Thank you to our sponsors:

Intervet Schering-Plough Animal Health

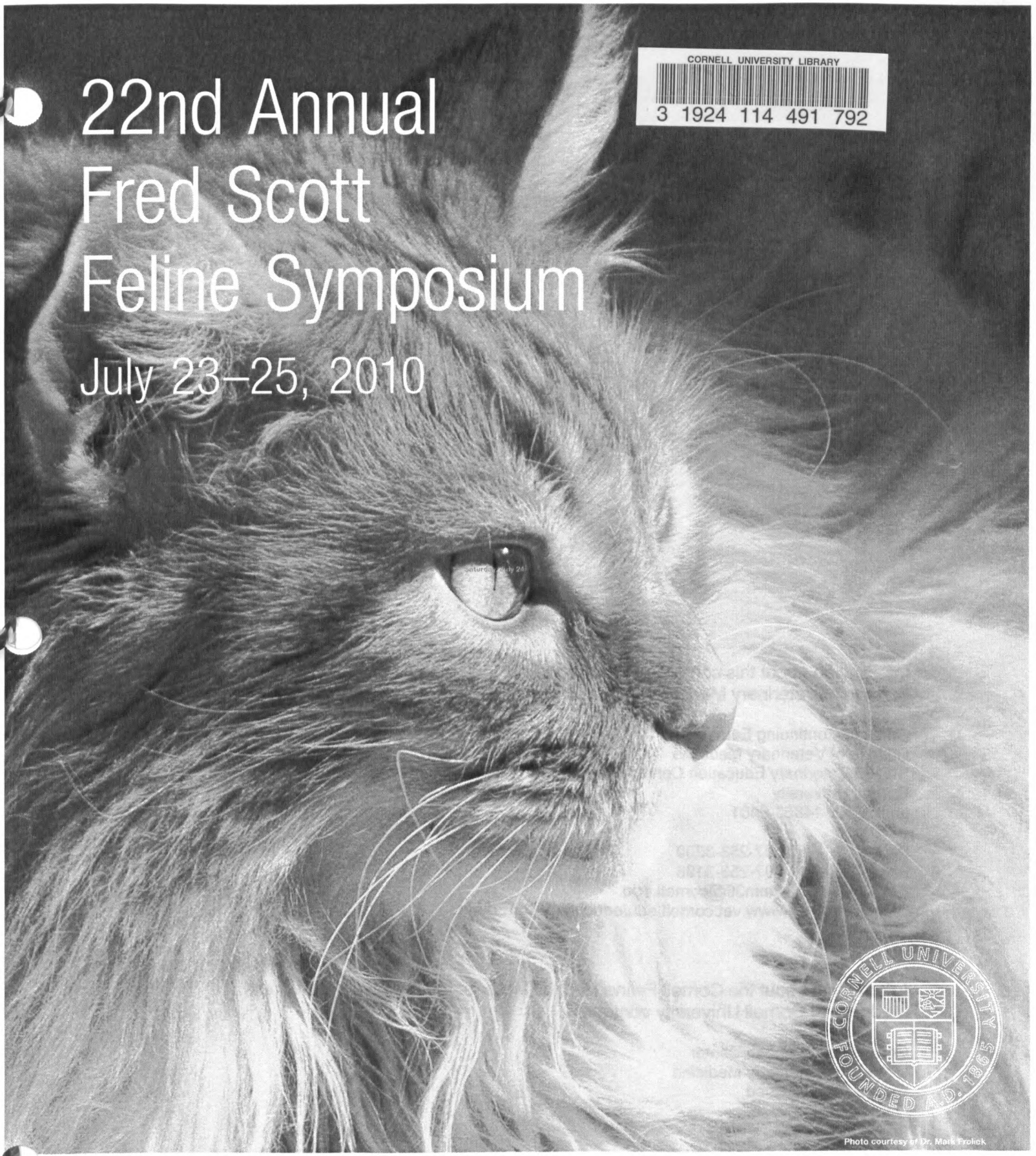
MERIAL

Fallon Wellness Pharmacy

ProLabs

Nate's PHARMACY AND SURGICAL SUPPLIES

Paris Hill Cat Hospital



22nd Annual Fred Scott Feline Symposium

July 23–25, 2010

Photo courtesy of Dr. Mark Frolick

Thank you to our sponsors:

Intervet Schering-Plough Animal Health

MERIAL

Fallon Wellness Pharmacy

ProLabs

Nate's PHARMACY AND SURGICAL SUPPLIES

Park Hill Cat Hospital

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

Office of Continuing Education
College of Veterinary Medicine
S2 169 Veterinary Education Center, Box 52
Cornell University
Ithaca, NY 14853-6401

Phone	607-253-3200
Fax	607-253-3198
Email	amm36@cornell.edu
Website	www.vet.cornell.edu/education/ConEd.htm

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

Cornell Feline Health Center
College of Veterinary Medicine
Hungerford Hill Road
Cornell University
Ithaca, NY 14853

Phone	607-253-3414
Fax	607-253-3419
Website	www.vet.cornell.edu/fhc/

General Information

General Information and Logistics

22nd Annual Fred Scott Feline Symposium
July 23-25, 2010

Course Overview

This year's 22nd 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.

RACE Accreditation and Continuing Education Credit

This program was reviewed and approved by the AAVSB RACE program for 17 hours of continuing education in jurisdictions which recognize AAVSB RACE approval. Please contact the AAVSB RACE program if you have any comments/concerns regarding this program's validity or relevancy to the veterinary profession.

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:

Office of Continuing Education
College of Veterinary Medicine
S2 169, VEC, Box 52
Cornell University
Ithaca, NY 14853-6401

Phone	607-253-3200
Fax	607-253-3198
Email	CVMERM@cornell.edu
Website	www.vet.cornell.edu/education/ConEd.htm

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.

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. Dennis Chew on Friday in S1 007 Schurman Hall. If you signed up to have lunch with Dr. Chew on Friday 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

There were no pages

in this section

Corporate Sponsors and Exhibitors

22nd Annual Fred Scott Feline Symposium
July 23-25, 2010

Corporate Sponsors

Fallon Wellness Pharmacy

www.fallonpharmacy.com/

Peace of mind is a precious commodity, and that's what you can expect when you rely on Fallon Wellness Pharmacy (one of the very few compounding pharmacies nationally that have earned Professional Compounding Accreditation Board (PCAB) accreditation. We strive to improve patient outcomes and experiences through compounding and wellness consultations.

Intervet/Schering - Plough Animal Health

www.intervet.com

Intervet/Schering-Plough Animal Health is a global leader in the research, development, manufacturing and sale of veterinary medicines. We offer one of the industry's broadest, most innovative portfolios, spanning products for the prevention, treatment and control of disease in all major farm and companion animal species.

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.

MERIAL

www.merial.com

Merial is a world-leading animal health company. We are a forward-looking company with a proven track record, producing pharmaceutical products and vaccines for livestock, pets and wildlife. We are on the cutting edge of product development and innovation, providing millions of doses worldwide annually to keep livestock and pets healthy.

Nate's Pharmacy

www.natespharmacy.com/

Nate's Pharmacy is dedicated to keeping the following promises to our patients and customers:

- We always give our patients and their caregivers an honest answer about their health care choices. Those answers will not be based on profit, they will be based on what is best.
- We apply our knowledge, experience, and skills to the best of our ability to assure maximal drug therapy outcome.
- We continue to learn and seek out the best medical options available for our patients and participate and advocate changes in the profession of pharmacy that improve patient care.
- We maintain the highest principles of moral, ethical and legal conduct. We focus on wellness, not sickness.

ProLabs

www.prolabsanimalhealth.com/

ProLabs Animal Health has been supplying veterinary practitioners with proven, popularly priced products for over 18 years. Today, with a rapidly growing product line, ProLabs offers more than 20 professional animal health care products for treatment of the disease problems most often encountered by companion animal veterinarians.

ProLabs was developed to be a reliable source of necessary veterinary supplies in today's changing markets. Consistent supply of quality products is making ProLabs one of the most rapidly growing lines of ethical products in the field.

Annual Picnic

The annual picnic will be held at the Six Mile Creek Vineyard and includes a wine tour for those who are interested. *Tuckers* will cater the picnic and the band will be *Aceto Lieberman Quartet.*

Exhibitors

Cornell Feline Health Center
DVM Solutions
Elsevier Medical Publishers
Fallon Wellness Pharmacy
Hill's Pet Nutrition, Inc.
IDEXX Laboratories
Intervet/Schering - Plough Animal Health
MERIAL
Nate's Specialty Pharmacy
Prolabs
RX Vitamins for Pets
Wiley - Blackwell

Faculty

Faculty

22nd Annual Fred Scott Feline Symposium
July 23-25, 2010

Dennis J. Chew, DVM , DACVIM, The Ohio State University

Dr. Dennis Chew is a 1972 graduate of the College of Veterinary Medicine at Michigan State University. He did a 1-year internship at South Weymouth Veterinary Associates (Massachusetts) and a 2-year residency in internal medicine and nephrology at the Animal Medical Center (NY, NY). He became a diplomate of the American College of Veterinary Internal Medicine (Internal Medicine specialty) in 1977. Dr. Chew has been an attending veterinarian at The Ohio State University College of Veterinary Medicine Teaching Hospital since 1975 and has been a Full Professor in the Department of Clinical Sciences since 1989. Most of his work in clinics, research, and publications involves urology/nephrology in small animals. He has special interest in disorders of calcium metabolism (idiopathic hypercalcemia in cats), treatment of renal secondary hyperparathyroidism (especially phosphorus, calcium, calcitriol and PTH dynamics), acute renal failure, disorders of the feline lower urinary tract (idiopathic/interstitial cystitis and urolithiasis). He has pioneered many of the diagnostic procedures for urinary endoscopy in dogs and cats.

Daniel J. Fletcher, PhD, DVM, DACVECC, Cornell University

Dr. Fletcher obtained a BS in Electrical Engineering at Drexel University and a PhD in Bioengineering from UC Berekely/UC San Francisco before completing his veterinary degree at UC Davis. He did his rotating internship and residency in Emergency and Critical Care at Penn and has been on the faculty at Cornell since 2006. Dr. Fletcher is currently an assistant professor of Emergency and Critical Care; his research interests include neurotrauma, cardiac output monitoring technologies, and the use of simulation in veterinary medical training.

Bruce Kornreich, DVM, PhD, DACVIM (Cardiology), Cornell University

Bruce Kornreich received his DVM from Cornell University in 1992. Following one year of small animal private practice experience in central New Jersey, he returned to Cornell as the first Cardiology resident in 1993. After one year as a postdoctoral associate in the Department of Pharmacology, he began graduate studies in the Department of Molecular Medicine and received his PhD in Pharmacology from Cornell University in 2005. He is board certified in Cardiology by the American College of Veterinary Internal Medicine and has been a Senior Research Associate in the Department of Clinical Sciences since 2007.

John Ludders, DVM Diplomate ACVA, Cornell University

Dr. John Ludders is a Diplomate of the American College of Veterinary Anesthesiologists and is a past-president of that college. He joined the Section of Anesthesiology at Cornell University in 1989 and currently serves as chief of section. His research has focused on veterinary anesthesia in general and more specifically as it relates to birds. More recently, Dr. Ludders has studied how and why errors are made during anesthesia.

Kathryn Meurs, DVM, PhD, DACVIM, Washington State University

Dr. Meurs is a Professor and the Richard L. Ott Chair of Small Animal Research in the Department of Veterinary Clinical Sciences at Washington State University - College of Veterinary Medicine. She completed her DVM in 1990 at the University of Wisconsin - Madison and completed a small animal internship at North Carolina State University in 1991. She completed a Cardiology residency at Texas A&M University and is board certified from the American College of Veterinary Internal Medicine (Cardiology). Dr. Meurs has a Ph.D. in Genetics from Texas A&M University and her areas of interest include familial aspects of cardiovascular disease, especially cardiomyopathy.

Mark Rishniw, BVSc, MS, PhD, DACVIM (Cardiology & IM), Cornell University

Dr. Mark Rishniw graduated from the University of Melbourne in 1987. After 4 years in general practice in Australia and UK, he completed 2 residencies. Subsequently, he was Board-certified in Internal Medicine and Cardiology. He spent 1 year at Melbourne University on staff, then 3 years at Cornell University as acting section chief of cardiology. In 2009, Dr. Rishniw completed a PhD program in Physiology. He began full-time employment with Veterinary Information Network in 2005, and has been a part-time post-doctoral associate with Dr. Ken Simpson since 2006. Currently, he is a visiting scientist at Cornell and a salaried employee of VIN. He has co-authored 60 peer-reviewed journal articles, is a section contributor to Advances in Small Animal Medicine and Surgery, and a reviewer for multiple scientific journals.

Catherine Rogers, DVM, DACVECC, Cornell University

Dr. Catherine Rogers graduated from Tufts Cummings School of Veterinary Medicine and completed a residency in emergency and critical care at Tufts in 2008. She joined the faculty at Cornell as a lecturer in 2009.

Gretchen Lee Schoeffler, DVM, DACVECC, Cornell University

Dr. Gretchen Schoeffler is a Diplomate of the American College of Veterinary Emergency and Critical Care and is currently the chief of Emergency and Critical Care at the Cornell Companion Animal Hospital. She completed two bachelor's degrees in Biomedical and Veterinary Science respectively, prior to obtaining her Doctor of Veterinary Medicine degree at Texas A&M University. After graduation she went on to complete a small animal rotating internship at the University of Georgia College of Veterinary Medicine. Following her internship, she moved to New England and completed a standard track residency in Veterinary Emergency and Critical Care Medicine at Tufts University. Prior to coming to Cornell, she worked to establish Emergency and Critical Care programs in two private specialty referral practices. Dr. Schoeffler's current interests are both clinical and academic. In addition to establishing and building the rapidly growing Companion Animal Hospital's Emergency and Critical Care Service, she is currently assisting in the development of simulator based teaching methodologies for veterinary professionals and paraprofessionals.

Danny Scott, DVM, DACVD, Cornell University

Dr. Danny Scott is a 1971 graduate from the University of California, Davis, and is currently Professor of Medicine and Co-Chief of the Dermatology Service at Cornell University. Dr. Scott's responsibilities include clinical service, teaching (students, interns, residents), clinical research, diagnostic dermatopathology, consultation service for regional veterinarians, and committee work. Dr. Scott has authored or coauthored over 540 publications (including the standard texts in small animal, equine, and farm animal dermatology), and presented over 375 continuing education programs around the world.

There were no pages

in this section

Chronic Kidney Disease (CKD) in Cats - The Pivotal Role of Phosphorus Control

Dennis J. Chew, DVM Dipl ACVIM
The Ohio State University College of Veterinary Medicine
Columbus, Ohio, USA

Introduction

Chronic kidney disease is diagnosed commonly in cats – from 2 to 3 times as frequently as in dogs and is especially common in geriatric cats. CKD is clinically characterized by the development of variably progressive irreversible intrarenal lesions and loss of renal functions. A variety of interventions (diet and drugs) can slow the progression of the renal disease, improve the quality of life for the patient, and/or extend the quantity of life. Compensatory increases (so called adaptations) in glomerular hemodynamics and glomerular volume may actually be maladaptive in some instances as shown in the figure below.

Figure 1. Concept of increased protein-trafficking as a consequence of intraglomerular hypertension and glomerular hypertrophy that occur in remnant nephrons associated with advanced CKD. Protein in urine is both a marker and a creator or more renal disease as shown in the graphic below.

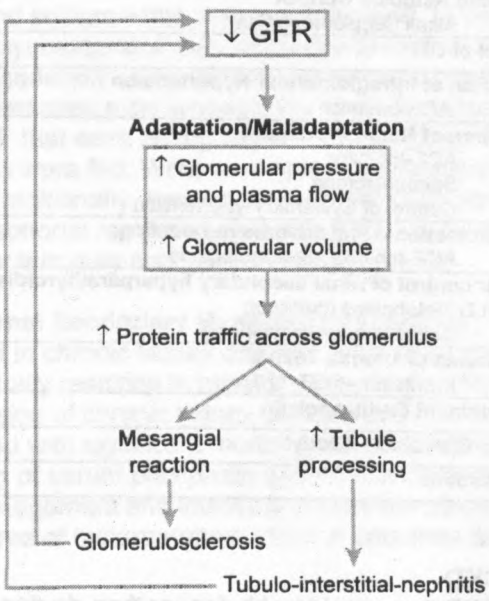


Table 1. The International Renal Interest Society (IRIS) has proposed a staging system for CKD based on the serum creatinine concentration for the stable patient (well hydrated) on at least 2 occasions.

IRIS Stage	Serum creatinine (dog)		Serum creatinine (cat) (mg/dL)	
Stage 1	< 1.4 < 125	mg/dL µMol/L	< 1.6 < 140	mg/dL µMol/L
Stage 2	1.4-2.0 125-180	mg/dL µMol/L	1.6-2.8 140-250	mg/dL µMol/L
Stage 3	2.1-5.0 181-440	mg/dL µMol/L	2.9-5.0 250-440	mg/dL µMol/L
Stage 4	> 5.0 > 440	mg/dL µMol/L	> 5.0 > 440	mg/dL µMol/L

Staging of CKD should allow more rational treatment strategies to be employed based on stage of disease. The goal of treatment is to slow or prevent progression of disease. Most studies of

treatment for CKD have been reported for dogs and cats with overt azotemia and clinical signs (i.e., IRIS stages 3 and 4). More cats than dogs with CKD are identified in IRIS stage 1 and 2. Serum creatinine at the time of diagnosis is quite variable. Initial serum creatinine (IRIS Stage) predicts survival in some but not other studies of cats with CKD. Many cats live for a long time (years) compared to dogs with CKD.

General goals for management of CRF are to reduce uremic signs, provide optimal nutrition, retard the progression of CRF, and provide endocrine replacement when possible.

Table 2. Treatment Considerations for CKD

Total Body Phosphate Burden Control: Dietary Modification Intestinal Phosphate Binders
H2-Receptor Blockers or Proton Pump Inhibitors
Systemic Hypertension Control: Calcium Channel Blocker (Amlodopine) ACE-Inhibitor (Enalapril/Benazepril)
Hypokalemia/Kaliopenia Control Potassium Supplementation
Metabolic Acidosis Control Alkali Supplementation
Control of UTI
Reduction of Intraglomerular Hypertension ACE-Inhibitor
Reduction of Renal Proteinuria ACE-Inhibitor Spironolactone Control of Systemic Hypertension
Renoprotection – anti adverse remodeling: ACE-Inhibitor, Spironolactone
Further control of renal secondary hyperparathyroidism Activated Vitamin D Metabolites (calcitriol) Calcimimetics (cinacalcet)
Adsorbents of Uremia Toxins Kremezin – AST-120
Recombinant Erythropoietin
Enteric Dialysis® - Azodyl
Ant-Fibrotics

Survival of Cats with CKD

Most cats with CKD live considerably longer than do dogs with CKD of similar severity based on IRIS staging. Renal survival time is usually defined as the time from the start of treatment to the time when parenteral fluid therapy is necessary, or when euthanasia or death occurs as a consequence of the advancing CKD. Increased serum creatinine, increased UPC, and increased WBC count were independent variables that were associated with shorter renal survival times in a study of 95 cats with CKD (58 were censored as they were still alive or owners failed to follow protocol; King JVIM 2007)). Entry into the study required a serum creatinine of 2.0 and higher along with a urinary specific gravity of 1.025 or lower. The median survival for all 95 cats was 319 days and 644 days in the censored cats. Increased risk not to survive was seen in cats at all levels of proteinuria > 0.2. Increased serum phosphate, urea nitrogen concentration, and lower hemoglobin or hematocrit concentrations were also associated with a shorter renal survival times, but are considered dependent variables since they correlated with serum creatinine at base line. Cats with 4.7 to 6.8 mg/dl serum phosphorus were at increased risk for shorter renal survival despite the fact that these values were still within the normal reference range. Cats with greater than 6.8 mg/dl serum phosphorus were at much greater risk for shorter renal survival. Cats with serum phosphorus of 2.8 to 4.7 mg/dl had the longest renal survivals (many censored since were still alive).

