammation, cytologic specimens alone are unreliable for detection of non-septic inflammation. Furthermore, cytologic preparations are unable to definitively diagnose nonsuppurative CCHS because of their inability to disclose hepatic architectural features needed to establish zonal involvement and confirmation of bile duct involvement. We have recognized a mixed inflammatory infiltrate in some cats in the absence of demonstrable or culturable bacteria, a negative PCR for eubacterial DNA, and negative in-situ fluorescence hybridization (FISH) for eubacteria.[1] Clinical significance of positive PCR results for enteric bacteria and Helicobacter spp DNA in liver or bile remains unclear.[5,6] Helicobacter was detected by PCR in bile from 4/15 (26%) cats with nonsuppurative CCHS, 8/51 (24%) cats with liver disease other than nonsuppurative CCHS, and 7/12 (58%) cats lacking liver disease.[5] One study in human beings investigating Helicobacter species in patients with primary biliary cirrhosis, primary sclerosing cholangitis, or other liver disease of known cause (alcoholism, hepatitis B, metabolic liver disease) discovered . 30% of each population was PCR positive. These findings contradict a role of Helicobacter as a primary cause or as a pathologic association with many inflammatory liver disorders.[7] A feline study[6] using archived paraffin embedded liver tissue found Helicobacter sp in 2/32 (6%) cats with CCHS and 1/17 (6%) control (non-inflammatory liver disease or healthy) cats by PCR amplification. Positive findings were speciated by sequence confirmation. Using FISH, a single semicurved bacterium (2-u long) with *Helicobacter*-like morphology was observed within an intrahepatic bile duct in one cat with suppurative CCHS. Although DNA of Helicobacter spp other than H. pylori were confirmed (suppurative CCHS: H. fennelliae or H cinaedi, H. bilis was amplified from a cat with portosystemic vascular anomaly). Silver staining (Steiner stain) was uniformly negative in PCR positive cats. Because discordancy between culture, in-situ localization, and positive PCR reports are frequent in experimental and clinical studies of Helicobacter, it is probable that PCR detection of bacterial DNA reflects enterohepatic circulation of intestinal organisms or DNA sojourning the liver rather than true colonization. However, positive reports might also reflect transient tissue colonization.

Histologic Characterization of Nonsuppurative CCHS: The study at Cornell[1] has better defined subcategorizations of nonsuppurative CCHS. Our findings contradict an overt initiating neutrophilic inflammatory process and describe an epitheliotropic immune-mediated disease process Observations confirm marked differences in disease activity among liver lobes that can compromise diagnostic accuracy when either a single liver lobe is biopsied or tissue is only retrieved by small 18g tru-cut core instruments.[8] Findings confirm that the best samples for histologic characterization are surgical wedge or laparoscopic cup samples. However, multiple 16g tru-cut needle samples collected under US guidance have successfully harvested enough tissue for confident lesion characterization from some cats. Nevertheless, in consideration of "best practice" for sample collection, it is important to acknowledge that collection of multiple tru-cut biopsies imposes greater risk of iatrogenic complication. Full thickness intestinal and pancreatic samples should also be considered in cats with suspected CCHS. More than 20 years ago, an affiliation between enteric and pancreatic inflammation and chronic interstitial nephritis was noted in cats with CCHS.[9]

Routine sampling of gallbladder bile by US guidance is <u>not advised</u> by the author unless septic inflammation is considered likely and diagnostic strategies will be altered by confirmation of bacterial

infection. Dull pressure on the gallbladder during cystocentesis can initiate a vasovagal response (severe bradycardia, respiratory arrest, death) requiring anticholinergics and resuscitation. A similar response may explain sudden death after needle biopsy of the liver described in some cats; perhaps the gallbladder or large bile ducts were iatrogenically traumitized.[10]

Our CCHS classification scheme defines 4 groups. *Group 1:* lymphocytic/lymphoplasmacytic inflammation confined within the portal triad or effacing the limiting plate. Biliary epithelial hyperplasia exists without apparent duct destruction derived from immunocyte epithelial targeting. *Group 2:* lymphocytic/ lymphoplasmacytic inflammation with biliary epithelial targeting, duct destruction, and extension of biliary hyperplasia effacing the limiting plate. Inflammatory cells follow replicating oval /biliary epithelial cells and leaving a trail of lipogranulomas and ductopenia within the original confines of the portal triad. Inflammatory infiltrates may extend into the wall of major bile ducts, the cystic duct, or gallbladder, and also may extend within the pancreatic ductal system. Pancreatic involvement may be associated only with periductal inflammation that may lead to duct involution. In some cats, disappearance of islets, accumulation of islet amyloid, and clinical diabetes mellitus has been observed. Overt pancreatitis has been found in a small subset. *Group 3:* ambiguous "inflammatory" infiltrates may represent clonal expansion (histomorphology, immunophenotyping) and/or evolving neoplasia. Affected cats may be ductopenic due immunotargeting of biliary epithelium. This group may represent a "paraneoplastic process" associated with evolving lymphoma. *Group 4:* overtly neoplastic lymphoid infiltrates often associated with demonstrable TCR-rearrangement clonality.

Distinction of Group classification is made with special stains (e.g. extent of fibrosis, lobular collapse, biliary epithelial hyperplasia, duct targeting, lipogranulomas, iron retention), immunophenotyping stains, cytokeratin immunohistochemistry (documenting duct dropout and duct location), PCR detecting T-cell antigen receptor rearrangements (PARR, primers for conserved regions of the V and J genes to amplify desired CDR3 regions, followed by product size separation to identify clonal expansions), PCR for detection of eubacterial DNA and FISH for identification of bacterial organisms. Pathologic findings are being correlated with clinicopathologic features, treatment response, and survival.

Treatment Nonsuppurative CCHS: nutritional support with a balanced protein replete feline diet, vitamin supplements (water soluble, ensure taurine, thiamine (B_1) and cobalamin (B_{12}) sufficiency), injectable vitamin K_1 before biopsy sampling, antioxidants (SAMe: 40-50 mg/kg of a proven bioavailable product with predominance of s-SAMe isomer [Denosyl®], Vitamin E: alpha tocopherol acetate 10 U/kg), ursodeoxycholic acid (15 mg/kg PO divided BID but given with meals to enhance absorption) with supplemental taurine (250 mg/day) as ursodeoxycholate must be conjugated in the cat to taurine, and immunomodulation. Prednisolone 2 mg/kg PO is prescribed initially; this is tapered to 1 mg/kg in tolerant cats (tolerance = no hyperglycemia). Prednisone should not be used as the source of glucocorticoid. A recent study at Cornell has confirmed that cats have low uptake of prednisone dosed orally. While we have used metronidazole (7.5 mg/kg PO BID, compounded into gel caps or given as a prepared flavored liquid) to allow glucocorticoid dose reduction, we have not observed chronic problems with neurotoxicity or consequences associated with recently described genotoxicity.[11] While some cats in Group 1 respond well to only oral SAMe treatment (Denosyl®, 40-60 mg/kg PO daily) with resolution of inflammatory infiltrates, most cats in Group 1 require prednisolone and antioxidants, +/- UDCA. Cats in Group 2 (sclerosing CCHS with duct immunotargeting) are not controlled with prednisolone and antioxidants and require more aggressive immunomodulation. We have achieved reasonable control in some cats using either methotrexate (0.3 mg total dose per cat on one day given at 0, 12, and 24 hrs, at 7-10 day intervals or chlorambucil given as 2 mg total dose PO every other day. Case presentations will be used to demonstrate treatment responses after accurate syndrome characterization.

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Advances in the Management of Feline Chronic Kidney Disease
Feline Health Center Symposium 2009

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Chronic kidney disease is an extremely prevalent disorder in companion animal practice. An estimated 0.5-1.0% of all dogs and1.5-2% of all cats presenting to US veterinary clinics suffer from some degree of kidney disease. These numbers are much higher in practices that see a large number of geriatric patients and emphasize periodical geriatric examinations. Some estimates claim that as many as 30% of small animal cases seen in referral institutions suffer from chronic renal disease.
Terminology – Chronic renal failure has been most commonly used in the past as a catch all term for any degree of chronic kidney disease.

Historical Terms:

1. "Renal disease" to describe a state of abnormal renal function with a decrease in GFR and possibly urine concentrating ability without azotemia. This condition would likely be associated with the functional loss of 50-75% of renal tissue, and is associated with very few clinical signs.
2. "Renal insufficiency" would describe a condition more severe than the above with mild azotemia. Typical serum creatinine values would be 2-4.0mg/dl.
3. "Renal failure", more severe azotemia (serum creatinine > 4.0mg/dl) likely associated with some or all of the systemic manifestations of renal disease, a syndrome called uremia.

Currently – IRIS Staging:

Stage	Plasma creatinine (mg/dl)	Comments
I	**<1.4 - dogs <1.6 - cats**	**Renal abnormality (lack of urine concentration etc..)**
II	**1.4-2.0 - dogs 1.6-2.8 - cats**	**Mild clinical signs (PU/PD)**
III	**2.1-5.0 - dogs 2.9-5.0 - cats**	**Many extra renal clinical signs may be present**
IV	**>5.0 – dogs & cats**	**Difficult to manage w/o invasive measures**

Qualifyers:

1. Proteinuria

Cut-off levels	Interpretation
<0.2 dogs & cats	**Non-proteinuric**
0.2-0.4 - cats **0.2 – 0.5 - dogs**	**Borderline proteinuric**
>0.4 - cats **>0.5 - dogs**	**Proteinuric**