In another study, CKD (Boyd JVIM 2008) was followed in 211 cats with a serum creatinine greater than 2.3 mg/dl and urinary specific gravity less than 1.035 in most cats. IRIS

staging based on initial serum creatinine predicted survival. Median survival in IRIS stage 2b (2.3 to 2.8 mg/dl creatinine was 1,151 days; stage 3 was 778 days; stage 4 was 103 days. Median survival for all 211 cats was 771 days. At the time of diagnosis, 37% cats were in stage 2b, 33% were in stage 3, and 30% were in stage 4. Thirty % of the cats diagnosed in stage 4 were later classified to a lower stage after fluid therapy corrected volume deficits. Median survival was 401 days in 142 cats identified with progressive weight loss , 273 days in 142 cats starting SQ fluids, 123 days in 145 cats with onset of a serum creatinine > 4.0 mg/dl, 44 days with onset of creatinine greater than 5.0 mg/dl in 98 cats, 83 days in 81 cats with >25% weight loss, 100 days in 121 cats with PCV < 25%, and 25 days in 42 cats with the start of specific treatment for anemia. IRIS stage alone was predictive for survival but individual serum creatinine values did NOT predict survival. The only parameter in this study that did predict survival was serum phosphorus concentration – unfortunately details of the phosphorus levels and their effect on survival were not provided.

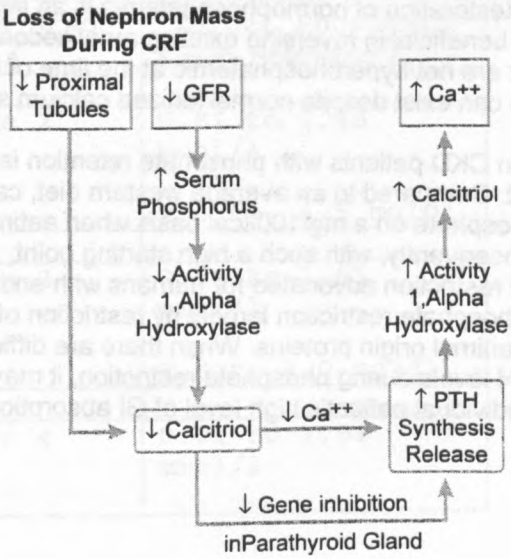
Dietary Intervention

Several evidence based medicine studies of clinical cats with chronic renal failure have emerged showing salutary effects of dietary modification to increase survival time and to decrease the number of uremic crises. "Renal-friendly" veterinary diets are generally restricted in protein, phosphorus, calcium, and sodium while supplemented with carbohydrates, sources of alkali (potassium citrate), and polyunsaturated fatty acids in a favorable ratio of omega-6:omega-3 fatty acids. Canned foods are generally more restricted in phosphorus than their dry counterparts and substantial differences exist amongst the available products. The survival time was 16 months for cats with CRF that were eating any of 7 renal kidney diets compared to 7 months when maintenance foods were fed. What exactly is in these renal diets that confers the extension in life is not known. Traditionally, benefits of such diets are attributed to the well-known protective effects of dietary phosphorus restriction (with or without lowering of PTH), but diets with higher eicosapentaenoic acid content may also confer protection.

Phosphorus Retention and Renal Secondary Hyperparathyroidism

Phosphorous is retained in chronic kidney disease, promoting renal secondary hyperparathyroidism, and eventually resulting in hyperphosphatemia. Phosphate retention is a major contributor to the progression of chronic kidney disease and it is well known that hyperphosphatemia is associated with significant mortality risk in humans with end-stage renal disease. With careful monitoring of serum phosphate and PTH and implementation of phosphate-restricted dietary management and intestinal phosphate binders, progression of chronic kidney disease and degree of hyperparathyroidism in cats may be reduced.

Figure 2- Development of Renal Secondary Hyperparathyroidism - calcitriol trade-off hypothesis



Serum phosphorous concentration depends on the dietary phosphorous intake, the degree of gastrointestinal absorption across the duodenum and jejunum, translocation into intracellular sites, and excretion of phosphorous into the urine. The kidney plays a crucial role in regulating serum phosphorous concentrations. Serum phosphate levels are maintained within a narrow range in health. Young growing animals often have higher levels of serum phosphorous than adults. The normal serum phosphorous range of many laboratories includes that of adults and growing animals which may make it difficult to detect early rises in serum phosphorous above normal. The typical normal range for phosphorous in the cat is 2.5-6 mg/dL (0.81 to 1.94 mmol/L). Phosphate retention and hyperphosphatemia are primarily due to impaired renal phosphate excretion. In the early stages of chronic kidney disease increased levels of parathyroid hormone (PTH) keep serum phosphorous within the normal range by increasing phosphate excretion into urine. This allows for normalization of serum phosphorous at the expense of hyperparathyroidism.

Pathophysiological Consequences of Hyperphosphatemia

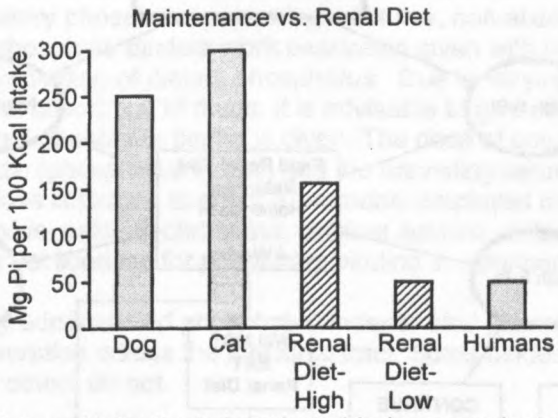
Deleterious effects of phosphate accumulation in cats are most often recognized to be a direct consequence of phosphate from calcium phosphate precipitates into the tissues (increased calcium x phosphate product). Indirect effects that increase PTH and decrease ionized calcium may also be important. It has been known since the early 1980s that dietary phosphorous restriction provided dramatic benefits to the histologic renal architecture of cats with the remnant model of chronic renal failure. Serum phosphorous and PTH concentrations were considerably increased in cats fed the normal phosphate diet compared to those fed the restricted phosphate diet. Hyperphosphatemia and renal secondary hyperparathyroidism are common in cats with IRIS stage 3 and 4 chronic kidney disease and can be documented in some with IRIS stage 2. Interestingly, thirteen percent of cats in this study had increased PTH despite normal concentrations of both ionized calcium and serum phosphorous.

Treatment of Hyperphosphatemia

Conventional wisdom and evidence dictates the importance of correcting hyperphosphatemia of CKD. Early phosphorus restriction in CRF has been shown in dogs and cats to blunt or reverse renal secondary hyperparathyroidism. In a study of cats with naturally-occurring CRF, renal secondary hyperparathyroidism was successfully managed by dietary restriction of phosphorus; one-third of the cats also required treatment with phosphorus binders. Survival times in CKD cats eating the renal diet was over twice that of those eating maintenance diets – this effect was attributed to phosphorus control and control of PTH. Renal diets may provide sufficient dietary phosphate restriction during early stages of CKD but often dietary phosphate binders are needed. Diet and binders should be prescribed to effect of serum phosphorus and PTH levels. Normal serum phosphorus concentrations are desirable but do not guarantee that PTH is normal. Restoration of normophosphatemia is an initial and main goal but phosphorous restriction may be beneficial in reversing existing renal secondary hyperparathyroidism in cats that are not hyperphosphatemic at the time of initial evaluation. Secondary hyperparathyroidism can exist despite normal ionized calcium and serum phosphorous status.

Phosphorus restriction in CKD patients with phosphate retention is initiated by feeding a low phosphorus, low protein diet. Compared to an average western diet, cats consume six times, and dogs five times as much phosphate on a mg/100kcal basis when eating grocery store pet foods (C. Buffington 2006). Consequently, with such a high starting point, it is difficult to achieve the degree of dietary phosphate restriction advocated for humans with end-stage renal failure. Veterinary renal diets achieve phosphate restriction largely by restriction of dietary proteins that contain phosphorus, especially animal origin proteins. When there are difficulties in achieving the target serum phosphorus or PTH levels during phosphate restriction, it may be due to too much dietary phosphorus intake, an individual patient's high level of GI absorption, or the formulation of the phosphate in the diet.

Figure 3. Dietary phosphorus intake between dogs and cats eating commercial or renal therapeutic foods compared to average western diet of humans. Note that dogs and cats consume 5 and 6 times as much phosphorus as the average human which makes it difficult to achieve adequate dietary phosphorus restricion (Developed by Nutritional Support Services The Ohio State University CVM, Dr. Tony Buffington 2006)



Dietary modification and intestinal phosphate binders are pivotal interventions to provide optimal phosphorous and PTH control. Extremely phosphorous-depleted diets may be unpalatable to cats due to the low levels of protein needed to provide this phosphorous restriction. Diets moderately restricted in phosphorous may provide adequate phosphate control during early stages of chronic kidney disease. As kidney disease progresses diet alone is usually not successful in adequate phosphorous control and phosphorous concentration increases above the normal range or stays in the upper half of the normal range.

Goals of Dietary Phosphorous Control

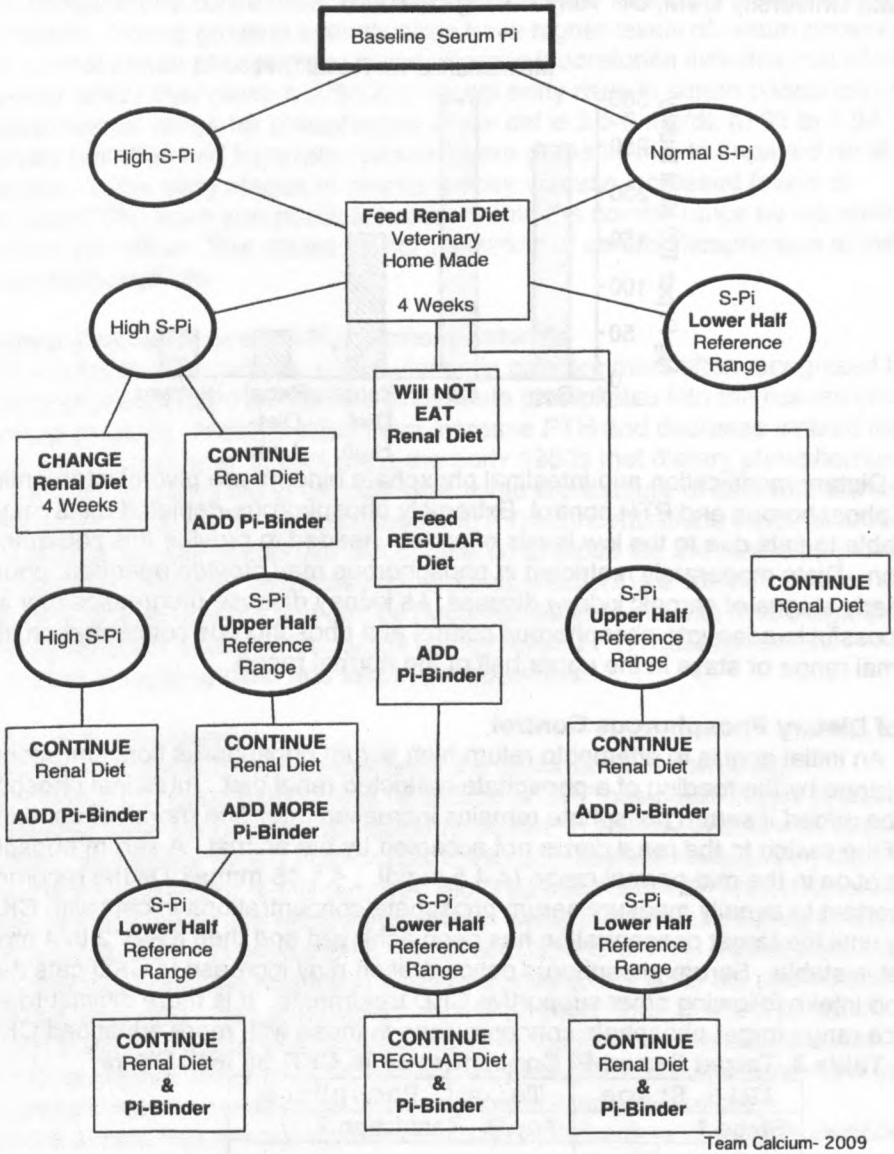
An initial goal is to attempt to return high serum phosphorus concentrations to within the normal range by the feeding of a phosphate-restricted renal diet. Intestinal phosphate binders should be added if serum phosphate remains increased after one month of consuming the renal diet or if the switch to the renal diet is not accepted by the animal. A serum phosphate concentration in the mid-normal range (< 4.5 mg/dL ; < 1.45 mmol/L) is the recommended target. It is important to serially measure serum phosphate concentrations in cats with CKD usually monthly until the target concentration has been achieved and then every 2 to 4 months thereafter if the cat is stable. Serum phosphorus concentration may increase in CKD cats that increase their food intake following other supportive CKD treatments. It is more difficult to achieve mid-reference range target phosphate concentrations in those with more advanced CKD.

Table 3. Target Serum-Pi Concentration in CKD by IRIS Stage

IRIS Stage	Target Phosphate
Stage 1	Any Pi- Restriction ?
Stage 2	0.81 to 1.45 mmol/l 2.5 to 4.5 mg/dl
Stage 3	0.81 to 1.61 mmol/l 2.5 to 5.0 mg/dl
Stage 4	0.81 to 1.94 mmol/l

	2.5 to 6.0 mg/dl

Figure 4. Algorithm for Feeding and Pi-Binders to Gain Control of Phosphorus



A second goal is to restore PTH to normal levels or to prevent it from increasing even if serum phosphorus is in the normal range. Further phosphorus restriction with diet and phosphorus binders can be titrated to the effect of lowering PTH if possible. In some instances, PTH cannot be controlled despite dietary intervention and use of intestinal phosphate binders. Other treatments with calcitriol and calcimimetics may be indicated in these cases. In addition to serial serum phosphate measurements, serial measurement of PTH and ionized calcium from the same time may be considered a gold standard for assessment of sufficient relief of body phosphorus burden and PTH control.

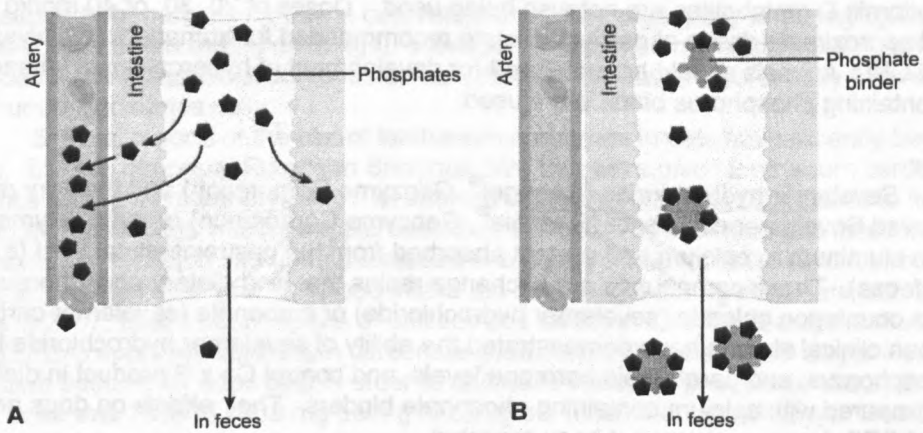
Adverse effects of phosphate restriction potentially can occur. Although hypophosphatemia is one such possible consequence, it is difficult for this to develop in those with initially high concentrations of serum phosphorus and reduced GFR. Hypercalcemia can be encountered when calcium salts are used for intestinal phosphate binding. Constipation and GI effects can occur following use of some of the intestinal phosphate binders. Absorption of

chemicals from the intestinal phosphate binder may occur with resulting accumulation in the tissues in some instances.

Intestinal Phosphate Binders

Phosphorus-binding agents are given orally to trap phosphorus in the gut and increase insoluble phosphate salt excretion into feces. Phosphate binders work because the cation in the binder combines with dietary phosphate, producing insoluble, non-absorbable, phosphate compounds. Intestinal phosphate binders work best when given with meals or within 2 hours of feeding to maximize their binding of dietary phosphorus. Due to varying effects of intestinal phosphate binders to limit absorption of drugs, it is advisable to give other drugs 1 hour before or 3 hours after any intestinal phosphate binder is given. The dose of any phosphate binder should be based on the meal size (phosphorus intake) and the prevailing serum phosphorus level for each CKD patient; the dose is titrated to effect. Commonly employed oral phosphorus binders include aluminum hydroxide, calcium carbonate, calcium acetate, chitosan, and lanthanum carbonate but no drug is yet licensed for phosphate binding in veterinary medicine.

Figure 5. Effect of orally administered phosphate binder to bind phosphate within the intestinal lumen preventing its absorption across the intestinal tract. Some binders undergo absorption across the intestine and others do not.



Aluminum Salts

Aluminum salts are the most widely used phosphate binders in cats. Aluminum based phosphate binding agents (aluminum hydroxide, aluminum carbonate) are highly effective in lowering serum phosphate levels, forming insoluble and nonabsorbable aluminum phosphate precipitates in the intestinal lumen. In humans with CKD, significant aluminum may be retained in the body, especially the bone, leading to osteomalacia, adynamic bone disease, microcytic anemia, and encephalopathy. **THERE IS NO KNOWN SAFE DOSE OF ALUMINUM SALTS FOR HUMANS WITH CKD**. Detrimental effects of aluminum based phosphate binders as described in humans seen in humans have not been systematically evaluated in small animal patients and are rarely clinically appreciated. As cats with CKD can live for years on treatment, concerns for aluminum accumulation deserve more study as to long-term safety.

Despite concerns for toxicity and stringent use guidelines in humans, aluminum salts remain the most commonly prescribed intestinal phosphate binders in veterinary medicine as they are very effective phosphate binders and are inexpensive. Aluminum hydroxide or aluminum carbonate is used at an initial dosage of 30 mg/kg q8h or 45 mg/kg q12h given with food. Constipation is the most common side effect encountered during treatment with aluminum phosphate binders. Lactulose treatment may help to alleviate constipation but may also contribute to dehydration due to extra fluid loss in the stool.

Sucralfate

Sucralfate is an aluminum hyrdoxide complex used mostly for treatment of GI ulcer disease. It has known phosphorous binding properties much like that from aluminum salts in general. Sucralfate has been used empirically by some clinicians as a phosphate binder though there are no reports of its use for such in cats or dogs. Sucralfate is reported to be an effective phosphate binder in humans with CKD though it is more expensive than aluminum hydroxide. Increased aluminum in the circulation and tissues is still of concern despite lower aluminum intake from sucralfate.