2. Arterial Blood Pressure

Blood Pressure	Systolic (mm Hg)	Diastolic (mm Hg)
Minimal Risk	**<150**	**<95**
Low Risk	**150-159**	**95-99**
Moderate Risk	**160-179**	**100-119**
High Risk	**≥180**	**≥120**

Each BP category is qualified
Clinical evidence of end-organ damage
Example:
Cat with:
Creatinine of 2.2 mg/dl
UPC of 0.6
BP of 180 with evidence of hypertensive retinopathy would be:
Stage III/P/HRC

It is well documented in humans and rodent models of renal disease that once a critical mass of kidney tissue has been damaged, there will be a spontaneous progression of the renal disease towards end-stage kidneys and uremic death. This progression will occur even if the underlying cause of the renal injury has been identified and removed. Although not well documented (yet) in naturally occurring disease, it appears to happen in small animal patients in a similar way. Obviously if the underlying disease has not been removed it can also continue to worsen the kidney function and hasten the progression of the disease. Chronic disease may be a result of an insult that caused acute disease as was described in the previous talk or it could also start out as a slow chronic process. Understanding the factors associated with the progression of chronic renal disease is vitally important so that appropriate steps to stop or at least slow this process may be taken. In general the factors thought to influence the progression of chronic renal disease are thought to include:

1. The primary cause of the renal disease
2. Mechanisms of inherent progression
    a. Intrinsic renal mechanisms, possibly including glomerular hypertension and hypertrophy, as well as proteinuria.
    b. Systemic derangements possibly including systemic arterial hypertension, anemia, mineral and acid base abnormalities.
3. Pre-renal factors.

The rest of this presentation will hopefully try and shed a practical light on the possible causes of progression of renal disease and the proposed management strategies to manage the clinical manifestations as well as possibly slow the progression of chronic renal failure. An emphasis on the influence of proteinuria on the progression of renal disease will be given.

<u>The minimal data base when assessing a patient with possible chronic renal disease should include:</u>

1. Thorough history, including a good dietary history, travel history and physical examination. Typically the clinical signs associated with CRD will have lasted for a few weeks. Common clinical signs and historical complaints may be similar to those of acute renal failure, with more of a gradual onset and may include:
    a. Lethargy, weakness, exercise intolerance
    b. Anorexia, vomiting. In some cases diarrhea and/or melena.
    c. Weight loss
    d. PU/PD
    e. Bruising and oral ulcerations
    f. Uremic breath
    g. Poor unkempt hair coat (cats)
    h. Hypothermia (a direct effect of the uremia)

Physical examination findings may include:

a. Small irregular kidneys (some chronic diseases are associated with large kidneys – polycystic kidneys, amyloidosis, neoplasia, peri-renal pseudocysts etc…)
b. Pale mucus membranes with CRT elongation
c. Dehydration
d. Tachycardia, possibly with bounding femoral pulses
e. Uremic bruising, ulceration, breath (less than in acute disease)
f. Rubber jaw (uncommon).

2. Complete blood count
    a. Non-regenerative normocytic, normochromic anemia. May be somewhat regenerative if there was some rather acute GI bleeding.
3. Serum chemistry profile
    a. Azotemia – elevations in BUN and creatinine, potentially higher than expected based on the clinical presentation when compared to acute disease.
    b. Hyperphosphatemia – Relatively mild when compared to acute disease of the same magnitude.
    c. Hypercalcemia – If present usually mild, with a normal ionized calcium. Hypocalcemia is quite rare in chronic disease.
    d. Albumin – Usually normal although may be low if marked proteinuria is present. May not appear to be as low as it really is on presentation because of dehydration. May also be low with GI bleeding.
    e. Globulin – Uncommon to be used through the kidneys but can be with severe glomerular disease. Would tend to be low in the case of GI bleeding. May not appear to be as low as it really is on presentation because of dehydration.
    f. Sodium and chloride – May be excessively lost with PU/PD or could be high if the kidneys are not able to excrete these electrolytes adequately. This is true especially in cats receiving IV or sub-cutaneous fluid therapy.
    g. Hypophosphatemia – Common in cats with a potassium losing nephropathy with or without other evidence of renal disease. May be masked by acidosis. Hyperkalemia is very rare and usually is only present in anuric/oliguric/post-renal renal disease or end stage chronic renal failure
    h. Low bicarbonate concentration – metabolic acidosis – Very common as bicarbonate is normally produced de-novo in the kidney and this capability is impaired with CRD.

4. Complete urinalysis
    a. Isosthenuria is a consistent finding. In mild disease urine my be slightly more concentrated but if dehydration and azotemia are present as well – then the degree of urine concentration will be inappropriate for the degree of azotemia.
    b. Proteinuria – usually mild to moderate unless there is a primary glomerulopathy. Use a urine protein/creatinine to assess severity

c. Crystalluria, hematuria, pyuria, bacteriuria all may be present. Remember – Never trust a urine sediment to give you all the information when the specific gravity is less than 1.012!