Calcium Salts

Calcium-based binders are not as effective as aluminum salts, having a lower affinity for phosphorous, thus effective binding of dietary phosphorous requires large doses of calcium, often enough to induce hypercalcemia in humans.

The most commonly used calcium based phosphate binders are calcium carbonate and calcium acetate. Calcium carbonate can be used in cats at a starting dosage of 30-mg/kg q8h or 45-mg/kg q12h given with food. Calcium carbonate binds phosphorous best in an acidic environment (pH approx. 5) and binding capacity is reduced in the neutral pH range. Many CKD patients receive inhibitors of gastric acid secretion potentially reducing calcium carbonates ability to bind phosphorous. Calcium acetate can bind phosphate over a wide range of pH, has about twice the phosphate binding capacity of calcium carbonate and as such can be used at lower dosage, and has been shown to cause less hypercalcemia than calcium carbonate when activated vitamin D metabolites are not also being used. Doses of 20, 30, or 40 mg/kg given with each meal approximate doses of calcium acetate recommended for humans with dialysis dependent CKD. Animals should be monitored for development of hypercalcemia whenever calcium-containing phosphorus binders are used.

Sevelamer

Sevelamer hydrochloride (Renagel®, Genzyme Corporation) and the very recently FDA approved Sevelamer carbonate (Renvela®, Genzyme Corporation) organic polymers that do not contain aluminum or calcium and are not absorbed from the gastrointestinal tract (excreted entirely in feces). These compounds are exchange resins that bind dietary phosphorous and release the counterion chloride (sevelamer hydrochloride) or carbonate (sevelamer carbonate). Many human clinical studies have demonstrated the ability of sevelamer hydrochloride to lower serum phosphorous, and parathyroid hormone levels, and control Ca x P product in dialysis patients compared with calcium containing phosphate binders. Their effects on dogs and cats with clinical CRF, however, have not been reported.

Sevelamer hydrochloride is hydrophilic and sevelamer carbonate is hygroscopic but both are insoluble in water. Pills should be given intact and will expand in water. Sevelamer may be associated with gastrointestinal side effects including constipation, and at extremely high dosages in dogs (6 to 100 times the recommended dosage in humans) sevelamer may be associated with impaired absorption of folic acid and vitamins K, D, and E.Sevelamer HCl is available in 400 mg and 800 mg tablets and Selelamer carbonate is available in 800 mg tablets. Sevelamer hydrochloride can also be compounded into a suspension. Sevelamer hydrochloride has been used effectively in children with end-stage renal failure. Reported doses of sevelamer hydrochloride used in children are extrapolated from adult humans ranging from initial dose of 100 mg/kg/day to 121 mg/kg/day divided every 8 hours and titrated to a final dose of 130 mg/kg/day to 163 mg/kg/day divided every 8 hours. These doses may be applied to small animal patients with careful monitoring for side effects and serial serum phosphate measurements with titration of the dose as needed.

Chitosan

Epakitin® (Vetoquinol USA, Inc.) is marketed as a complementary feed on the veterinary market. It contains the adsorbent chitosan (8% crab and shrimp shell extract), 10% calcium carbonate, and 82% lactose and is designed to reduce GI phosphorus absorption and to lower urea nitrogen due to effects of reduced protein digestibility. One short-term study of a small number of normal and CKD cats showed a reduction in protein and phosphorus digestibility along with the decreases in BUN and serum phosphorus in cats eating a normal maintenance diet

supplemented with the chitosan and calcium carbonate product.Another longer-term study showed the ability of a chitosan and calcium carbonate intestinal phosphate binder to significantly decrease serum phosphorous and plasma parathyroid hormone levels when added to a maintenance diet for cats with CKD created by 11/12. The results of these two studies suggest that this supplement could be an alternative to prescription of renal veterinary diets thereby allowing some cats to continue on their regular diets while still reducing the risks for progression of CKD associated with total body phosphorus burden. We have, however, observed the development of hypercalcemia in a few CKD cats with the use of this product probably as a consequence of the calcium carbonate.

Lanthanum Salts

Lanthanum carbonate (Fosrenol®, Shire Pharmaceuticals) is another newly developed non-aluminum and non-calcium containing intestinal phosphate binder and is indicated for use in human patients with end-stage renal failure to reduce serum phosphorous. Very little lanthanum is absorbed across GI tract and lanthanum accumulates to a far less degree following absorption compared to aluminum since lanthanum undergoes extensive hepatic excretion whereas aluminum is excreted mostly by the kidneys. Lanthanum appears to have minimal toxicity in humans. Toxicity studies performed in dogs show that lanthanum increases in many tissues (especially GI tract, bone and liver) during treatment. Intact tablets should not be swallowed. Tablets may be crushed to aid in chewing. Initial daily doses of Fosrenol® that may be extrapolated from humans for use in cats range from 12.5 mg/kg/day to 25 mg/kg/day (based upon an average human weight of 60 kgs). However doses of 35 mg/kg/day to 50 mg/kg/day are often needed since commercial cat foods contain more phosphate proportionally than what an average human consumes daily.

Several reports of the use of lanthanum carbonate in cats have recently been published. Studies of normal European Shorthair cats that were given lanthanum carbonate in maintenance food or a veterinary renal diet showed similar results when compared to findings in cats eating the same diets without supplementation. Phosphorus excretion into feces increased while phosphorus excretion into urine decreased in a dose-related manner; serum phosphorus did not differ between dose groups. Food intake did not change during treatment with lanthanum carbonate.In 2007, based upon reports of efficacy and safety in cats, the European Food Safety Authority (EFSA) approved lanthanum carbonate octahydrate (Lantharenol® Bayer HealthCare AG) as a feed additive for adult cats in order to decrease intestinal phosphate absorption. The approved dose was 1500 to 7500 mg per kg of complete feed. Renalzin® (Bayer HealthCare AG) is the proprietary name for the delivery system of Lantharenol® was launched in 2008. In addition to Lantharenol®, Renalzin® also contains kaolin, for uremic toxin binding effects, and vitamin E, for its anti-oxidant effects, but the benefits of these other compounds have not yet been demonstrated. It comes as a liquid with a pump to deliver the appropriate liquid dose to food.

Cats with experimental sub-total nephrectomy (asymptomatic, mildly azotemic, and normophosphatemic following renal mass reduction)were fed wet cat food supplemented with Lantharenol® for two weeks. Food intake was not altered in cats of this study and a dose-dependent decrease in phosphorus availability was demonstrated. Urinary phosphorus excretion was increased unlike that seen with decreased urinary phosphorus excretion in normal cats. This may be due to excretion of phosphate from cellular stores that accumulated during renal failure. In another study of experimental cats, cats with subtotal nephrectomy were fed a standard feline maintenance diet supplemented with Renalzin® (5mg/kg original moist feed) for 6 months. Serum urea, creatinine, and phosphorous values were significantly improved and pH was increased, from starting values, after two months of Renalzin® administration. These parameters, however, tended to deteriorate towards the end of the six month trial period possibly due to a progressive decline in kidney function. Renalzin® was tolerated by all cats and did not affect body weight.

In a dose tolerance study, normal cats were fed an escalating dose of Lantharenol. A dose of 1 g/kg bodyweight was well tolerated by all cats. However at 2 g/kg Lantharenol® repeated vomiting of feed occurred in all cats which resolved 2 days after discontinuation of test item and re-occurred with re-challenge of 2 g/kg Lantharenol®. A dose of Lantharenol® of 1

g/kg bodyweight corresponds to a concentration of 84 g Lantharenol® per kg complete feed. Given the approved feed concentration range of 1.5 to 7.5 g/kg complete feed Lantharenol® has a safety margin of ten.

Twenty-three cats with naturally-occurring CKD (decreased urinary specific gravity, increased BUN and serum creatinine) finished an 8-week study comparing those fed a veterinary renal diet (9 cats) or a maintenance diet supplemented with Renalzin® at 400-600 mg Lantharenol ® per day (14 cats). The Renalzin® treated group showed an improvement in serum phosphorus control, overall clinical status, and behavioral scores for quality of life compared to cats fed the veterinary renal diets. Due to an unintended but relavant group difference at randomization and enrolment into the study – the Renalzin® group comprised a higher proportion of animals with hyperphsophatemia as well as impaired quality of life and overall clinical status – a comparison of the effects in Renalzin® and the renal diet in this study became impossible and requires further testing. Nevertheless, the evidence suggests that Renalzin®, similar to Epakitin ®, may be beneficial in cats on regular maintenance diets.

TABLE 4. Treatment of cats with intestinal phosphate binders: dose rates and approximate costs

Intestinal Phosphate Binder	Dose (Cat)	Approximate Cost	Approximate cost for 4 kg cat/mo.
Aluminum hydroxide (Alternagel® 600 mg/5ml)	30 mg/kg PO q 8 hr; 45 mg/kg PO q 12 hr (give with meal)	$8.50/360 mls* (£0.60) (€0.69)	$1.42-$2.13 (£0.86–1.29) (€0.98–1.47)
Calcium carbonate (Tums® regular strength 500 mg/tablet)	30 mg/kg PO q 8 hr; 45 mg/kg PO q 12 hr (give with meal)	$0.04/tablet* (£0.02) (€0.03)	$1.00 (£0.60) (€0.69)
Sevelamer hydrochloride (Renagel® 400 mg tablets)	33-54 mg/kg PO q 8 hr; 50-80 mg/kg PO q12 hr (give with meal)	$1.40/tablet* (£0.84) (€0.97)	$42.00-$68.00 (£25.37–41.07) (€28.98–46.92)
Epakitin®	1 gm/10lbs twice daily with food	$15/50 gms# (£9.05) (€10.35)	$18.00 (£10.87) (€12.42)
Lanthanum (Fosrenol® 500 mg chewable tablets)	12.5-25 mg/kg/day PO; 6.25-12.5 mg/kg PO q12 hr starting dose (give with meal, do not swallow tablet whole)	$6/tablet* (£3.62) (€4.14)	$45.00-$90.00 (£27.18–54.36) (€31.05–62.10)
Lanthanum (Renalzin®) Not available in US	2 mls applied to cats food once or twice daily	$10/50 mls^ (£6.04) (€6.90)	$12.00-$24.00 (£7.25–14.50) (€8.28–16.56)

* Prices obtained from drugstore.com (accessed April 6, 2009)
\# Price obtained from amazon.com (accessed April 6, 2009)
^ Price obtained from petdrugsonline.co.uk/ (accessed April 6, 2009)
Currency conversions correct as of September 8, 2009 (1$ ≡ £0.604/€0.690)

ACE-Inhibition

Angiotensin-II plays a pathophysiologic role in proteinuria and the progression of renal disease. Angiotensin-converting enzyme (ACE) inhibitors (e.g. enalapril, benazepril) may have protective effects in patients with chronic renal disease due to their ability to block adverse effects of angiotensin II. ACE-inhibition reduces glomerular capillary hydraulic pressure by decreasing postglomerular arteriolar resistance. Proteinuria is decreased secondary to decreased glomerular hydraulic forces and development of glomerulosclerosis is limited when protein trafficking across the glomerulus is decreased. Remnant nephrons in animals with CRF have glomerular hypertension that can benefit from reductions in transglomerular forces. An additional potential benefit from ACE-inhibition is improved control of systemic blood pressure. This beneficial effect must be balanced against their potential to worsen azotemia since glomerular pressure provides the driving force for GFR in the "super-nephron".

Benazepril is licensed for treatment of CRF in cats in many regions of the world (Fortekor®), but not in the USA. Average survival of benazepril treated cats of one study was 501 days vs. 391 days for placebo treated cats but this effect did achieve statistical significance. When a subset of cats in this study with proteinuria (UPC> 1.0) was considered, survival was not significantly improved for those treated with benazepril (401 days in benazepril treated cats vs. 126 days for control cats) but this subgroup only contained 13 cats. Plasma protein concentration was maintained at higher levels in CKD cats treated with benazepril if the initial UPC < 1; better appetite was maintained in those with UPC > or = 1. Benazepril consistently reduces proteinuria in various stages of chronic kidney disease in cats in this and other studies even when the base line level of proteinuria is seemingly trivial. In another study of 61 cats with CKD, benazepril treatment for 180 days appeared to stabilize those in IRIS stage 2 or 3 with less transition to stage 4 compared to treatment with placebo though this effect did not achieve statistical significance (low number of cats and short duration of study). The overall efficacy of treatment rated by the attending veterinarian was statistically higher during benazepril compared to placebo treatments.

General guidelines for use of ACE-inhibitors in CKD include rechecking renal function in 1 week following start of ACE-inhibition to make sure that GFR has not been reduced too much. It is common to see a small increase in serum creatinine at this time (20 to 30% increase over baseline). If creatinine has increased too much, reduce the dose of the ACE-inhibitor. Some dogs and cats are ACE-inhibitor intolerant in that their renal function will be much worse during initial treatments so that treatment must be discontinued. We also recommend to recheck the UPC 1 and 3 months after the start of ACE-inhibition. The goal is to achieve a 50% decrease in UPC in those in which it was initially increased. There does not appear to be much difference between benazepril or enalapril for clinical use in the dog or cat with CKD. Benazeprilat is cleared by both the kidney and liver compared to enalaprilat being cleared only by the kidney.

Hormone replacement: Calcitriol

Calcitriol treatments help to decrease PTH or prevent its increase in those with renal secondary hyperparathyroidism. This occurs mostly by genomic effects to block PTH synthesis in addition to a mild calcemic effect, and antiproliferative effect that prevents parathyroid gland hyperplasia. During treatment of CRF patients with calcitriol, simultaneous monitoring of serum ionized calcium, serum phosphorus and PTH concentrations is the ideal way to document successful and safe control of renal secondary hyperparathyroidism.

Calcitriol should not be administered until hyperphosphatemia has been controlled. If the Ca X P solubility product exceeds 60-70, calcitriol should be avoided because of the risk of soft-tissue mineralization. The beneficial effects of calcitriol are also lessened within the parathyroid gland when ionized calcium remains low. Phosphorus restriction relieves phosphate-mediated inhibition of the renal 1α-hydroxylase system, resulting in enhanced endogenous synthesis of calcitriol and subsequent inhibition of PTH synthesis. The effectiveness of calcitriol in control of hyperparathyroidism has been noted to increase in patients in whom serum phosphate was lowered.

Supplementation with calcitriol in CRF was initially designed as a daily therapy for life in veterinary patients as long as serum phosphorus remains within the normal range and serum calcium does not become increased. An extremely low dosage of calcitriol (2 to 3 ng/kg/day) has been used in dogs and cats with stable CRF to reverse renal secondary hyperparathyroidism. Serum PTH concentrations decrease during calcitriol administration over a period of weeks to months. Calcitriol is manufactured in capsule (250 or 500 ng) and liquid (1000 ng/mL) forms. Reformulation by a compounding pharmacy may be necessary to provide accurate dosing. In a recent study, dogs with CRF treated with calcitriol survived for a median of 365 days compared to 250 days in dogs treated with placebo. Similar studies were done in cats by the same investigators who concluded that there is no advantage to calcitriol treatments in cats with CRF but the study followed cats for just one year. In order to show a difference in treatment effect if one exists, studies in cats with CRF must be conducted for at least 2 and possibly 3 years due to the inherently slow nature of the progression of chronic renal disease in this species.

Intermittent rather than daily dosing treatment protocols are likely to become the standard of care since less hypercalcemia occurs during this protocol. The equivalent dose given at 2.5

ng/kg daily is given instead every 3.5 days. This works out to a dose of 9 ng/kg (8.75 ng/kg rounded to 9 ng/kd). It is important to give the dose every 3.5 days, rather than on day 1 & 4. For example if a dose is given Tuesday PM the next dose should be given Saturday AM. This is the longest time in between dosing that will still suppress the parathyroid gland. This method of dosing is especially attractive for cat owners since medication will only be given twice weekly.

Hormone replacement: erythropoietin

Recombinant human erythropoietin (rhEPO) has been used to successfully correct nonregenerative anemia in CKD cats. Treated animals demonstrate resolution of anemia, weight gain, improved appetite, improved haircoat, increased alertness, and increased activity. Therapy may be started in symptomatic cats with PCV values < 20% if clinical signs of anemia are present and problematic. The starting dosage is 100 U/kg administered subcutaneously 3 times per week. Iron deficiency is avoided by monitoring serum iron and total iron binding capacity and providing oral supplementation with ferrous sulfate (5 to 50 mg per cat per day). When the lower end of the target PCV range (30-40%) is reached, frequency of administration is reduced to twice a week. Depending upon the severity of anemia, it may require 3-4 weeks for the PCV to enter the target range. Although initially effective in correcting the anemia of CRF, use of rhEPO is associated with antibody formation in up to 50% of treated dogs and cats after 1 to 3 months of treatment. The resulting anemia can be more severe than that present before treatment because the induced antibodies can cross-react with the animal's native EPO. The canine EPO gene has been isolated, and recombinant canine EPO has been used to stimulate erythropoiesis in normal dogs and in those with naturally occurring CRF. It is not as effective when used in dogs that have developed red cell aplasia from previous treatment with rhEPO. Feline recombinant EPO also has been produced, but unfortunately unexplained red cell aplasia developed in some treated cats. Other adverse effects have been observed during administration of rhEPO to dogs and cats including vomiting, seizures, hypertension, uveitis, and hypersensitivity-like mucocutaneous reaction.

Control of Systemic Hypertension

Systemic hypertension occurs in 20 to 65% of cats with chronic renal failure when determined by methods that indirectly measure blood pressure. It is essential that cats be in a quiet environment before and during blood pressure measurements. Cats especially are prone to "white coat artifact" making it difficult to determine if a given cat is truly hypertensive. The correlation of unregulated arterial hypertension to the progression of CRF has not been established in cats, but there are some studies in dogs and humans that suggest a positive relationship. It is likely that high systemic blood pressure is transmitted to the glomerular vessels, which promotes further injury. Cats that have systemic hypertension from a variety of causes have been shown to survive longest when their blood pressure is well controlled.

Patients with systolic blood pressure readings > 170 mm Hg or those CKD patients with lower levels of blood pressure readings that also have fundic lesions consistent with hypertensive retinopathy (e.g., retinal edema, retinal hemorrhages, arterial tortuosity, retinal detachment) are candidates for anti-hypertensive therapy. Angiotensin-converting enzyme (ACE) inhibitors (e.g. enalapril, benazepril) may have protective effects in patients with CRF due to their ability to block adverse effects of angiotensin II. Beneficial effects include reduction in proteinuria, limitation of glomerular sclerosis and slowing of progression of renal failure as well as improvement in systemic blood pressure. Enalapril has not been very effective for treatment of hypertensive cats. The calcium channel blocker, amlodipine has been used successfully in cats at a dosage 0.625 to 1.25 mg per cat given orally once per day. Follow-up evaluations should be scheduled for one week after beginning treatment with amlodipine. Adverse effects (including hypotension) are very uncommon with the use of amlodipine in cats.

Control of Proteinuria

The detection of proteinuria is a diagnostic index in cats with CRF. Based on the theories of glomerular hypertension that occur in "super nephrons" of the adapted kidney, protein gaining access to tubular fluid and the mesangium is also a creator of further renal injury. The magnitude

of proteinuria is a function of the integrity of the glomerular barrier, GFR, tubular reabsorptive capacity, and effects from elevated systemic and intraglomerular blood pressure.

Cats with CRF increased their risk for death or euthanasia when the UPC was 0.2 to 0.4 compared to <0.2 and was further increased in cats with UPC of >0.4. The prognosis for survival is influenced by the UPC despite what has traditionally been thought to be low-level proteinuria. The effect of treatment that lower proteinuria on survival have not been specifically studied. Since even low-level proteinuria is a risk factor to not survive, it is prudent to consider treatments that lower the amount of proteinuria in those with CKD and CRF. Benazepril has been shown in two recent clinical studies to reduce the UPC in cats with CRF. Cats treated with benazepril in one study did not progress from IRIS stage 2 or 3 to the next stage as rapidly as those treated with placebo but over 6 months. Despite reduction in proteinuria in CKD cats with initial UPC > 1.0 that were treated with benazepril in another study, a significant increase in survival time was not found over placebo.

Selected Reading

1. Boyd LM, Langston C, Thompson K, Zivin K, Imanishi M: Survival in Cats with Naturally Occurring Chronic Kidney Disease (2000-2002). *J Vet Intern Med*, 2008.
2. Brown SA, Brown CA, Jacobs G, Stiles J, Hendi RS, Wilson S: Effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency. Am J Vet Res 62(3): 375-383, 2001.
3. Brown SA, Rickertsen M, Sheldon S. Effects of an intestinal phosphorous binder on serum phosphorous and parathyroid hormone concentrations in cats with reduced renal function. Intern J Appl Res Vet Med 2008; 6: 155-160.
4. Elliott J, Rawlings JM, Markwell PJ, Barber PJ: Survival of cats with naturally occurring chronic renal failure: effect of dietary management. J Small Anim Pract 41(6): 235-242, 2000.
5. Elliott J, Barber PJ, Syme HM, Rawlings JM, Markwell PJ. Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases. J Small Anim Pract 2001; 42:122-9.
6. Jepson RE, Elliott J, Brodbelt D, Syme HM: Effect of control of systolic blood pressure on survival in cats with systemic hypertension. J Vet Intern Med 21(3): 402-409, 2007.
7. King JN, Gunn-Moore DA, Tasker S, Gleadhill A, Strehlau G: Tolerability and efficacy of benazepril in cats with chronic kidney disease. J Vet Intern Med 20(5): 1054-1064, 2006.
8. King JN, Tasker S, Gunn-Moore DA, Strehlau G: Prognostic factors in cats with chronic kidney disease. J Vet Intern Med 21(5): 906-916, 2007.
9. Mizutani H, Koyama H, Watanabe T, Kitagawa H, Nakano M, Kajiwara K, King JN: Evaluation of the clinical efficacy of benazepril in the treatment of chronic renal insufficiency in cats. J Vet Intern Med 20(5): 1074-1079, 2006.
10. Plantinga EA, Everts H, Kastelein AM, Beynen AC: Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets. *Vet Rec* 157(7): 185-187, 2005.
11. Ross SJ, Osborne CA, Kirk CA, Lowry SR, Koehler LA, Polzin DJ: Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. J Am Vet Med Assoc 229(6): 949-957, 2006.
12. Spiecker-Hauser U, Kraemer F, Epe C, Schmidt B. Efficacy of Lantharenol to reduce intestinal phosphorous absorption from feline renal diet. Proceedings of the 11th European Society of Veterinary and Comparative Nutrition Congress; 2007 Nov 2-3; Leipzig, Germany, p.133.
13. Schmidt B, Delport P, Spiecker-Hauser U: Bay 78-1887, a novel lanthanum-based phosphate binder, decreases intestinal phosphorus absorption in cats. J Vet Pharmacol Therap 29((Supplement 1)): 206-207, 2006.
14. Schmidt B, Spiecker-Hauser U, Gropp, J: Effect of Lantharenol® on apparent phosphorus absorption from a conventional feline maintenance diet and a renal diet for cats. Proc Soc Nutr Physiol 17:87, 2008.

15. Schmidt B, Spiecker-Hauser U, Murphy M: Efficacy and safety of lantharenol® on phosphorus metabolism in cats with chronic kidney disease. J Vet Intern Med 22(3): 798, 2008.
16. Schmidt B, Adler K, Hellmann K. The use of Renalzin, a new intestinal phosphate binder, in feline chronic renal failure. Proceeding of the Vetoalp 2008 Conference; 2008 March 31; Chamonix, France; p.69.
17. Schmidt BH, Murphy M. A study on the long-term efficacy of Renalzin® (Lantharenol® suspension 20%) in cats with experimentally induced chronic kidney disease. Vet Clin Pathol. In Press 2009.
18. Schmidt B, Spiecker-Hauser U. Overdose acceptance and tolerance of Lantharenol in adult healthy cats. J Vet Pharmacol Ther. In Press 2009
19. Syme HM, Markwell PJ, Pfeiffer D, Elliott J: Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. J Vet Intern Med 20(3): 528-535, 2006.
20. Wagner E, Schwendenwein I, Zentek J: Effects of a dietary chitosan and calcium supplement on Ca and P metabolism in cats. Berl Munch Tierarztl Wochenschr 117(7-8): 310-315, 2004.

ADVANCES IN THE TREATMENT OF HYPERCALCEMIA

Dennis J. Chew, DVM ; Columbus Ohio
Patricia A. Schenck, DVM, PhD; Lansing MI

SHOULD ALL PATIENTS WITH HYPERCALCEMIA BE TREATED?

Most patients are initially determined to have hypercalcemia based on evaluation of serum total calcium. Adverse effects of circulating calcium only occur when increased ionized calcium is the cause of the increased total serum calcium. There is considerable diagnostic discordance in the ability of serum total calcium to predict true ionized calcium status in both dogs and cats, so ionized calcium should be used as the gold standard to determine if the hypercalcemia is a damaging one or not.[1,2] The magnitude of the hypercalcemia, its rate of development, whether the serum calcium concentration is stable or increasing, and the modifying effects of other electrolyte and acid-base imbalances must be considered while developing a treatment plan. The clinical condition of the animal based on history and physical examination ultimately dictates how aggressive treatment should be. Concurrent presence of neurologic, cardiac, and/or renal dysfunction as well as calcium-containing uroliths increases the urgency for correction of hypercalcemia. Acidosis can magnify the effects of hypercalcemia at all concentrations of serum calcium by shifting more calcium to the ionized fraction. Soft tissue mineralization is potentiated when hyperphosphatemia exists at the same time as hypercalcemia.

Animals with rapid and progressive increases in serum calcium usually display serious clinical signs (vomiting, anorexia, dehydration, depression/coma, weakness, cardiac arrhythmia) that require aggressive therapy.[3] Supportive therapy is often necessary to decrease serum calcium concentration to a less toxic level while awaiting a diagnosis to be determined, for definitive treatment to permanently reduce serum calcium concentration, and for chronic management of hypercalcemia when the underlying cause cannot be removed. Treatments are designed to decrease the magnitude of hypercalcemia by increasing renal calcium excretion, inhibiting bone resorption, and decreasing calcium transport across the intestine, or some combination of these. Correction of extracellular volume contraction with subsequent dilution of circulating calcium is an initial goal of parenteral fluids, usually administered as 0.9% NaCl. Emergency rescue with sodium bicarbonate infusions can be used, rarely, to shift ionized calcium to the protein-bound fraction. Clinical signs often improve when ionized calcium decreases to some degree even when it does not return completely to normal.

Some animals with hypercalcemia have minimal to no observed clinical signs, or are normal following physical examination (e.g., primary hyperparathyroidism, idiopathic hypercalcemia of cats). Usually, the magnitude of hypercalcemia is minimal to moderate and stable in these instances, so urgent treatment to correct hypercalcemia is not warranted as there is time for further diagnostics and to observe the trend in serum calcium. If the hypercalcemia is known to be ionized, measures should be taken to restore normocalcemia even in the absence of obvious clinical signs, since clinical signs may develop and the magnitude of the hypercalcemia can become more severe. Even at stable levels of hypercalcemia, some patients will develop urolithiasis, renal mineralization, and chronic renal injury. Animals with weight loss, vomiting, constipation, or other vague GI signs along with chronic low-grade hypercalcemia often improve their clinical sings following restoration to normocalcemia. If present, polyuria and polydipsia usually greatly diminish following restoration of normocalcemia, if calcium-associated chronic renal injury has not been too great.

In studies by the authors,[1,2] about 20% of dogs and cats with chronic renal failure were found to have hypercalcemia based on serum total calcium. When ionized calcium was measured in the same animals, about 10% of dogs and 30% of cats were found to be hypercalcemic. This indicates that serum total calcium overestimates ionized hypercalcemia in dogs and underestimates ionized hypercalcemia in cats. The discrepancy between serum total and ionized calcium in dogs with chronic renal failure is due to an increase in the complexed fraction of calcium, possibly due to increased circulating organic anions capable of complexing calcium.[4] We suspect that the higher number of cats with ionized hypercalcemia during their chronic renal failure is in association with idiopathic hypercalcemia, a syndrome that occurs in cats but not in dogs. Tertiary hyperparathyroidism (elevated ionized calcium concentration and excessive PTH secretion that is not inhibited by high serum iCa concentration), aluminum-induced bone disease (elevated ionized calcium concentration and low PTH secretion), toxicity from calcium-containing intestinal phosphate binders, and excess effects of prescribed activated vitamin D compounds are considerations when ionized hypercalcemia is discovered in both dogs and cats with chronic renal failure

(in addition to other differentials not associated with renal disease). Measurement of ionized calcium should be performed in all cases with chronic renal failure to determine if hypercalcemia based on serum total calcium is dangerous or not, and to determine if ionized hypercalcemia is a problem despite normocalcemia based on serum total calcium. Dogs and cats with chronic renal failure and increased ionized calcium are at increased risk for accelerated progression of their chronic kidney disease, presumably due to enhanced renal mineralization. As far as we know, those with increased total calcium and normal to low ionized calcium concentrations (high concentration of complexed or protein-bound calcium) are not at increased risk for further kidney damage, and do not need any specific therapy to lower circulating calcium.

STANDARD INITIAL TREATMENT – ACUTE STABILIZATION

The first step in treatment of severe hypercalcemia is with IV fluids to create volume expansion, dilution of calcium, and calciuresis. Fluid therapy alone will reduce the magnitude of pathological hypercalcemia somewhat, but is often not sufficient by itself to provide adequate amelioration of clinical signs or enough decline in circulating levels of calcium (hypoadrenocorticism and severe dehydration with hemoconcentration are exceptions). Usually the fluid of choice is 0.9% NaCl as it floods the renal tubules with sodium that competes for reabsorption of calcium resulting in calciuresis. Intravenous fluids increase renal perfusion, glomerular filtration rate, and calciuresis. Furosemide as a CRI or intermittent injection is a calciuretic diuretic that is often chosen next (thiazides should not be chosen as they promote renal calcium reabsorption). Furosemide CRI may be preferred since more urinary sodium and calcium as well as less urinary potassium were excreted compared to bolus intermittent injection in a small study of Greyhounds.[5] Care must be taken during furosemide therapy to avoid dehydration that can occur during intense diuresis. If the hypercalcemia is severe, salmon calcitonin can be added as treatment for the acute lowering of circulating calcium (within a few hours) due mostly to its effects that decrease osteoclastic bone resorption. The effects of calcitonin may only last a few days due to down-regulation of calcitonin receptors on the osteoclast, and some animals develop anorexia and vomiting as an adverse effect. Glucocorticosteroids can also lower circulating calcium levels by salutary effects on gut, bone, and kidney; they can also have dramatic effects to lower calcium levels in those with lymphoma, myeloma, or hematopoietic neoplasm from cytotoxicity, so their use should be avoided if possible until a definitive diagnosis has been made. Glucocorticosteroids also can exert beneficial effects in patients whose hypercalcemia is associated with hypervitaminosis-D or hypoadrenocorticism.

DIETARY CHANGE

A change in diet is not helpful for most cases with pathological hypercalcemia, since hypercalcemia most commonly develops from increased bone resorption along with some increased renal tubular reabsorption of calcium. A change to a diet low in calcium is helpful only if the mechanism responsible for the development of hypercalcemia features increased absorption of calcium across the gut, as happens in hypervitaminosis D. Renal diets are typically low in calcium and are somewhat alkalinizing, which can be helpful in those with hypervitaminosis D. All dairy products should be specifically avoided in those with hypervitaminosis D. In those with malignancy-associated hypercalcemia, gut absorption of calcium is usually already reduced due to effects of low PTH and calcitriol. Rarely some malignancies are associated with increased concentrations of calcitriol and hypercalcemia; in these instances, dietary restriction of calcium could be useful.

Attempts to reduce serum calcium concentration are sometimes successful following dietary modification in cats with idiopathic hypercalcemia; the mechanism for this beneficial effect has not been specifically studied. Mechanisms could include reduced intestinal absorption of calcium and reduced bone resorption of calcium. Intestinal absorption of calcium depends on the amount and bioavailability of calcium, dietary fiber type, the amount of fiber, and also other nutrients present in the diet. Feeding of increased dietary fiber has been reported to restore normocalcemia in some cats with IHC and calcium-oxalate urolithiasis,[6,7] but not in another study.[8] Intestinal absorption of calcium may be decreased with the feeding of high fiber diets by decreasing the gastrointestinal transit time. Most pet food manufacturers have taken this potential decrease in absorption of calcium into account, and have increased the quantity of dietary calcium in high fiber diets to enhance calcium absorption. Serum ionized calcium concentration and the degree of calciuria is increased in cats that eat acidifying and magnesium-restricted diets.[9] It is

possible that in some cats hypercalcemia will resolve when fed a less acidifying diet. Renal diets are less acidifying and possibly alkalinizing so these may be chosen as therapy, but their degree of phosphorus restriction may enhance calcitriol synthesis that could blunt the salutary effects of the alkalinization.

BISPHOSPHONATES

Bisphosphonates are organic pyrophosphate analogues that inhibit bone resorption following deposition into areas of active bone turnover. Their presence in bone interferes with hydroxyapatite dissolution and exerts direct effects that reduce osteoclastic function. Induction of osteoclast apoptosis appears to be the main effect of bisphosphonates.[10] Bisphosphonates that contain a nitrogen side chain have enhanced antiresorptive activity, and are called aminobisphosphonates (pamidronate, zolendronate, ibandronate). Early generation bisphosphonates such as etidronate and clodronate are lacking in nitrogen side chains and so are less active. Intravenous administration of bisphosphonates is preferred over oral administration for treatment of severe hypercalcemia as some patients will be vomiting and cannot tolerate oral medication. Bisphosphonates are very poorly absorbed across the GI tract; usually less than 5% is absorbed and this can decrease to nearly zero with food in the stomach at the time of administration. High dose oral bisphosphonate treatment can achieve similar results as the IV route in some instances in people.[11] Administration of oral bisphosphonates can be considered for maintenance control of normocaclemia after IV doses or for initial treatment in those whose hypercalcemia is not severe. Following IV administration, there is a delay in the onset of action that lowers circulating calcium that may range from 1 to 5 days. The magnitude of effect in lowering circulating calcium concentrations is related to the initial level of hypercaclemia, the dose, route administered, and the specific bisphosphonate administered. The duration of initial beneficial effect following IV administration of bisphosphonates may last 1 to 4 weeks.

Acute renal injury/renal failure attributed to precipitation of insoluble calcium-bisphosphonate salts in the renal tubules was reported in the early days of IV bisphosphonate treatment in humans, often after multiple doses and some with pre-existing chronic kidney disease. This is very uncommon today due to efforts to ensure hydration before, during, and after bisphosphonate infusion. People with relatively severe azotemia can be safely given IV infusions of bisphosphonates when given slowly, and adequate hydration is maintained.[12] Acute intrinsic renal failure can occur in dogs given greater than or equal to a dose of 10 mg/kg, according to the package insert for pamidronate. Hypocalcemia can occur following treatment with bisphosphonates but this is not usually a clinical problem.

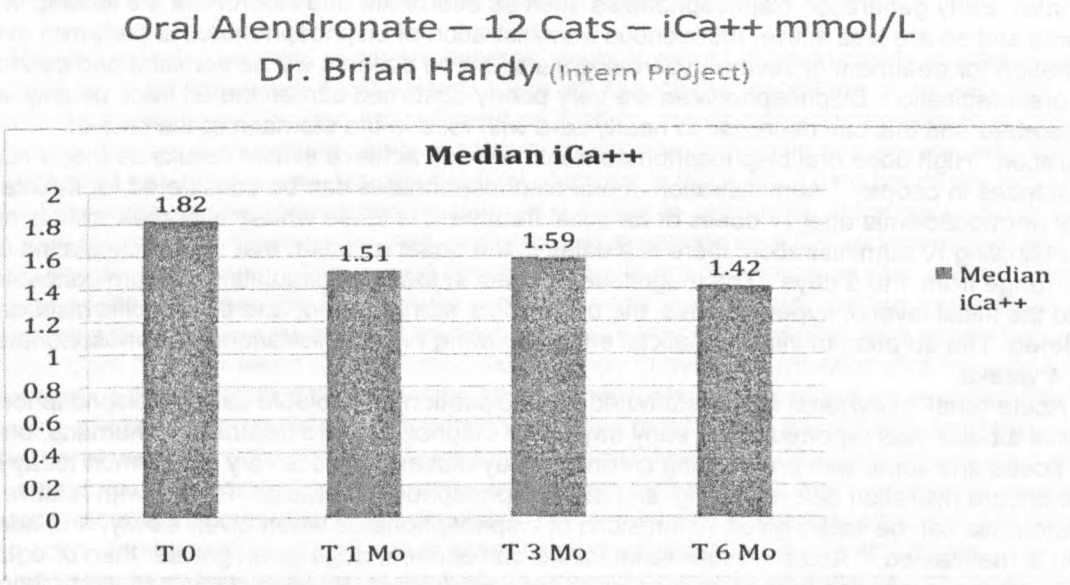
Intravenous pamidronate infusions at 1.0 to 2.0 mg/kg have been safely and effectively used to treat hypercalcemia in dogs and cats with malignancy, calcipotriene toxicity, granulomatous disease, and idiopathic hypercaclemia of cats. Beneficial effects were seen in these animals despite the presence of initial azotemia in over 40% of these cases.[13] It is important to deliver the pamidronate as an infusion over at least 2 hours during mild volume expansion after dehydration has been corrected. Intravenous pamidronate at 1.3 to 2.0 mg/kg was highly effective in lowering serum calcium in dogs with an experimental model of cholecalciferol intoxication,[14,15] and in dogs with clinical calcipotriene toxicity.[16] Though not specifically reported, we have used this dose range to treat dogs with primary hyperparathyroidism prior to surgical correction in an effort to reduce crisis-level hypercalcemia and to reduce post-operative "hungry-bone" syndrome.