5. Urine culture.
6. Blood pressure measurement. A very large percent (50-75%) of CRD dogs and cats are hypertensive. They commonly even present for acute blindness with retinal detachment. Blood pressure, even if just systolic via Doppler, should be assessed in every patient.

Additional testing may be warranted:

1. Blood tests – serum iron concentrations, coagulation profiles, erythropoietin levels, parathormone concentrations.
2. Imaging – abdominal ultrasound, radiographs, excretetory urograms, double contrast cystograms, nuclear scintigraphy
3. Renal biopsies or aspirates
4. Search for cause of intrinsic renal disease (leptospira titers, Lyme titers, cancer search…), or underlying systemic disease (tick borne disease etc…)

Once the diagnostics have been performed our goal is then to:

1. Treat underlying disease – impossible in most cases of intrinsic CRD
2. Identify and try and correct all metabolic abnormalities.
3. Attempt and slow the progression of the disease.

<u>The attempt to correct all measurable metabolic abnormalities</u>

Azotemia

Dietary management is at the foundation of the medical management of CRD. Specially formulated diets attempt to minimize uremic effects and to provide adequate nutrition.

a. Dietary protein

Degradation products of protein must be excreted by the kidney. When GFR declines the products build up. These products then become "uremic toxins". Urea and creatinine are easily measured and serve as markers for a larger group of nitrogenous waste products. The use of protein restricted diets in dogs and cats with renal disease appears to be associated with a decrease in clinical signs, and seems very worth while. There is some dispute as to how severe this restriction should be and when in the disease process it should be implemented. I believe there is no doubt that some restriction is beneficial when azotemia becomes apparent.

b. Sub-cutaneous fluid administration

This is very beneficial in some of our smaller small animal patients (usually <10kg). This may help eliminate some of the small acute episodes that hasten the progression of the renal disease because of bouts of anorexia, adipsia, and

dehydration. This is usually tolerated well even on a daily basis. One must watch the electrolytes and especially sodium to make sure it is not rising on high sodium containing fluids.

Gastrointestinal symptoms including anorexia, vomiting, GI bleeding

These symptoms can be quite severe and be the reason that a patient with CRF is euthanized. In human patients this is one of the main determinants of when maintenance dialysis is started. The cause of these symptoms are not entirely known and are likely multifactorial. There is some evidence in cats that hypergastrinemia is present and may be associated with some of the GI upset and bleeding. Other factors may be gastric mineralization, as well as direct effects of uremic toxins on the chemoreceptor trigger zone and GI mucosa. Another very important cause of the anorexia is likely the anemia associated with CRD. This will be addressed separately. Attempted management (in addition to decreasing uremic toxins):

1. Histamine-2 receptor antagonists. Decrease gastric acidity and possibly negate the effects of hypergastrinemia. Remember that these medications are renally excreted and therefore a dose reduction is necessary in CRD.
2. In severe cases of vomiting antiemetics may be used. Metoclopramide is the most common medication used.
3. In refractory cases of anorexia and malnutrition, placing a gastrostomy (PEG) tube is extremely beneficial. The whole appetite issue is not important at this time and the owners can ensure that the patient is getting adequate nutrition of the proper diet as well as the large amount of medication recommended. All this is done without the owner having to fight with the pet over eating and taking medications, and in most cases turns out to be an excellent palliative solution for all.

Anemia of chronic renal disease

Bone marrow hypoplasia and anemia are specific and well defined sequela of chronic renal disease in small animals as well as in people. In people and likely in small animal patients one cannot overemphasize the impact of the anemia on the well being of the patient. The anemia appears to contribute to the inappetence, weakness, fatigue, cold intolerance and dehydration, these patients experience. Ideally all patients should be treated for their anemia; unfortunately this is not always possible.

The role of erythropoietin –

The factors that have been shown to contribute to the anemia of humans with CRD include:

a. Reduced RBC survival
b. Platelet dysfunction
c. GI bleeding
d. Bone marrow failure from lack of erythropoietin
e. Lack of iron.

All these factors may play a role but today there is no question that the most important factor is the erythropoietin deficiency. In dogs (and people) with renal disease erythropoietin levels are low or inappropriately low for their degree of anemia – a relative deficiency. The introduction of recombinant human erythropoietin (r-HuEPO) therapy has completely changed human nephrology and has made a big difference in small animal practice.

The use of r-HuEPO –

Advantages – Will likely normalize Hct within a number of weeks and GREATLY improve the well being of the small animal CRD patient.

Disadvantages – Expensive

- The potentially catastrophic risk of clinically significant anti – EPO antibodies developing. Such antibodies also bind endogenous EPO lowing Hct to extremely low numbers possibly for many months and excluding the re-introduction of r-HuEPO again.

- Must be given with iron
- Blood pressure must be controlled prior to initiation of EPO therapy.

Because of these potential side effects and cost we tend to only treat animals who are not doing well because of moderate to severe anemia, with recommended cut off Hct values of 20-25% in cats and 25-30% in dogs.

Suggested protocol for r-HuEPO

1. Measure BP and control hypertension if present
2. Supplement iron (usually 100-300mg/day for dogs and 50mg/day for cats)
3. Start EPO at 100u/kg 3 times a week and check PCV weekly
4. When Hct reaches low normal value decrease to twice a week and if reaches high normal value decrease to once a week. Most patients will end up at 1-2 times a week dosing. If 100u/kg once a week is still too much then go to 75u.

If antibodies develop a relatively steep drop in Hct will occur. An increased myeloid:erythroid ratio on a bone marrow of >7-10 is the best way today to diagnose this disorder. If this occurs then EPOGEN® must be stopped immediately and the patient supported with transfusions (usually for months) until the antibody titer drops.

Canine and feline recombinant erythropoietin – Unfortunately - Currently under investigational use only and not available.

Darbopoietin – A new BETTER alternative that r-HuEPO will be discussed

Analogue of erythropoetin
Slightly different sequence

More potent different immunogenicity
So far appears safer than epo

Dosage:

1/3 of the frequency
200IU epogen ~ 1µg darbo
PCV monitoring as in epo
Go to every other week after target PCV is reached
Dose adjustments not more frequently than 4 weeks apart
Given with iron

rHuEPO dose U/week	Weekly Darbopoetin µg/week
<2,500	6.25
2,500-4,999	12.5
5,000-10,999	25
11,000-17,999	40
18,000-33,999	60

Systemic hypertension

Hypertension may play a role in the progression of chronic renal disease in small animal patients. It is also harmful in itself causing ocular, cardiac, vascular and CNS pathology. Therefore the control of at least severe hypertension (systolic blood pressure over 180 and diastolic blood pressure over 100) is highly recommended. You must be able to measure at least systolic pressure via Doppler to properly manage these patients. Management:

1. Sodium restriction – All renal diets are sodium restricted, this may help in the management of hypertension. We do not recommend adding salt to diets of patients with CRD to encourage drinking.
2. Commonly used medications:
    a. ACE inhibitors – Benazapril, enalapril
        i. Relatively weak at controlling blood pressure ion their own.

ii. Apparently extremely beneficial in slowing progression of renal disease – possible mechanisms:
    1. Decreased glomerular hypertension
    2. Decreased proteinuria
    3. Inhibitory effect on growth factors
iii. Possible side effects
    1. Transient decrease in GFR and increased azotemia

b. Calcium channel blockers – amlodipine
    i. Excellent yet gentle control of blood pressure resulting from renal disease in cats.
    ii. Easy to dose in cats (1/4 of a 2.5mg tab SID).
    iii. Likely beneficial in dogs as well although possibly not as predictable.
    iv. May take a few days to achieve effect

c. Arterial dilators – Hydralazine
    i. Very effective and potent
    ii. Injectable and oral dosaging
    iii. Can cause severe hypotension – Not recommended for use unless refractory to other therapies and pressure needs to be dropped quickly.

Acid base disorders

The kidney is the major site for regeneration, production and regulation of bicarbonate, as well as the major site for excretion of additional acidic compounds like sulfates and phosphates. Therefore, moderate to severe metabolic acidosis is a consistent finding with CRD. Management:

1. Reduction of acid load by reduction of dietary protein content.
2. Discontinue any acidifying medications in use
3. Consider oral bicarbonate therapy when bicarbonate concentration is less than 15mEq/L. Initial dose is 8-12mg/kg 2-3 times daily to achieve a bicarbonate concentration of 18-24. This can be given as tablets or a solution made up with baking soda.

Mineral disorders of CRD

The following are the common mineral derangements seen with CRD. The first two are primary disorders caused by reduction in GFR and functional renal mass, the rest are mostly consequences of the first two:

1. Hyperphosphatemia
2. Hypovitiminosis D (also contributed to by high phosphorus directly)
3. Hypercalcemia (common only in severe disease, ionized calcium usually normal)
4. Markedly increased phosphorus and calcium product, predisposing to soft tissue mineralization.

5. Increased PTH concentration – secondary renal hyperparathyroidism. This occurs even with mild CRD. This increase is caused by 2 factors:
    a. The rising phosphorus binds calcium and the slight drop in calcium cause a rise in PTH to bring calcium back to normal levels.
    b. Vitamin D is usually an important inhibitor of PTH, when it decreases PTH goes up.

Why do we care about all this?

1. Some people feel that PTH in itself is a uremic toxin in small animals.
2. Soft tissue mineralization likely contributes to the progression of renal disease
3. In extreme cases this syndrome causes severe bone mineral depletion.