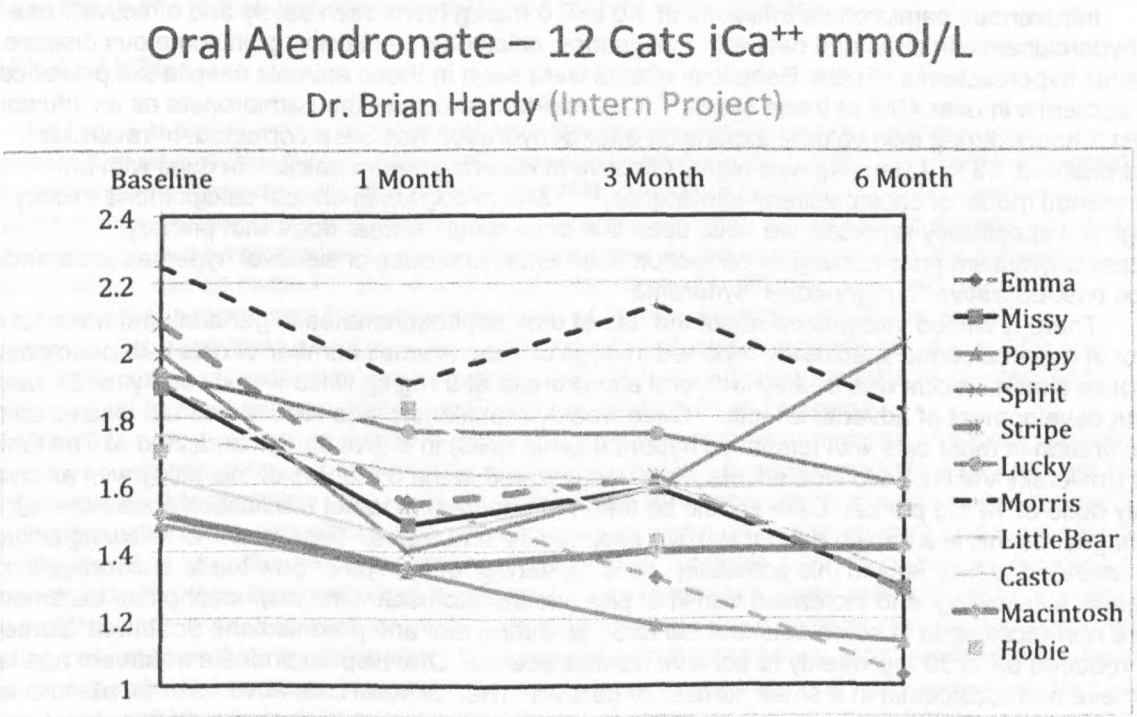
There is limited information about the use of oral bisphosphonates in general, and none for control of hypercalcemia specifically reported in dogs or cats. A small number of cats with odontoclastic resorptive dental lesions was treated with oral alendronate at 9 mg/kg twice weekly orally for 27 weeks without development of adverse effects.[17] Once weekly oral alendronate reduced serum ionized calcium concentration in most cats with idiopathic hypercalcemia (IHC) in a pilot study conducted at The Ohio State University VMTH.[18] No side effects were documented in the 6 months of this study with an average weekly dose of 10 mg per cat. Care should be taken to ensure that tablet medication does not stick in the esophagus, as this is a known risk for erosive esophagitis in humans. Tap water PO following pilling is recommended to help lessen this possibility, as is "buttering" of the lips or paw top to encourage licking, salivation, swallowing, and increased transit of pills into the stomach. Oral bisphosphonate treatment can restore normocalcemia in some cats that fail to do so during diet and prednisolone treatment. Some cats have required up to 30 mg weekly to achieve normocalcemia. Oral bisphosphonate treatment has failed to achieve normocalcemia in a small number of cats with IHC. Several cats have been on alendronate treatment for years without known adverse effects. We have observed one cat with IHC to develop hypocalcemia and clinical signs. The salutary response during bisphosphonate treatment indicates that

blunting of osteoclastic bone resorption can be effective to decrease serum ionized calcium but it does not prove that accelerated bone resorption is the underlying cause of IHC.

REFERENCES

[1]Schenck PA and Chew DJ. Am J Vet Res 2005;66(8):1330; [2]Schenck PA and Chew DJ. Can J Vet Res 2010 (in press); [3]Schenck PA et al. In:SP DiBartola, ed. Fluid Therapy in Small Animal Practice 2005, 3rd ed: 122; [4]Schenck PA and Chew DJ. Am J Vet Res 2003;64(9):1181; [5] Darcy B et al. J Vet Intern Med 2003;17:632–636; [6]Osborne CA. Vet Clin North Am Small Anim Pract 1996; 26(2):217-32; [7]McClain HM. J Am Anim Hosp Assoc 1999;35(4):297-301; [8]Midkiff AM. J Vet Intern Med 2000; 14(6):619-26; [9]Ching SV. J Nutr 1989;119(6): 902-915; [10]Body JJ et al. Cancer Treat Rev 1996;22:265-287; [11]Pecherstorfer M et al. Treat Endocrinol 2003; 2(4):273-292; [12]Machado CE et al. Clin Nephrol 1996; 45(3):155-9; [13]Hostutler RA et al. J Vet Intern Med 2005; 19:29-33; [14]Rumbeiha WK et al. Am J Vet Res 1998; 60:1092-1097; [15]Rumbeiha WK et al. AVJV 2000; 61:9-13; [16]Hare WR et al. Vet Med 2000; 95:770-778; [17]Harvey CE et al. 2004; [18]Hardy B unpublished observations.





HYPERCALCEMIA IN DOGS AND CATS – HOW MUCH SHOULD I REACT ?

Dennis J. Chew, DVM , Diplomate, ACVIM (Internal Medicine)
The Ohio State University, Columbus, Ohio, USA
Patricia A. Schenck DVM, PhD
Michigan State University, East Lansing, Michigan, USA

An increased serum calcium is typically first noted when total calcium (tCa) is measured as part of a biochemistry profile. Abnormalities in tCa warrant further diagnostic investigation. First it should be verified that the abnormality is repeatable. If the abnormality is repeatable, ionized calcium (iCa) should be measured for an accurate assessment of calcium status. Total or adjusted tCa are not reliable measurements of calcium status as noted by a high degree of diagnostic discordance between total, adjusted, and ionized calcium measurements.

Small increases in ionized serum calcium concentration can have adverse consequences in some animals whereas others with a similar or greater degree of hypercalcemia may not manifest obvious clinical signs. A mild degree of hypercalcemia may not be immediately dangerous and there is time to establish a definitive diagnosis before starting treatment. In those with severe clinical signs associated with hypercalcemia, diagnostic and therapeutic efforts may need to proceed concurrently. Interaction with serum phosphorus is important, as those with a tCa (mg/dL) times phosphorus concentration product greater than 70 are most likely to have severe tissue changes associated with mineralization. Hypercalcemia can be toxic to all body tissues, but major deleterious effects are on the kidneys, nervous system, and cardiovascular system. Most animals with tCa greater than 15.0 mg/dL will show systemic signs, and those with tCa concentrations greater than 18.0 mg/dL are critically ill.

Polydipsia, polyuria, and anorexia are the most common clinical signs attributed to hypercalcemia, though depression, weakness, vomiting, and constipation can also occur. Uncommonly, cardiac arrhythmias, seizures, and muscle twitching are observed. Severe hypercalcemia that has developed rapidly (hypervitaminosis D) can result in death. Cats with hypercalcemia do not display polyuria, polydipsia or vomiting as commonly as do dogs with a similar degree of hypercalcemia. Cats with idiopathic hypercalcemia may have no obvious clinical signs.

Hypercalcemia is initially defined on results of serum total calcium from obviously sick animals, but also fortuitously during wellness examinations, pre-anesthesia screenings, evaluation of urolithiasis, and from those evaluated for vague GI signs. The initial finding of a mild increase in serum tCa should be repeated to see if the hypercalcemia is persistent. A transient increase in serum tCa is documented in some cats with minor increases in serum tCa; further workup is not indicated in these instances in which the serum tCa concentration is normal on subsequent analysis. Measurement of serum iCa is the next step in the diagnostic evaluation of those with persistent or more substantial increases of serum tCa. Prediction of iCa status from tCa measurement is not accurate, and iCa needs to be specifically measured. Increased iCa concentration is documented in all cats with IHC, but may be normal or low in other conditions associated with increased serum tCa, especially chronic renal failure (CRF). Serum iCa can be measured alone, or preferably at the same time that parathyroid hormone (PTH) concentration is measured.

Differential Diagnoses for Hypercalcemia

There are many potential causes of hypercalcemia (See HARDIONS Eponym). Though cancer-associated hypercalcemia has traditionally been noted to be the primary cause of elevated serum in both dogs and cats, IHC appears to be the most prominent cause in cats followed by renal failure, and then malignancy in primary care practice. In some cases with persistent hypercalcemia, the diagnosis of the cause of the hypercalcemia will be obvious after analysis of history (vitamin D exposure, drugs, ingestion of houseplants), and findings from physical examination (masses, organomegaly, cancer or granulomatous disease). In other cases, the cause will not be obvious and information from hematology, serum biochemistry, body cavity imaging, cytology, and histopathology will be necessary.

Hypercalcemias can be classified as parathyroid-dependent (primary hyperparathyroidism), or parathyroid-independent (normal parathyroid gland). In hypercalcemic dogs, neoplasia is the most common diagnosis, followed by hypoadrenocorticism, primary hyperparathyroidism, and chronic renal failure. Approximately 70% of hypercalcemic dogs are also azotemic, with azotemia uncommon only in dogs with hyperparathyroidism. In hypercalcemic cats, neoplasia is second to renal failure or idiopathic hypercalcemia.

H = Hyperparathyroidism (1°,3°, hyperplasia), Humoral Hypercalcemia of Malignancy, Houseplants, Hyperthyroid
A = Addison's Disease, Aluminum Toxicity,Vitamin A, Milk-Alkali
R = Renal Disease, Raisins(Grapes)- dogs
D = Vitamin D Toxicosis (Granulomatous Dz),
Drugs, Dovonex, Dehydration, DMSO (calcinosis cutis), Diet
I = Idiopathic (Cats), Infectious, Inflammatory,
Immobilization
O = Osteolytic (osteomyelitis, immobilization,Local Osteolytic Hypercalcemia, bone infarct)
N = Neoplasia (HHM and LOH), Nutritional
S = Spurious, Schistosomiasis , Salts of Calcium, Supplements

Treatment

Excessive calcium ions are toxic to cells. Although all tissues may be subject to the dangerous effects of hypercalcemia, effects on the central nervous system, gastrointestinal tract, heart, and kidneys are of most importance clinically. Mineralization of soft tissues (especially the heart and kidneys) is an important complication of hypercalcemia. The serum phosphorus concentration at the time hypercalcemia develops is important in determining the extent of soft tissue mineralization. Soft tissue mineralization occurs regardless of the serum phosphorus concentration in severe hypercalcemia.

The impetus to prescribe therapeutic intervention becomes more pressing when the magnitude of ionized hypercalcemia continues to increase or clinical signs become more obvious. Aggressive treatment to decrease iCa concentration is warranted in patients with chronic kidney disease, chronic kidney failure, and or those with calcium-containing urinary stones. Continued ionized hypercalcemia poses a risk for further development of renal lesions and for development of new stones and enlargement of existing stones.

Acute rescue from hypercalcemia related to IHC (idiopathic hypercalcemia) is rarely indicated, as hypercalcemia has been gradual in development and relatively longstanding, and dramatic clinical signs are usually absent. Most cats with IHC will be treated as outpatients with either dietary change alone or in combination with drug therapy.

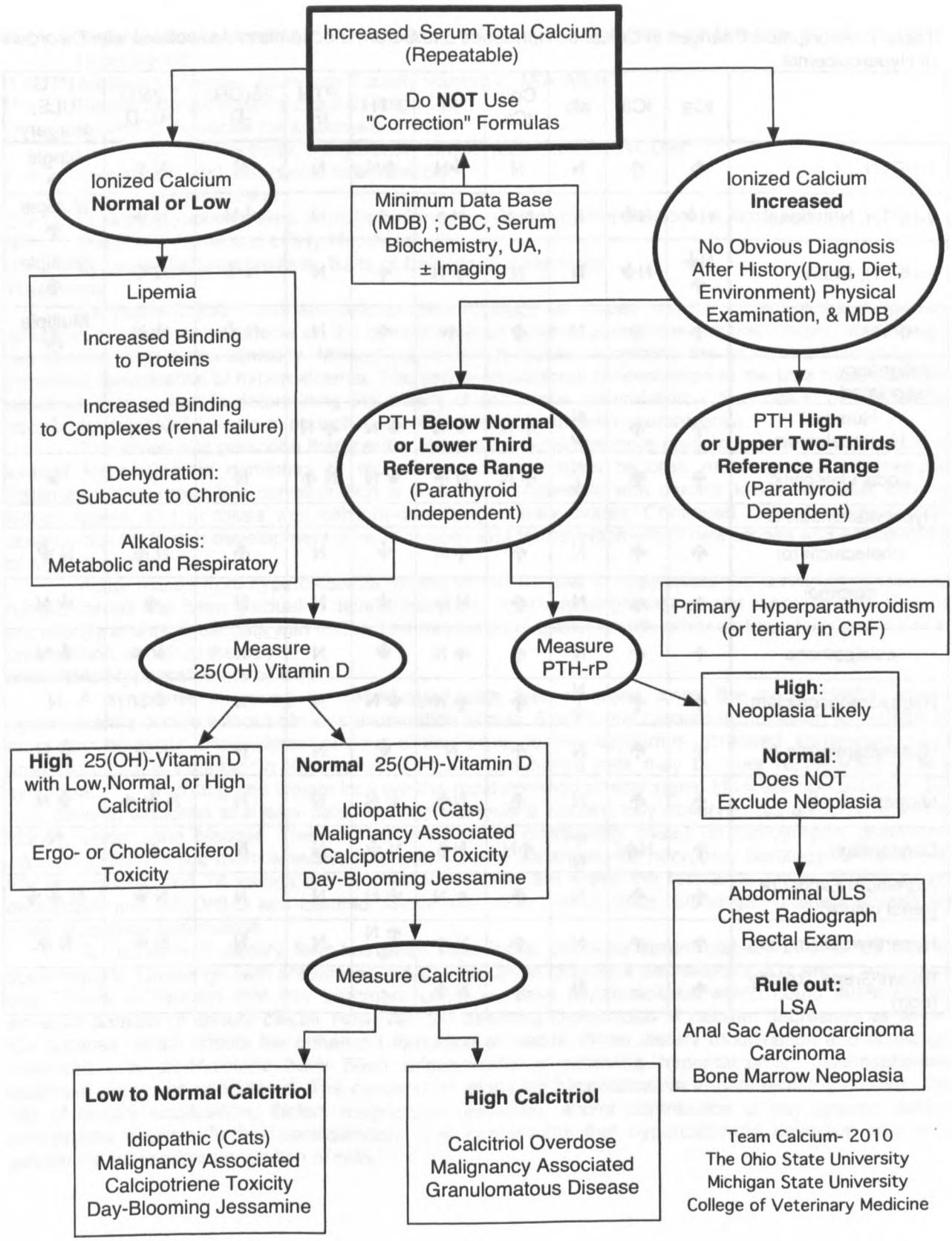
Idiopathic Hypercalcemia of Cats

A syndrome in young to middle-aged cats has emerged since the early 1990's, where hypercalcemia occurs without obvious explanation in cats. Serum total calcium is increased for months to more than one year, often without obvious clinical signs. Ionized calcium is increased, sometimes out of proportion to the increase in total serum calcium. Longhaired cats may be over represented in this syndrome. Vomiting and weight loss are the most common clinical signs. Most are nonazotemic, but may develop azotemia at a later date. Nephrocalcinosis is occasionally observed, as are uroliths in the kidney, ureter, and bladder. There is no evidence of malignancy based on radiography, abdominal ultrasonography, bone marrow evaluation, and in some instances, full necropsy. Serology for FeLV and FIV is negative, and T4 values are normal. PTH levels are within the reference range, PTHrP is not detectable, and 25-(OH)-D and calcitriol levels are within normal limits. Blood gas analysis reveals no major acid-base disturbance.

An increase in dietary fiber has been reported to decrease serum calcium in affected cats in some reports. Challenge with prednisone therapy results in long-term decreases in iCa and tCa in some cats. There is concern that this treatment could increase hypercalciuria, which could subsequently enhance genesis of urinary calculi. However, the declining filtered load of calcium decreases as serum iCa declines, which offsets the enhanced formation of calculi. When dietary modification and challenge treatment with prednisolone have been unsuccessful in resolving hypercalcemia, bisphosphonate treatment should be considered. The cause(s) of idiopathic hypercalcemia in cats remains elusive. The role of dietary acidification, dietary magnesium restriction, and/or contribution of any specific dietary constituents deserve further consideration. It is conceivable that hypercalcemia develops only in a genetically susceptible population of cats.

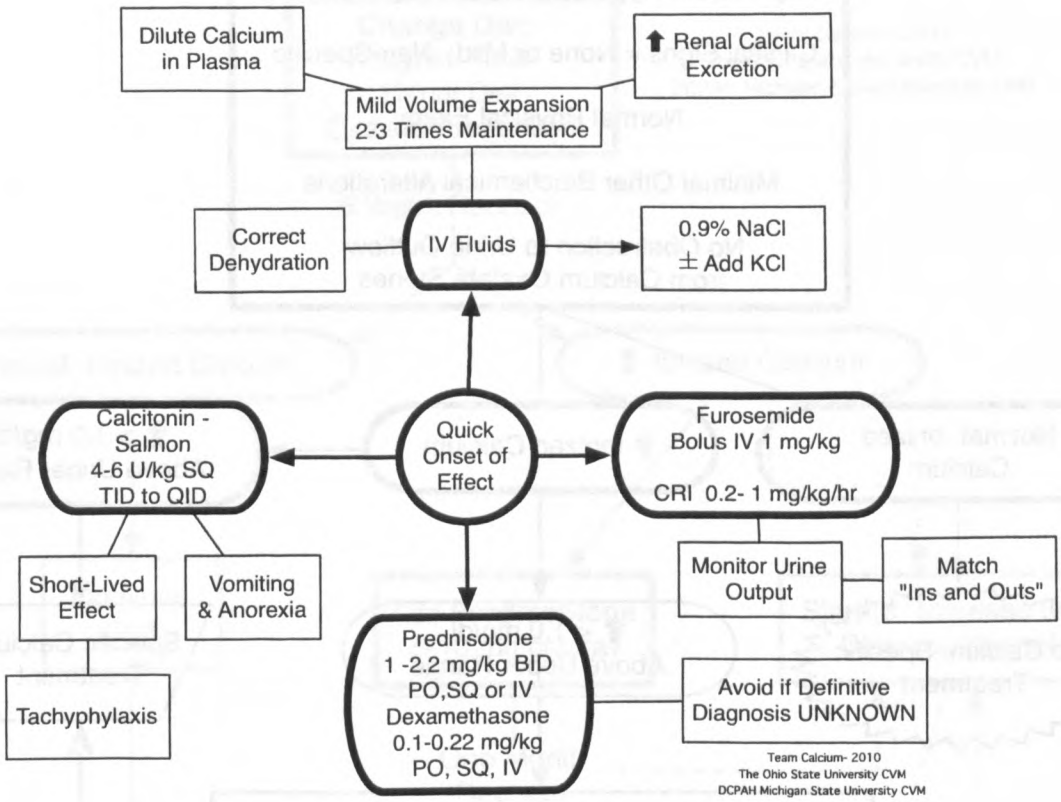
Table 1. Anticipated Changes in Calcemic Hormones and Serum Biochemistry Associated with Disorders of Hypercalcemia

	tCa	iCa	alb	Corr tCa	Pi	PTH	PTH rP	25(OH) -D	1,25(OH)$_2$-D	PTG ULS, Surgery
1-HPTH	↑	↑	N	N	↓N	↑N	N	N	N ↑	Single ↑
2-HPTH, Nutritional	N↓	N↓	N	N↓	N↑	↑	N	↓N	N ↓	Multiple ↑
2-HPTH, Renal	N↓ ↑	N↓	N	N	↑ N	↑	N	N ↓	N ↓	Multiple ↑
3-HPTH	↑	↑	N	↑	↑	↑	N	N ↓	↓ N	Multiple ↑
Malignancy Associated										
Humoral Hypercalcemia	↑	↑	N ↓	↑ N	↓ N	↓ N	↑ N	N	↓N ↑	↓
Local Osteolytic	↑	↑	N ↓	↑ N	N ↑	↓ N	N ↑	N	N	↓
Hypervitaminosis D										
cholecalciferol	↑	↑	N	↑	↑ N	↓	N	↑	N ↑	N ↓
calcitriol	↑	↑	N	↑	N ↑	↓	N	N	↑	↓ N
calcipotriene	↑	↑	N	↑	↑ N	↓	N	N	↓ N	↓ N
Hypoadrenocorticism	↑	↑	N ↓	↑	↑ N	↓ N	N	N	↓ N	N
Hypervitaminosis A	↑	↑	N	↑	N	↓	N	N	N ↓	↓ N
Idiopathic (cat)	↑	↑	N	↑	N↑	↓ N	N	N	N ↓ ↑	↓ N
Dehydration	↑	N↑	↑ N	↑N	N↑	N ↓	N	N	N	N
Aluminum Exposure (renal failure)	↑	↑	N	↑	↑ N	↓ N	N	N	N ↓	N ↑ ↓
Hyperthyroidism (cat)	↑	↑	N	↑	N ↑	↑ N ↓	N	N	N ↓	N ↑
Raisin/Grape Toxicity (dog)	↑	-	N	↑	N ↑	-	-	-	-	-