Management:

1. Phosphorus must be controlled!!
    a. Diets low in phosphorus – All kidney diets
    b. Phosphate binders, given MIXED in to the food
2. IF phosphorus is within normal limits and calcium is within or below (rare in chronic disease) normal limits one may consider vitamin D (Calcitriol) supplementation to lower PTH concentrations

So to summarize this portion of the notes –

1. Perform a thorough diagnostic work-up
2. Assess with problems are present from the above list in your patients
3. Treat each problem to try and achieve resolution or improvement.

Problems not easily measurable or addressable (except decreasing azotemia)

1. Uremic encephalopathy
2. Effects of uremia on platelet function
3. Effects of uremia on white cell function and the immune system

Proteinuria

Proteinuria has been found to be a negative prognostic indicator for survival in dogs and cats with CRD! It appears that all efforts to decrease proteinuria are warranted.

Measuring Urine Protein

As our understanding of proteinuria and our ability to detect small amounts of protein increases so does our knowledge of its importance. Cats and dogs with renal disease can have proteinuria which is likely detrimental to their kidneys even when the primary insult is tubular and not glomerular. There is recent evidence showing that even a protein creatinine ratio of 0.4 (normal for most laboratories) is a negative prognostic indicator for

cats with renal disease. There are problems with relying on a dipstick though to evaluate protein:

1. The amount the dipstick picks up depends on urine concentration therefore it has to be normalized for concentration or urine creatinine (P/C ratio).
2. There are many false negatives and false positives. A more accurate method employed in many labs (not on the dip stick) is the SSA (sulfasalycilic acid) technique.
3. Minute concentrations of albumin (microalbuminuria) measurement require a specific test. The value and clinical use of this test is questionable because of a high percentage of positive dogs and cats that are considered to be clinically normal.

A P/C over 0.5 (canine) and 0.4 (feline) is considered abnormal and should be investigated and possibly treated including:

1. Search for underlying cause (infectious, neoplastic, immune mediated)
2. Treat with:
    a. Low protein diet
    b. ACE inhibitor
    c. Possibly omega 3 fatty acid supplementation
3. If no improvement over time consider renal biopsy.

Renal diet (k/d) has recently been shown to slow progression and decrease uremic episodes in cats with chronic kidney disease. The diet was testes in comparison to a maintenance diet and each component was not tested separately. Phosphate restriction, omega3 fatty acid supplementation, potassium and bicarbonate supplementation and sodium restriction among others are likely reasons for the success of the renal diet.

Additional measures that MAY help slow the progression of CRD in dogs and cats

Little is known in this fascinating area about naturally occurring CRD. Most of the data is extrapolated from canine and feline experimental models or even from human studies or rodent models.

Current thoughts:

1. ACE inhibitors (besides proteinuria)
    a. Decreases glomerular hypertension
    b. Inhibits growth factors to hopefully help negate deleterious nephron hypertrophy
2. Ω3 fatty acid supplementation
    a. Decreases inflammation apparent in the progression of renal disease
    b. Decreases glomerular hypertension
    c. Decreases negative effects of uremia on platelet function
3. Specific growth hormone and cytokine inhibitors – The wave of the future?

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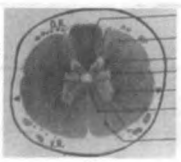
What's new in pain control and anesthesia for cats

Andrea Looney, DVM, DACVA, CCRP

Pain management and rehabilitation service, CUHA

How is pain defined?

- An unpleasant sensory or emotional experience
- Associated with actual, perceived, or potential tissue damage
- A physiologic and psychological experience
- A very subjective experience
  - Formed by a neural matrix
  - Evolving=Subject to change
    - immediate
    - long term



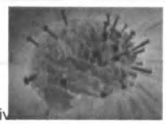
"New age" definitions

- **Acute pain**
  - Known causative factor
  - Treatment usually satisfactory
  - Examples:
    - Myocardial pain
    - Traumatic MS pain
    - Headache

- **Chronic pain**
  - Causative factors?
    - Known
    - Unknown
  - Ongoing duration
  - Difficult to treat
  - Examples:
    - Oncologic pain
    - Osteoarthritis
    - Diabetic pain
    - Nerve injury pain

What do these new definitions mean to us clinically?

- There's no straight line from tissue alteration to pain response
- A tiny insult can result in exponential damage
  - Autonomic changes
  - Supportive and neural Tissue changes
    - Structural
    - functional



- What decreases these problems?
  - Early aggressive treatment of pain
  - Preventative treatment of pain=preemptiv
  - Multimodal treatment of pain

Why bother treating pain?

- Immediate effects
  - Increased sympathetic tone
  - Hypercoagulability
  - Increased myocardial work
  - Diminished pulmonary function
  - Translocation and altered GI blood flow
- Long term effects
  - Thromboembolic disease
  - Chronic pain
  - Myocardial disease
  - Immune supression
  - Poor wound healing

Lascelles B, 1999. A survey of current british veterinary attitudes to perioperative analgesia for cats and small mammals

- Veterinarians asked their opinion on an exploratory laparotomy in dogs and cats
  - Most considered this procedure painful in both species
  - Only 56% cats received analgesics
    - Compared to 71% of dogs

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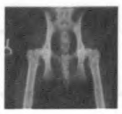
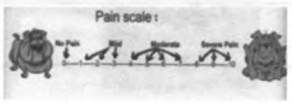
Why are cats undertreated?

- Difficulty in recognizing signs of pain in this species
- Limited number of analgesics with label indications for cats
- Perceived frailty of the species
- Fear of adverse side effects
- Lack of published information



Assessment of pain is important



Normal cat spontaneous behaviors

- Stretching
- Back arching
- Climbing
- Grooming
- Laying lateral or curled up
- Yawning
- Wide eyed and slow blinking
- Tail movements
- Play or trouble making!

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Pain assessment

- Acute vs. chronic
- Physiologic and behavioral signs
- Knowing the norm for the animal
- Experience the animal outside the acute environment (in the case of chronic pain)

Common clues to the presence of pain in cats

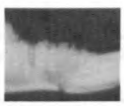
- Decreased movement
- Scratching or overgrooming affected areas
- Poor coat quality
- Lack of grooming and hair matting
- Decreased appetite and water consumption
- Hiding and isolation
- Escape attempts
- Slow cautious movement

Common clues to the presence of pain in cats

- Facial expression
  - Half mast pinna position
  - Squinting eyes
- Failure to urinate and defecate
- Toaster position
- Over sleeping
- Quietness or voice changes
- Drooling or difficulty prehending or chewing

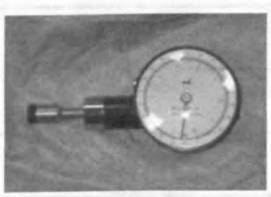
Systematic approach to determining pain in cats

- Detailed history
  - Typical day, current medications, recent life changes, vaccinal history
- Observation from a distance
  - Cat on the ground, dim lights
- Assess response to owner's approach
- Stranger interaction
  - Your Non invasive interaction
- Physical exam
  - Area of interest last



Other more objective means of identifying pain

Fisher algometer



The bottom line in feline pain determination

- Acute pain
  - Respiratory rate
  - Respiratory character
  - Heart rate
  - Interactive behavior score near and far from area of interest
  - Adminster an analgesic and watch response
- Chronic pain
  - Appetite?
  - Movements?
  - Interaction with owners normal?
  - Urinary and bowel habits?
  - Administer an analgesic and watch response

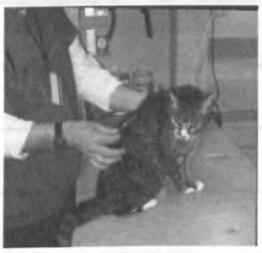
A great way to determine the presence or absence of pain

- Document pre-existing state
- Administer an analgesic
- Note and document response
  - Spontaneous behaviors
  - Induced or reactive (interactive) behaviors
  - Physiologic parameters
    - Heart rate and rhythm
    - Respiratory rate and character

What to administer?

- Hydro or Oxymorphone 0.05-0.1mg/kg SQ
- Buprenorphine 0.01-0.02mg/kg SQ or lingual
- Morphine 0.1-0.2mg/kg IM
- Meloxicam 0.1-0.2mg/kg
- Dexmedetomidine 5-10mcg/kg lingual, SQ, or IM

Other factors which have great impact on pain control for cats



- Hydration and volume status
- Blood presure control
- Stress reduction
- Nutrition
- Electrolytes
- Glucose
- Movement
- Urinary and bowel habits
- Sleep

Drugs and therapies used to treat feline pain

Slow Acting Disease Modifying Agents

Feline physiotherapy





Feline physiotherapy






OPIOIDS






Opioid usage

For typical acute analgesia

- Buprenorphine 0.02mg/kg lingual, SQ, IM, IV q. 12 hr
  - Alternate with nsaid and/or dexmedetomidine
- Morphine 0.1-0.2mg/kg IM or SQ q. 12 hr
  - Alternate with nsaid and/or dexmedetomidine

For typical premed, pre anesth

- Buprenorphine 0.02mg/kg IM or IV
- Hydromorphone 0.05mg/kg IM, IV, SQ
- Morphine 0.1-0.3mg/kg IM
  - All with dexmedetomidine and/or nsaid

Opioid usage

- For typical chronic analgesia:
  - Buprenorphine 0.01-0.02mg/kg buccal mucosa sid to bid
  - Oxycodone 5mg/5ml syrup: 0.05-0.1mg/kg orally sid to bid
  - Methadone 0.05-0.1mg/kg sq sid to bid
  - Oxymorphone 0.05-0.1mg/kg sq sid
  - Fentanyl patch 12.5 and 25mcg/hr q. week