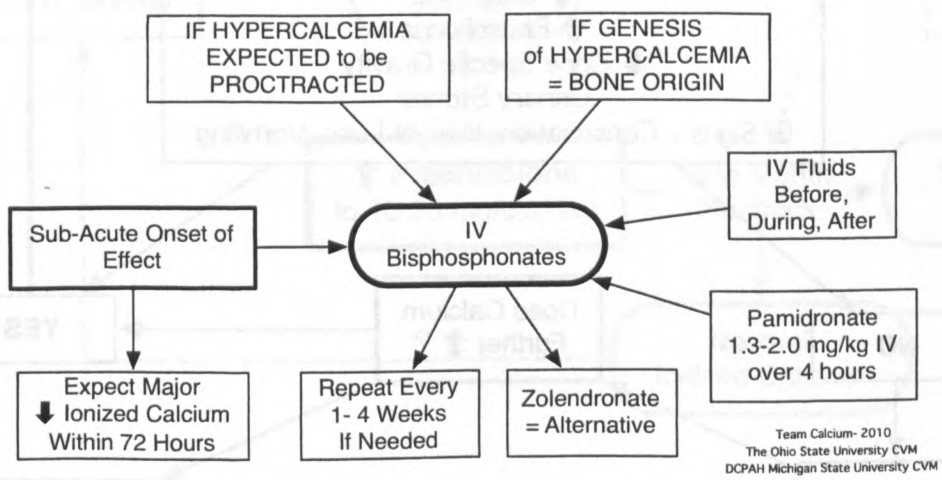


Team Calcium- 2010
The Ohio State University
Michigan State University
College of Veterinary Medicine

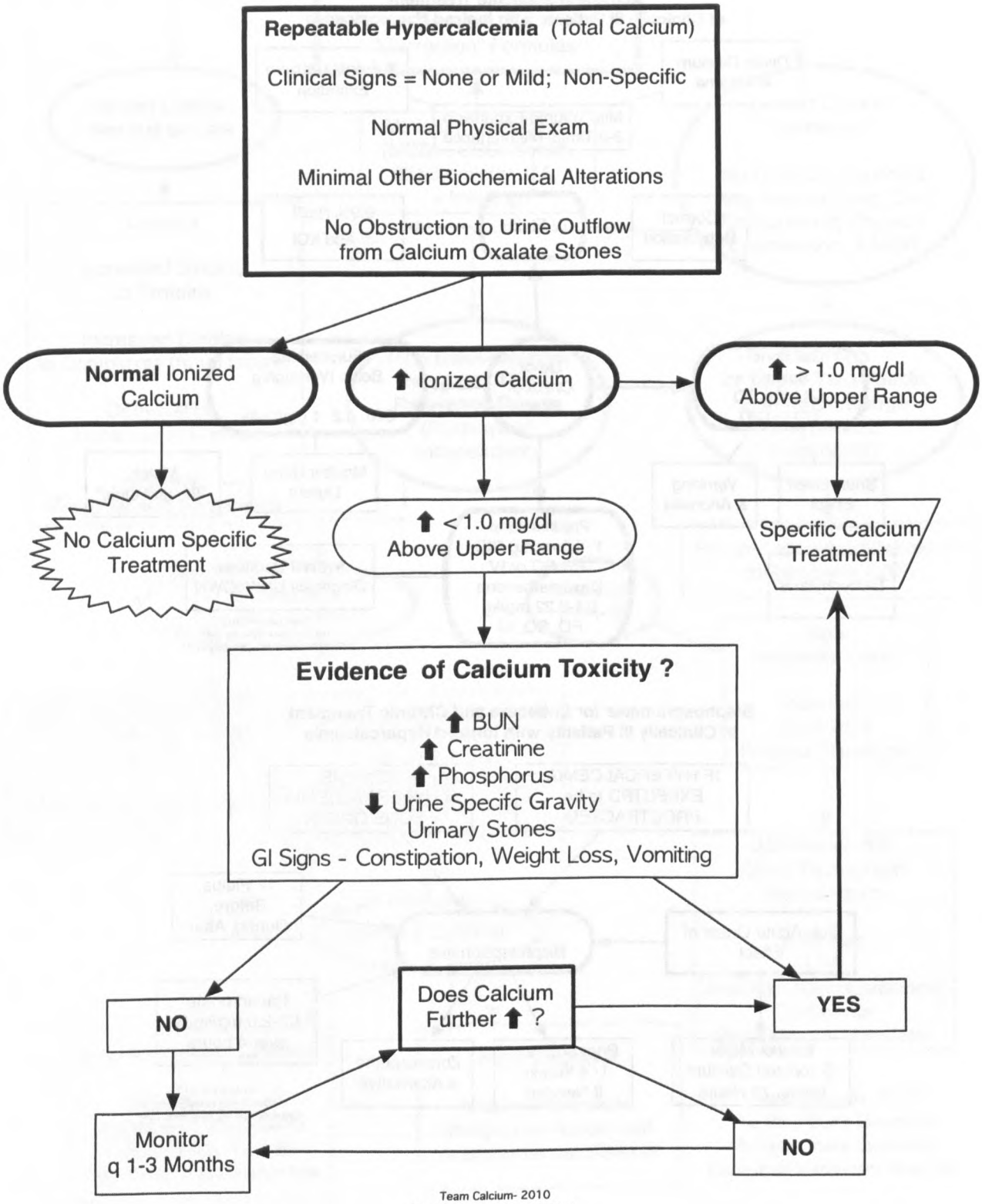
Acute and Subacute Treatment of Clinically Ill Patients with Ionized Hypercalcemia



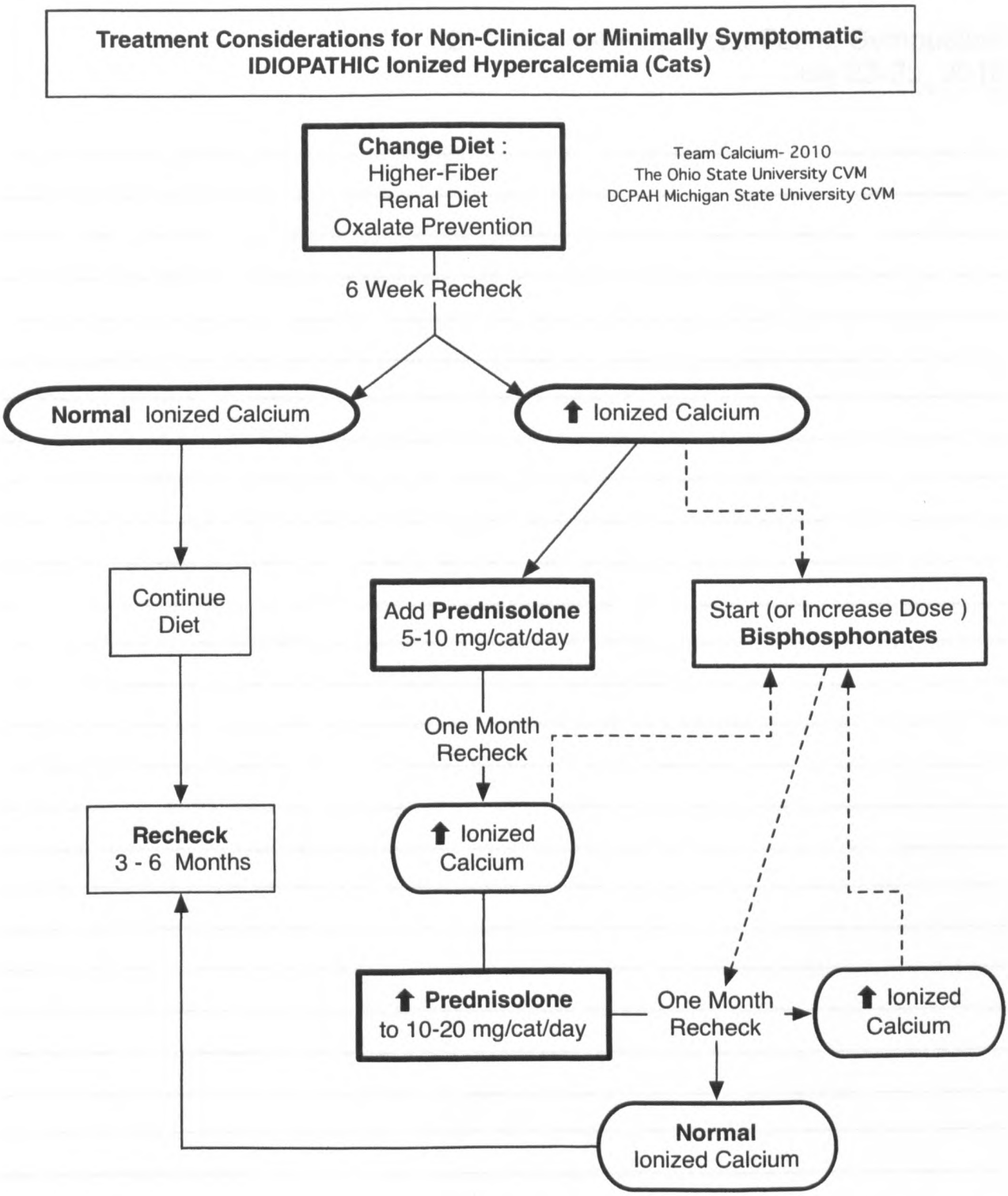
Bisphosphonates for Subacute and Chronic Treatment of Clinically Ill Patients with Ionized Hypercalcemia



Chronic Hypercalcemia - Not Sick
Intent to Treat or Not ?



Team Calcium- 2010
The Ohio State University CVM
DCPAH Michigan State University CVM


Treatment Considerations for Non-Clinical or Minimally Symptomatic IDIOPATHIC Ionized Hypercalcemia (Cats)
Change Diet : Higher-Fiber Renal Diet Oxalate Prevention
Team Calcium- 2010
The Ohio State University CVM
DCPAH Michigan State University CVM
6 Week Recheck
Normal Ionized Calcium
⬆ Ionized Calcium
Continue Diet
Add Prednisolone 5-10 mg/cat/day
Start (or Increase Dose) Bisphosphonates
One Month Recheck
Recheck 3 - 6 Months
⬆ Ionized Calcium
⬆ Prednisolone to 10-20 mg/cat/day
One Month Recheck
⬆ Ionized Calcium
Normal Ionized Calcium

There were no pages

in this section

CLINICAL USE OF GENETIC TESTING FOR FAMILIAL HYPERTROPHIC CARDIOMYOPATHY

Kathryn M. Meurs, DVM, PhD, DACVIM (Cardiology)
meurs@vetmed.wsu.edu


Genetic screening of familial feline HCM

- Known feline HCM mutations
  - Maine Coon cat
  - Ragdoll cat


Genetic Screening - Issues

- Adult onset
- Genetic penetrance
- Genetic heterogeneity
- Diagnostic criteria

Adult Onset

- Hypertrophic cardiomyopathy is adult onset disease
  - This complicates screening issues since animals are used for breeding BEFORE they develop the disease
    - Inevitably pass on trait
    - Led to increased demand for early genetic screening

Genetic Penetrance

- Hypertrophic cardiomyopathy is impacted by "Genetic Penetrance"
- Phenomenon that determines how much of a trait is demonstrated in the individual
- Animals with the exact same genetic etiology demonstrate great variation in severity of disease

Maine Coon Hypertrophic Cardiomyopathy

- Maine Coons (MC) with the MC HCM mutation may have significant ventricular hypertrophy & heart failure
- Litter mates with the same mutation may not even ever show the disease!!

Genetic Penetrance

- Mechanism of variable penetrance is poorly understood
- Likely involves environmental or genetic factors
  - Diet ?
  - Genetic background ?
  - Daily activities?

Genetic Penetrance

- Pet owners and pet breeders MUST understand that not all individuals with the same disease will have same severity
  - Even siblings
- Failure to understand this concept will lead to lack of confidence in testing (clinical or genetic)

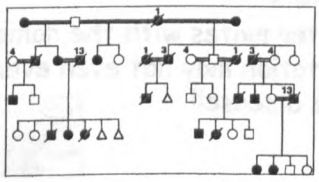
Genetic Heterogeneity

- Causative mutations identified in > 1 gene that result in the same disease
  - Hypertrophic cardiomyopathy in human beings - 400 mutations/ 20 genes
  - How many will cats have?

MAINE COON AND RAGDOLL HYPERTROPHIC CARDIOMYOPATHY

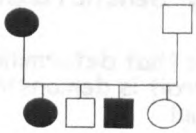
Maine Coon HCM

- Inherited as autosomal dominant trait



Autosomal dominant

Affected Unaffected



- All affected should eventually show the trait (no silent carriers)
- Breeding affected animals may produce both affected and unaffected (not a carrier) offspring
- Silent carriers should not exist

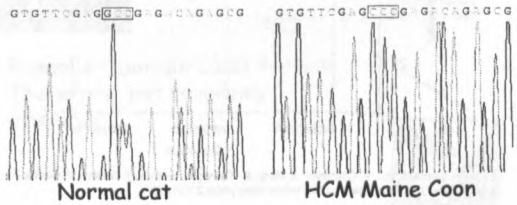
Autosomal dominant

Breeding recommendations:

- Emphasize characterization of disease prior to breeding
  - Breeding of affected animals has at least 50% chance of producing affected
  - Affected individuals should not be used for breeding if possible
  - Breeding of unaffected to unaffected will not transmit trait (no silent carriers)

Maine Coon HCM

A genetic mutation has been identified in the myosin binding protein C gene (MYBPC3)



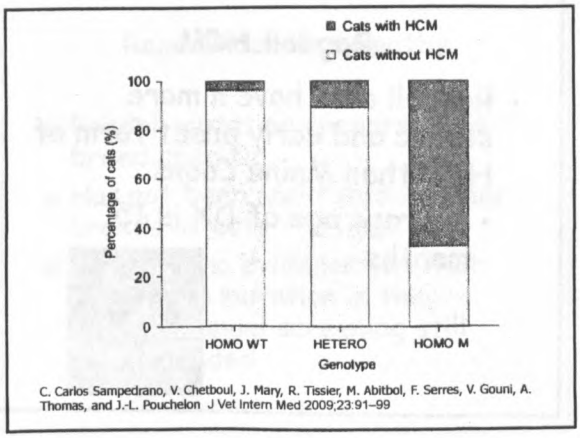
Normal cat HCM Maine Coon

Maine Coon HCM

- Myosin binding protein C is an important cardiac sarcomeric protein
- Also involved with the development of familial HCM in human beings

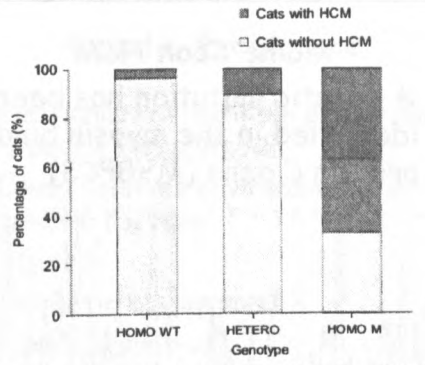
Maine Coon HCM

- The mutation is inherited with incomplete penetrance and variable expressivity
  - Not all cats with mutation will show disease, or show same severity of disease
- Cats that are homozygous for the mutation appear to be more likely to show the disease and perhaps have a more severe form



C. Carlos Sampedrano, V. Chetboul, J. Mary, R. Tissier, M. Abitbol, F. Serres, V. Gouni, A. Thomas, and J.-L. Pouchelon J Vet Intern Med 2009;23:91–99

- However, not all Maine Coons with HCM have the mutation
- In people there are > 400 HCM mutations
- It is likely that there is > 1 in the Maine Coon cat



C. Carlos Sampedrano, V. Chetboul, J. Mary, R. Tissier, M. Abitbol, F. Serres, V. Gouni, A. Thomas, and J.-L. Pouchelon J Vet Intern Med 2009;23:91–99

Maine Coon HCM

6455 samples analyzed from 2005-2010- Washington State Univ

- 33% of Maine Coon samples were positive for the mutation
  - 92% were heterozygotes

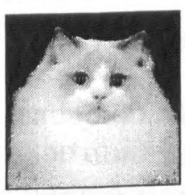
Distribution and % of Cats with the Mutation by Continent

Continent	Total MC	% Positive
North America	2,120	31.70
Europe	775	37.55
Asia	69	30.94
Australia	121	46.28

Fries R, Heaney AM, et al.J Vet Intern Med. 2008

Maine Coon HCM

- Mutation appears to be quite breed specific it has only been identified in:
  - 1 DLH
  - 1 DSH
  - 1 Siberian
  - 5 Ragdolls
- It does not appear to be associated with familial HCM in other breeds of cats



RAGDOLL CARDIOMYOPATHY

Ragdoll HCM

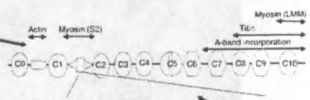
- Ragdoll cats have a more severe and early onset form of HCM than Maine Coons
  - Average age of DX is 15 months

Ragdoll Hypertrophic Cardiomyopathy

- Mode of inheritance is not well understood but likely- autosomal dominant
- Mutation identified in the same gene - MYBPC3, but different location as Maine Coon

Both mutations are in the MYBPC3 gene

Maine Coons- Domain C0-C1 of protein



Ragdolls - Domain C6 of Protein
Therefore, not commonly inherited

Ragdoll Cardiomyopathy

- Heterozygous cats appear to have a more mild form of the disease that may include only mild papillary muscle hypertrophy

Ragdoll Cardiomyopathy

- Homozygous cats appear to be very severely affected with development of heart failure and thromboembolic episodes < 2 years of age

Ragdoll Cardiomyopathy

- Ragdoll mutation appears to be breed specific
- Has not been identified in other breeds of cats
- Although no evidence yet that there is >1 mutation in the Ragdoll, annual screening still recommended

Hypertrophic Cardiomyopathy in Other Breeds

Also appears familial in other breeds the:

Norwegian Forest Cat 

British Shorthair 

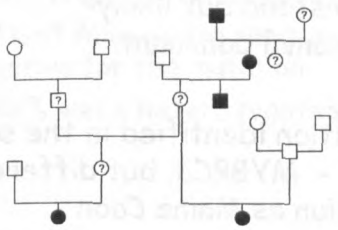
Sphynx 

- None of these breeds have the MC or RD mutation

Sphynx HCM

Sphynx cat HCM

- Likely autosomal dominant



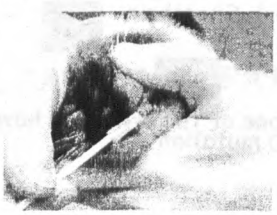
Sphynx cat HCM

- Familial
- Early onset disease (2.5 years)
- Do not have MC or RD mutation
- Do not have a mutation in the 8 most common genes for human HCM

CLINICAL TESTING FOR HCM MUTATIONS

Mutation Screening for the Ragdoll and Maine Coon mutations

- Mutation screening can be performed on a blood sample in EDTA or a buccal swab

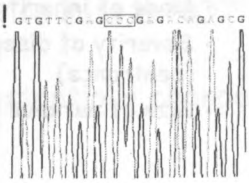


Mutation Screening

- Screening can be performed by two methods
  - PCR based Sequencing (Gold Standard)
  - http://www.vetmed.wsu.edu/deptsVCGL/test.aspx
  - Taqman Assay

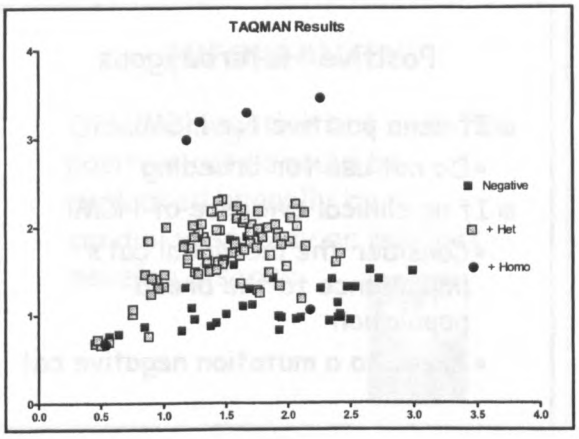
PCR based Sequencing

- Sequence the area of interest to look at mutation
- Higher financial and time expense
- Gold Standard !



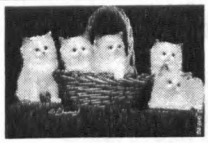
TAQMAN

- DNA is fluorescently labeled, colored dyes are detected and quantified for each allele - for instance "C" or "G" or both
- Quick, less labor intensive
- Inexpensive
- ACCURACY ?

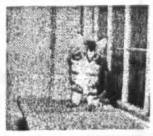


Mutation Screening

- Not all genetic tests are the same!
- Breeders should be strongly encouraged to pay for more expensive PCR BASED SEQUENCING tests

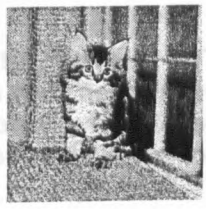


GENETIC SCREENING RECOMMENDATIONS FOR MAINE COONS AND RAGDOLLS



Mutation Screening

- Mutation screening is helpful for breeders interested in pre-breeding screening



Developing Breeding Recommendations

- Genetic testing (molecular or clinical) is often requested
- Most pure breeds have a closed, fairly small gene pool
- If aggressive removal of too many animals occurs it could have a detrimental impact on the breed

Developing Breeding Recommendations

- Screening information should be used to make educated decisions based on :
  - Heterozygous or homozygous mutation (if known)
  - Mode of inheritance
  - Severity of disease in parents (pentrance)
  - Size of national breed organization

Mutation Negative

- Annual echocardiography is still recommended, especially in Maine Coons
  - Since is at least one more mutation

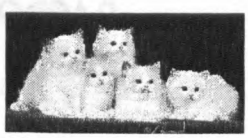
Positive Heterozygous

- If echo positive for HCM:
  - Do not use for breeding
- If no clinical evidence of HCM:
  - Consider the individual cat's importance to the breed population
  - Breed to a mutation negative cat

- Screen offspring of the mating of a Heterozygous X Negative for mutation
- Try to select kittens from this generation that are negative to replace the mutation positive parent in the breeding pool

Over a few generations:

Decrease the prevalence of the disease mutation in the population without greatly altering the gene pool



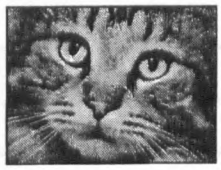
Breeding recommendations

Due to the large number of cats with the mutation in the population, removal of all mutation positive cats is NOT recommended

* And could substantially change the gene pool!

Positive Homozygous

Since both copies of the gene carry the mutation, these cats should not be used for breeding



IMPORTANTLY

Disease negative but mutation positive cats should be evaluated annually by a cardiologist, may or may not develop disease

Clinical Implications

In both breeds, cats that are homozygous for the disease are more likely to develop a severe form of the disease

- **This was especially true in Ragdolls where all homozygotes developed severe dz < 24 months**

Conclusion

Genetic screening for mutations is just one of many TOOLS used to understand and manage this disease

Preliminary data suggests that the mutations do not appear to be causative for HCM in all breeds (NWFC, BSH, or Ragdoll) or in all MC or RD

Not all cats with the mutation will develop the disease, modifiers are likely!

FELINE CARDIOMYOPATHY- CLINICAL DIAGNOSIS AND MANAGEMENT

Kathryn M. Meurs
meurs@vetmed.wsu.edu

Discussion Outline

- Feline Cardiomyopathy
- Feline Hypertrophic Cardiomyopathy
  - Pathophysiology
  - Etiology
  - Therapy
- Miscellaneous Cardiomyopathies

Remember….

Valvular disease in the cat is very rare!!!!

- They do not really get ENDOCARDIOSIS, Endocarditis is RARE!

Always think MYOCARDIAL Disease first

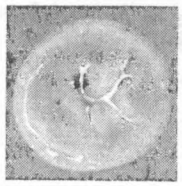
Feline Cardiomyopathy

- Feline cardiomyopathies:
  - Primary muscle disease
  - Adult Onset
- Hypertrophic cardiomyopathy (HCM)
- Dilated cardiomyopathy (DCM)
- Restrictive cardiomyopathy (RCM)
- Arrhythmogenic right ventricular cardiomyopathy (ARVC)
- Unclassified cardiomyopathy (UCM)

Feline Cardiomyopathy

- In many cases, there is significant overlap between HCM, DCM, RCM and even ARVC for:
  - clinical signs
  - ECG
  - radiographic findings
- **Echocardiography is needed to complete the diagnosis.**

Feline Hypertrophic Cardiomyopathy (HCM)

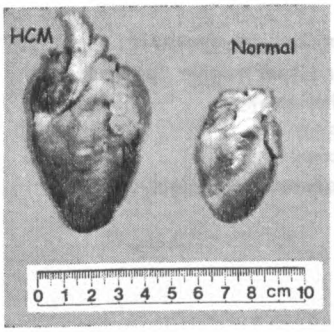


LV hypertrophy w/o causative systemic or other cardiac disease.

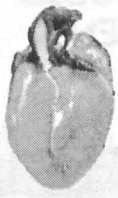
Most common form of heart disease in the cat!

If they are Hyperthyroid, or hypertensive, it is NOT HCM

Hypertrophic cardiomyopathy



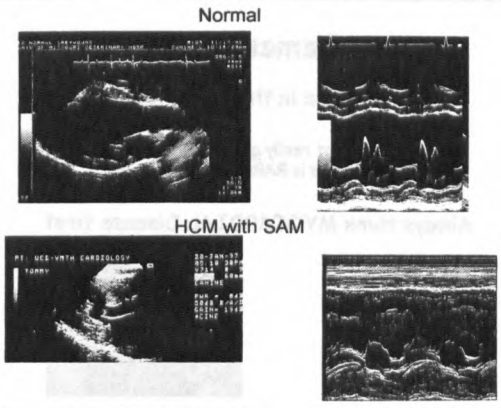
Feline HCM - Pathophysiology



- Diastolic Dysfunction
  - Hypertrophy of the left ventricular free wall and/or IVS
    - myocardial stiffness and decreased lumen size

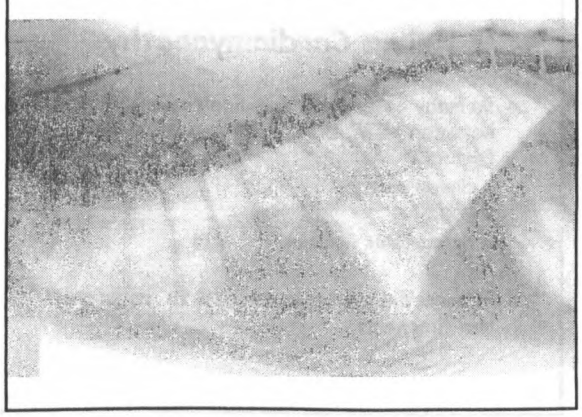
Feline HCM - Pathophysiology

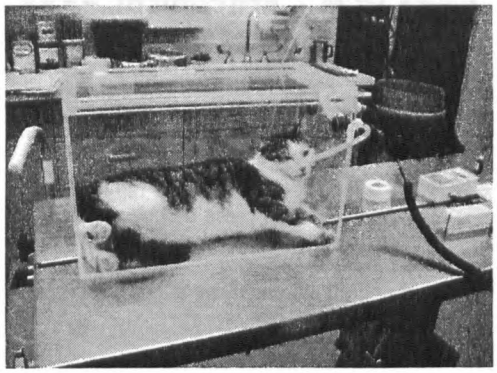
- Mitral regurgitation may develop:
  - from distortion of the LV cavity
  - from systolic anterior motion of the mitral valve (SAM)



Feline HCM - Pathophysiology

- Increased left atrial pressure develops to fill the stiffened left ventricle
  - Elevated pulmonary venous pressure and pulmonary edema may result





Feline HCM - Pathophysiology

- Right Heart Failure secondary to left sided disease
  - Pulmonary hypertension
  - Right ventricular enlargement may occur secondary to the left sided heart disease and generalized fluid retention
- Thrombi
  - may develop in the stretched, dilated atria and subsequently break free and lodge in the systemic circulation (typically the distal aorta)

ETIOLOGY

Feline HCM

- The etiology for the majority of cases is unknown
- Inherited in Maine Coon cats and Ragdolls and is believed to be in the American Shorthair, Rex and a few other cat breeds

Familial Feline HCM

- Causative genetic mutation have recently been identified in the Maine Coon and Ragdoll breeds

Familial Feline HCM

- Cats of other breeds (Sphynx, Bengal, Norwegian Forest Cat, Siberian) do not have the mutation

CLINICAL DIAGNOSIS

Feline HCM - Preclinical ---- Clinical Stages

Feline HCM is a progressive disease with individual variation:

- Affected cats may be asymptomatic
- Dyspnea, and shortness of breath may be presenting complaints due to congestive heart failure
- Acute hindlimb paralysis suggests distal aortic embolization
- Sudden death can occur

Feline HCM - Physical exam

- A systolic murmur consistent with left ventricular outflow tract obstruction and/or mitral regurgitation is common.
- Heart murmurs are never "normal" in a cat, thus a cat with a new murmur deserves discussion of echocardiography

Feline HCM - Physical exam

- A gallop rhythm may be ausculted indicating abnormal LV filling
- Tachypnea, dyspnea may be observed with CHF but crackles are infrequently heard and cats with CHF rarely cough!

Feline HCM - ECG

- Often within normal limits
- Conduction disturbances and arrhythmias (ventricular and supraventricular) may be noted.

Feline HCM - Radiography

- Radiographs may be useful to evaluate :
  - Cardiac size
  - Chamber enlargement patterns
  - Evidence of heart failure
    - Remember that echocardiography does not indicate presence or absence of heart failure, only radiographs can!

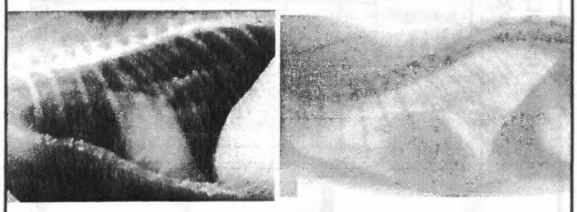
Feline HCM – Radiography

- Radiographs are NOT very useful to diagnose :
  - the specific form of feline heart disease

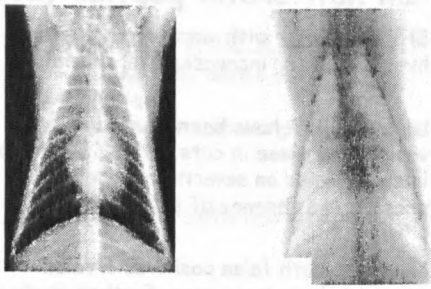
Feline HCM – Radiography

- Range from normal to significant cardiac enlargement depending on stage of disease
- May have evidence of heart failure (pulmonary venous distension, patchy pulmonary edema)

Normal HCM

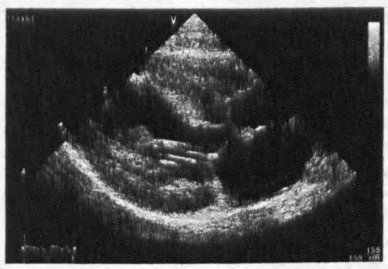


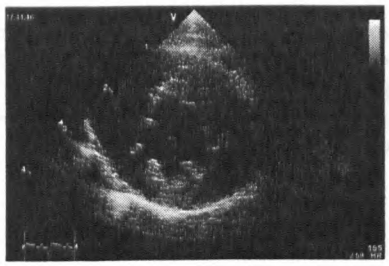
Normal HCM

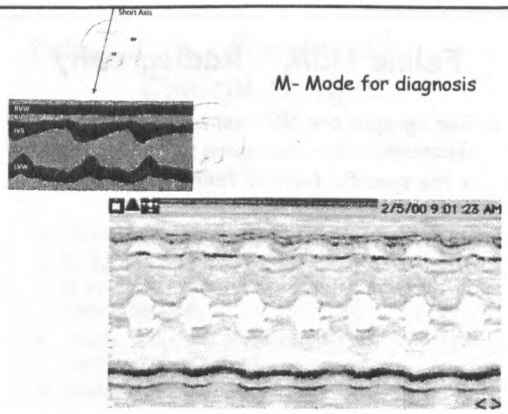


Feline HCM - Echocardiography

- Best diagnostic test !!!
- May have generalized concentric LHV
- Localized left ventricular free wall and / or interventricular septal hypertrophy
- Most use a wall thickness > 6 mm (diastole) as dx

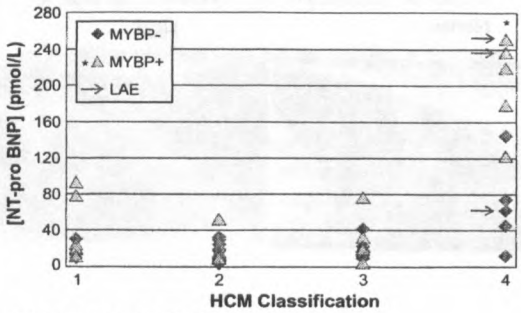






Brain natriuretic peptide (BNP)

- BNP released - with ventricular dilation, hypertrophy or increased wall tension.
- Levels of BNP have been found to have a variable increase in cats with HCM. Increase likely depends on severity of disease & presence or absence of with CHF
- However, both false positives & false negatives have been seen, further study is needed



Hsu A, Kittleson MD, Paling A. J Vet Cardiol 2009;11(S1):S63-70.

Current recommendations for the interpretation of the feline NT-proBNP assay

Concentration (pmol/l) Interpretation

<50 NT-proBNP concentration is not elevated. Heart disease is unlikely.

50-100 NT-proBNP concentration is elevated. Heart disease may be present. **Consider an echocardiogram or repeating test in 3 months if clinical suspicion persists**

100-270 NT-proBNP concentration is elevated and consistent with heart disease or heart failure. An echocardiogram is recommended. If signs of heart failure are present, a chest radiograph is also recommended.

>270 NT-proBNP concentration is significantly elevated. Congestive heart failure is highly likely. Where clinically stable, a complete cardiac workup should be performed. Where clinically unstable, assess whether therapeutic stabilization is required if additional diagnostics prove stressful to the patient

- Connolly , DJ 40, 559-570, 210

Feline HCM - Differential Diagnosis

- Always rule out both hyperthyroidism and systemic hypertension since these can cause similar hypertrophy/ clinical presentation.

Feline HCM - Therapy (Tx)

- Therapy is directed at:
  - Decreasing the heart rate to allow for maximum filling time
  - Decreasing the left ventricular outflow tract gradient if SAM is present
  - Controlling CHF if present
  - Antiarrhythmic needs

Feline HCM - Tx

????

Enalapril?

????

Atenolol?

Diltiazem?

Feline HCM - Tx

- Optimal therapy for asymptomatic cats is uncertain. In general, mildly affected cats are not treated
- Tachycardiac (>220) and outflow obstruction on echo may be considered indications for therapy

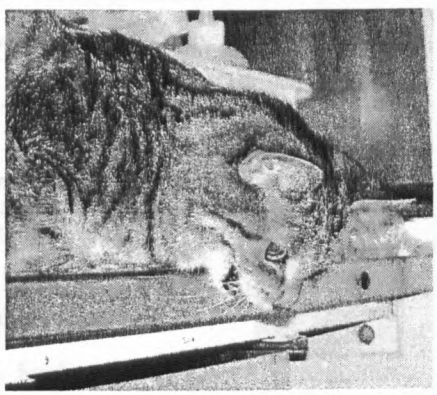
Feline HCM - Tx

- Beta blocker (ATENOLOL, B_1 selective)
  - 6.26-12.5 mg orally twice a day
  - Decreases HR
  - Decreases LV outflow tract gradient if SAM

Do NOT start until out of CHF !!