ALPHA TWO AGENTS

Alpha two agonist usage

For typical acute analgesia

- Dexmedetomidine 3-10mcg/kg q. 12 hr buccally, SQ
- Medetomidine 7-15mcg/kg q. 12 hr buccally, SQ
  - either alternate with opioid of choice +/-nsaid sid

For typical premed, preanesthesia

- Dexmedetomidine 10-20mcg/kg
- Medetomidine 20-30mcg/kg
  - Either with opioid of choice +/- nsaid

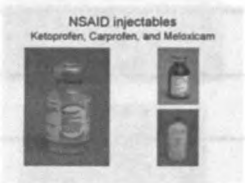
Alpha agonist usage

- For typical chronic analgesia
  - Dexmedetomidine 3-10mcg/kg buccally sid to bid
  - Given alternating with
    - opioid
    - nonsteroidal of choice

NSAIDS

My favorite acute NSAID options

- Meloxicam 0.1mg/kg SQ, IV, PO q. 2 days for 2-3 doses
- Carprofen 1mg/kg SQ, PO q. 2 days for 2-3 doses
- Flunixin 0.25mg/kg SQ q. 2 days for 2-3 doses
- Ketoprofen 1mg/kg SQ q. 2 days for 2-3 doses



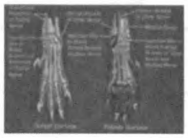
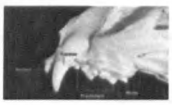
My favorite chronic NSAID options

- Meloxicam 0.05-0.1mg/kg PO q. 2-4 days
- Aspirin 5-10mg/kg PO q. 2-4 days
- Ketoprofen 0.2-1m/kg PO q. 3-5 days
- Carprofen 1mg/kg PO q. 2-4 days

Adequan for cats

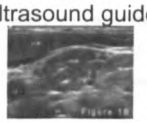
- Indications
  - Osteoarthritis
  - Tendonitis
  - Polymyositis/myopathy
  - Chronic toxoplasmosis
  - Chronic cystitis
- Doses
  - 4mg/kg lean bw sq every 4-7 days for one month

LOCOREGIONAL BLOCKS


Locoregional blockade can be performed blindly or guided

- Blind blockade
  - Pick nerve or plexus
  - Dilute local anesthetics
  - Deliver
    - with eyes open
- Ultrasound guided

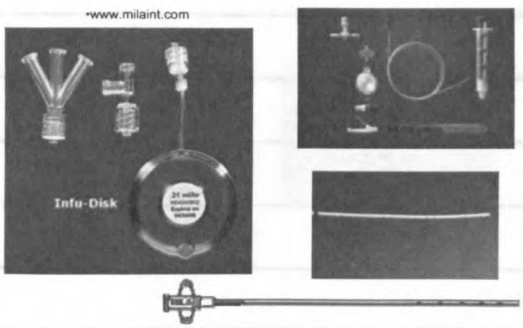


- Electrostimulation guided

Common blocks, common doses

- Bupivicaine 0.2mg/kg with Lidocaine 1mg/kg and saline to dilute if needed
- Saline:
  - Reduces toxicity potential
  - Reduces sting
  - Spreads the love

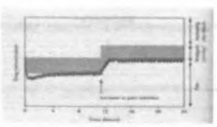

Catheters extend life of local blockades for acute pain



Different additives extend the life of local blockades for chronic pain=neurolytic blocks

- Sarapin
- Alcohol
- Ammonium chloride
- Triamcinalone
- Methylprednisone

Continuous rate infusions

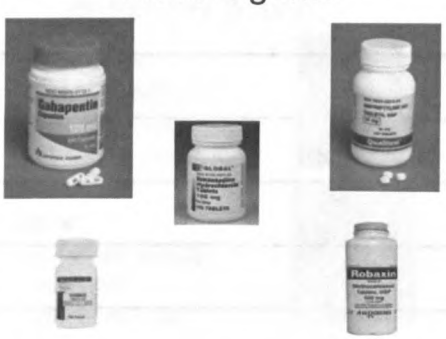

My favorite intraop infusion rates

- Fentanyl-expect MAC reduction
  - 0.3-0.5mcg/kg/min
- Remifentanil-expect MAC reduction
  - 0.3-0.7mcg/kg/min
- Ketamine
  - 3 mcg/kg/min
- Dexmedetomidine-expect MAC reduction
  - 0.5 mcg/kg/HOUR

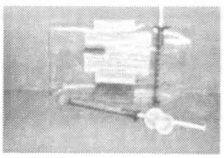
My favorite post op infusion rates

- Fentanyl
  - 0.1mcg/kg/min
- Lidocaine
  - 5mcg/kg/min
- Ketamine
  - 1-3mcg/kg/min
- Dexmedetomidine
  - 0.5-2mcg/kg/HOUR

Novel agents



Transdermal gels



Going into feline practice? Have these by your side