Feline HCM - Tx

- Calcium channel blocker (Diltiazem)
  - Less effective than previously thought
    - Decreases HR less than Atenolol
  - Ability to decrease left ventricular outflow tract gradient with oral medications is unclear
  - Probably also should wait until out of CHF to start



Feline HCM – Tx for CHF

- Initial hospitalization
  - Furosemide, oxygen, nitrate paste
  - Thoracocentesis if pleural effusion
- When discharged from the hospital
  - Furosemide + ACE Inhibitor (Enalapril or others)
  - +\- atenolol (but not until chf is under control)

Feline HCM- TX plan

Asymptomatic Normal HR	Tachycardia, No CHF	SAM with outflow obstruction	CHF
No Treatment Or Dilatizem or Atenolol	Atenolol	Atenolol	Enalapril, furosemide

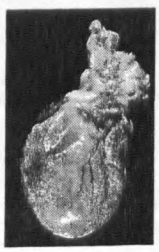
Feline HCM - Prognosis

- Prognosis may vary dependent on etiology:
  - some progress rapidly to CHF
  - some plateau and never progress, live with mild disease
  - Advise owners that prognosis may be determined after observing progression over months
  - CHF or thromboembolic episodes have poorer prognosis

Feline Cardiomyopathy

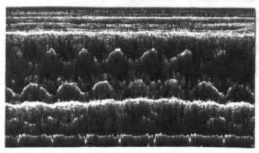
- In many cases, there is significant overlap of clinical signs, ECG and radiographic findings between cats with hypertrophic, dilated and restrictive cardiomyopathy.
- Echocardiography is needed to complete the diagnosis.
- Some forms of myocardial disease defy simple classification

Feline Dilated Cardiomyopathy (DCM)

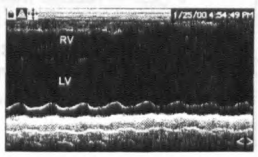


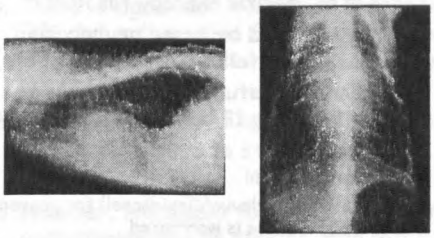
- A functional abnormality of the myocardium causing systolic dysfunction – similar to the canine form
- Uncommon in cats

Normal cat



Dilated cardiomyopathy





Feline DCM - Etiology

- The most common cause is Taurine (an essential feline amino acid) deficiency.
- Although most commercial cat foods are well supplemented, special diets or owner created diets may be deficient

Feline DCM - Etiology

- A small percentage of cats have dilated cardiomyopathy and normal plasma taurine levels, the cause in these cases is unknown.
- Myocarditis may have preceded development of DCM
  - Panleukopenia & histopathologic findings of myocarditis have been ID'd in a small % of DCM cases

Feline DCM - Laboratory evaluation

- Whole blood taurine levels should always be measured (normal mean is >200 nmol/ml)
- Taurine levels should be evaluated even if the diet is "normal"
- Taurine levels are typically low (< 100 nmol/ml) with taurine deficiency.

Feline DCM- Tx

- Treatment should be based on individual problems (heart failure, arrhythmias, etc)
- Positive inotrope
  - Pimobendan (Vetmedin) – 1.25 mg/cat orally q 12 hours
    - Not yet approved for use in cats however so offlabel use
- Taurine supplementation should be given until Taurine deficiency is ruled out. Taurine is given at 250 -500 mg PO BID

Feline Restrictive Cardiomyopathy - (RCM)

- A myocardial disorder characterized by endomyocardial fibrosis, stiffened ventricular wall and impaired ventricular filling.
- This is mainly a **diastolic** disorder
- Systolic function may be normal or decreased.
- Etiology is unknown.

Feline Restrictive Cardiomyopathy - (RCM)

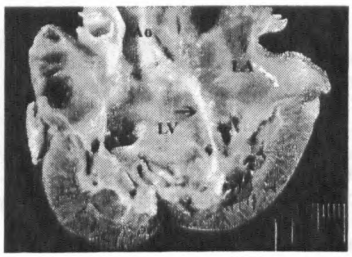


Photo from Dr. Kris MacDonald, Ettinger's Canine and Feline Internal Medicine

Feline RCM -Tx

- There is no specific therapy for RCM
- Treatment should be based on individual problems (heart failure, arrhythmias, etc)
- If myocardial dysfunction - Pimobendan - 1.25 mg-1.5/cat q 12 hours may be beneficial
- Cats with RCM are at a high risk of thromboembolism!
  - Anticoagulents (Plavix/Clopidogrel) for prevention of embolic disease is warranted

Feline Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

- Feline ARVC is an uncommon form of cardiomyopathy
- Although it shares the same name with the Boxer cardiomyopathy it is not the same disease!

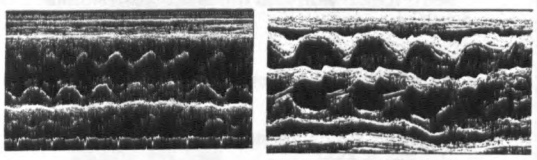
Feline Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

- Disease is characterized by right atrial and ventricular enlargement
- Supraventricular and ventricular tachyarrhyhmias may be observed
- Right heart failure may develop

Feline ARVC

Normal cat

Feline ARVC



Feline ARVC -Tx

- There is no specific therapy for ARVC
- Treatment should be based on individual problems (heart failure, arrhythmias, etc)
- If myocardial dysfunction - Pimobendan - 1.25 mg-1.5/cat q 12 hours may be beneficial
- Cats with RCM are at a high risk of thromboembolism!
  - Anticoagulents (Plavix/Clopidogrel) for prevention of embolic disease is warranted

Feline Cardiomyopathy

- There is significant overlap of clinical signs, ECG and radiographic findings between cats with different forms of cardiomyopathy
- Echocardiography is needed to complete the diagnosis
- However, treatment for heart failure and arrhythmias may be started even without knowing the form of cardiomyopathy

Conclusions

- There is significant overlap between the three forms of cardiomyopathy for:
  - clinical signs
  - ECG
  - radiographic findings
- **Echocardiography is needed to complete the diagnosis.**
- The best therapies are not well understood and may not be the same for all CM Cases

Cardiac Clinical Decision Making

Bruce Kornreich DVM, PhD, DACVIM (Cardiology)
Cornell University

In working up clinical cases, I find it helpful to ask a series of questions regarding a number of physiologic parameters for each case. The majority of these questions and their associated parameters are common to all cardiac cases, while a few are more clinically relevant in particular species (i.e. likelihood of thrombosis in cats). Asking these same questions and answering them appropriately for each case provides an organized means of making clinical decisions regarding cardiac cases.

The Questions

1) Does the patient need **preload** modification?

   Preload is roughly defined as the pressure that stretches the ventricle immediately prior to the onset of systole. According to the Frank-Starling Law, an increased preload will result in an increased stroke volume unless the ventricle is stretched beyond the point of optimal actin/myosin overlap, providing a mechanism to synchronize cardiac output with venous return. Decreased preload may result in decreased stroke volume, which may decrease cardiac output unless a compensatory increase in heart rate occurs (CO = SV x HR). Increased preload may cause increased ventricular wall stress with resultant increase in myocardial oxygen demand, which may predispose to arrhythmias or myocardial cell death. Patients that are dehydrated may require an increase in preload via fluid therapy, while patients with volume overload may require a decrease in preload, most commonly achieved by diuretic and/or angiotensin converting enzyme inhibitors (ACEI).

2) Does the patient need **afterload** modification?

   Afterload is roughly defined as the load against which the ventricle must eject its stroke volume. Common causes of increased left ventricular afterload include systemic hypertension (not uncommon in the cat) and fixed aortic stenosis (rare in the cat). An increase in afterload may increase ventricular wall stress, with subsequent increase in myocardial oxygen demand, which may predispose to arrhythmias or myocardial cell death. Afterload reduction may increase stroke volume and decrease ventricular wall stress and myocardial oxygen consumption. Afterload reduction may be achieved with ACEI, calcium channel blockers, alpha 1 adrenergic receptor blockers, or phosphodiesterase inhibitors.

3) Does the patient need a reduction in **congestion**?

   Patients commonly present with clinical signs that are due to congestive failure. Left sided congestive failure results in the development of pulmonary edema, while right sided congestive failure most commonly results in the development of

pleural effusion. Pleural effusion may also be seen in cats with apparent left sided congestive failure. Cats that present in respiratory distress (most commonly due to pulmonary edema secondary to left sided congestive failure) are in a tenuous physiologic state and are prone to respiratory and/or cardiac arrest. Reduction in pulmonary congestion is the primary treatment goal in patients with left sided congestive failure. This is most commonly and most effectively achieved by diuretic administration.

4) Does the patient need **inotropic** support?

Inotropic function refers to the ability of the ventricle to generate positive pressure during systole to eject its blood volume. Cats with decreased inotropic function either due to primary dilated cardiomyopathy, chronic volume overload, or long standing hypertrophic cardiomyopathy may benefit from positive inotrope administration. Positive inotropes have historically relied upon increasing intracellular calcium concentration. This increases the likelihood of calcium binding to troponin C, which disinhibits troponin I, allowing cross bridging to occur between actin and myosin (the final event in excitation-contraction coupling). More recently, calcium sensitizers, which increase the affinity of calcium for troponin C, have been developed. These compounds increase the likelihood of a binding event between calcium and troponin C without incurring the potentially deleterious effects of elevated intracellular calcium. Although not as commonly used in cats as in canine patients, positive inotropes may benefit feline patients with systolic dysfunction.

5) Does the patient need **lusitropic** support?

Lusitropy refers to myocardial relaxation, or the ability of the ventricle to generate negative pressure during diastole to promote ventricular filling. Hypertrophic cardiomyopathy (HCM), which is the most common cardiac disease in cats, is a disease of diastolic, or lusitropic, dysfunction. While calcium channel blockers and beta blockers may improve diastolic function (this is controversial), we most often strive to improve diastolic function by promoting an equalization between myocardial oxygen demand and supply. This can be achieved by controlling heart rate (see below) and by decreasing wall stress (see above).

6) Does the patient need **rhythm** control?

This issue may be roughly divided into two categories. The first, which is a common issue in feline patients, is rate control. Cats with HCM, for example, commonly present with tachycardia (i.e. sinus tachycardia) due to the compensatory mechanisms that strive to maintain cardiac output in the setting of decreased stroke volume (CO = SVxHR). Tachycardia can increase myocardial oxygen demand, which can promote ischemia, arrhythmias, and ultimately myocardial cell death. Control of tachycardia in cats is most commonly achieved by administration of beta blockers, although calcium channel blockers may also

be used for this purpose. Cats in atrial fibrillation most commonly have significant structural heart disease that precludes conversion to normal sinus rhythm. In these cases, ventricular rate control with calcium channel blockers, digoxin, and/or beta blockers is commonly employed. In rare cases, cats may present with bradycardias (i.e. sinus bradycardia, second and third degree AV block), which may decrease cardiac output and cause clinical signs of weakness/collapse. In these cases, although parasympatholytics and/or phosphodiesterase inhibitors may be used to maintain heart rates as high as possible, the definitive therapy is permanent pacemaker implantation. The second category of rhythm disturbances that may require intervention is arrhythmias that may degrade into rhythms that decrease cardiac output (most commonly by increasing heart rate). Ventricular ectopy (i.e. VPCs, VT) may require antiarrhythmic therapy with sodium channel blockers such as lidocaine, although beta blockers are most commonly used chronically. Generally speaking, antiarrhythmics are less commonly used in cats than in dogs.

6) Does the patient need **antithrombotic** medication?

This is an example of an issue that is of greater concern with feline patients. Cat platelets are highly aggregable, and cats with dilated left atria are prone to the formation of intracardiac thrombi, which may embolize systemically. Thromboembolism most commonly occurs at the bifurcation of the abdominal aorta (saddle thrombus), and this is a devastating sequela of HCM that is a poor prognostic indicator. Intracardiac thrombi may be visualized with echocardiography, and spontaneous contrast (smoke like appearance within left atrium/ventricle) may be a harbinger of impending thrombosis. Aspirin and/or clopidogrel therapy may be used to decrease the likelihood of further thrombosis, and the results of a large, ongoing clinical study (FATCAT) carry promise of determining whether aspirin or clopidogrel monotherapy is superior for the prevention of feline thromboembolism. While thrombolytic agents (i.e. streptokinase, urokinase, and tissue plasminogen activator) carry theoretical benefit, the side effects/reperfusion phenomena associated with these agents most commonly precludes their clinical use.

NON-OBSTRUCTIVE IDIOPATHIC/INTERSTITIAL CYSTITIS IN CATS: THINKING OUTSIDE THE (LITTER) BOX

Dennis J. Chew, DVM Diplomate ACVIM (Internal Medicine)
CAT Buffington, DVM PhD Diplomate ACVN
Department of Veterinary Clinical Sciences
The Ohio State University College of Veterinary Medicine, Columbus, Ohio

Introduction

A diagnosis of interstitial cystitis in people and cats requires identification of the presence of characteristic (although non-specific) sub-mucosal petechial hemorrhages-referred to as glomerulations) by cystoscopy, though the diagnostic value of this criterion is under debate. It is likely that the term idiopathic or interstitial cystitis in cats will be supplanted by more specific diagnoses as we improve our understanding of this frustrating syndrome. Results of studies over the past decade indicate that idiopathic cystitis in cats is the result of complex interactions between the bladder, nervous system, adrenal glands, husbandry practices, and the environment in which the cat lives (further detailed under pathophysiology).

Differential Diagnosis

Dysuria, stranguria, pollakiuria, macroscopic hematuria, and urinating in places other than the litterbox (inappropriate urination or periuria) are non-specific signs that, individually or in some combination, cause clients to bring their cats to a veterinarian due to apparent nonobstructive problems with the lower urinary tract regardless of the underlying cause. In cats less than 10 years of age, idiopathic cystitis accounts for clinical signs of irritative voiding in 60 to 70% of cats. Urolithiasis is encountered in 10 to 20% of cases with most, being associated with either calcium oxalate or struvite. About 10 % may have an associated structural abnormality such as urachal diverticulum or urethral stricture, another 10% have what appears to be a behavior disorder, less than 2 % of cases will be associated with urinary infection, and less than 1% can be expected to have bladder or urethral neoplasia.In cats older than 10 years of age at first presentation, only about 5% can be expected to be idiopathic. More than half of cats in this age category will have bacterial urinary tract infection, either alone or in association with urolithiasis. Many of these cats with positive quantitative bacterial cultures will have renal disease and sub-maximally concentrated urine.

Diagnosis

Idiopathic cystitis affects males and females equally, although neutered males and females are at increased risk compared to their intact counterparts. An affected cat typically is 1 to 10 years of age (peak risk 2-6 years), spends all or nearly all of its time living indoors with humans, is expected to use a litter pan for urination and defection, and eats 75 to 100% dry food. Obesity and a variety of other comorbid conditions may be associated with idiopathic cystitis. Owners sometimes note that affected cats are unusually nervous, fearful, or aggressive, and are overreactive to their environment compared to healthy cats. Cats with access to the outdoors still can be affected, especially when the cat population in the outdoor area is dense. Abdominal palpation may reveal pelvic organ pain and/or thickening of the bladder wall in some affected cats. The bladder is usually small during active bouts of cystitis. The rest of the examination is often normal. Rarely, barbering of hair in the caudal abdomen may represent referred pain. It is our impression that cats with IC have more heart murmurs and gallop rhythms than cats with other disorders.

Urinary tract imaging is recommended for all cats with recurrent LUTS. Survey radiographs are helpful to identify radiodense calculi such as calcium oxalate or struvite, which usually are observed if ≥ 2-3mm in size. In those cats with multiple recurrences or persistence of clinical signs, advanced urinary imaging should be pursued to exclude radiolucent calculi and anatomical defects if the survey radiographs were normal. Abnormalities that can be identified during double-contrast cystography include focal or diffuse thickening of the bladder wall, permeation of contrast agent into the bladder wall or through the bladder and into the abdomen, and filling defects in the contrast pool (blood clots and cellular debris). Ultrasonography (ULS) can be a useful, less invasive method of imaging than contrast urethro-cystography. The proximal urethra can be examined with ULS, but ULS is not a good method to image the urethra, as most of the urethra cannot be examined. Cystoscopy (uroendoscopy), which provides direct visualization of the internal surface of the bladder, is available at some referral centers. Excellent evaluation of the urethra and bladder lumen usually is possible in female cats weighing at least 3 kg using

a rigid pediatric cystoscope. The bladder of idiopathic cystitis cats will often display a varying degree of increased vessel density and tortuosity, edema, and sub-mucosal petechial hemorrhages (glomerulations). Increased number or size of glomerulations and increasing edema can be observed when higher bladder filling pressure (~80 cm water) is used during the scoping, findings that do not happen in cats with normal bladders.

Findings from urinalysis are useful, but are neither sensitive nor specific. The classical findings of hematuria and proteinuria in cats affected with idiopathic cystitis often wax and wane between days and even within the same day. Additionally, it is impossible to know with certainty that red cells and protein in the urine did not enter during collection when cystocentesis is performed. The classical positive finding is "hemorrhagic inflammation", which means that there is a preponderance of red blood cells with few neutrophils in the urine sediment. Crystals often are not present when fresh urine is evaluated. If crystals are observed, they usually are present in low numbers. Refrigeration can cause the formation of crystals ex vivo that were not present in vivo. Regardless, the presence of crystals has NO known diagnostic or pathophysiologic impact on non-obstructive forms of idiopathic cystitis. Struvite or calcium oxalate crystals do not damage a healthy urothelium. Conventional wisdom previously held that crystals formed and subsequently caused damage to the lower urinary tract, but it is more likely that sterile (neurogenic) inflammation occurs first, plasma proteins exude into urine, urinary pH increases, and then struvite crystals precipitate as a secondary event. It is physiologically normal to observe a few crystals in urinary sediment, especially when the urine is highly concentrated. The urine specific gravity (USG) in healthy cats should be greater than 1.025 in those eating mostly canned foods, and greater than 1.035 in those eating exclusively dry foods. In cats with LUTS and USG less than 1.025, some systemic disease (renal disease, renal failure, hyperthyroidism, diabetes mellitus) may be present that is interfering with the formation of more concentrated urine. Though not specifically studied, our impression is that cats with extremely high USG (1.060-1.080) are at higher risk for perpetuation of idiopathic cystitis once initiated if not transitioned to a therapy that produces a lower USG.

Pathophysiology

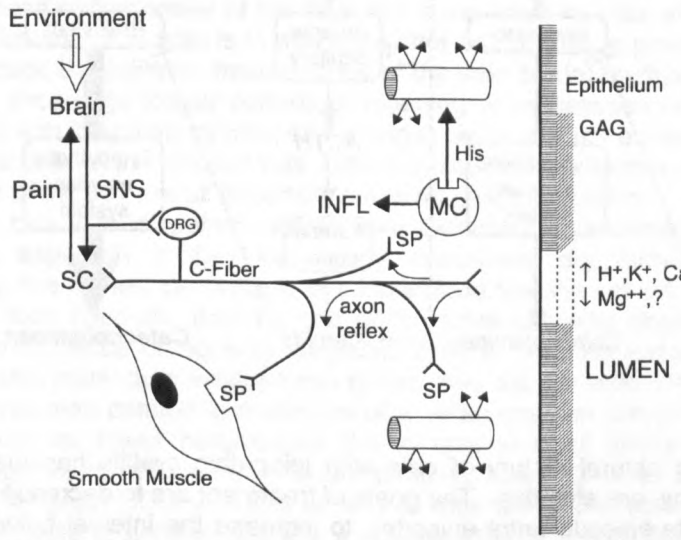
Idiopathic cystitis can be acute or chronic. Clinical signs associated with an initial or recurrent episode of idiopathic cystitis often resolve within about 7 days with or without treatment. Nearly 50% of cats with idiopathic cystitis will have recurrent signs within one year based on recent studies. It appears that most cats with recurrence have episodic signs of idiopathic cystitis, but some have persistent clinical signs that do not abate.

The pathophysiology of chronic idiopathic cystitis appears to involve complex interactions between multiple body systems. Abnormalities have been found in the bladder, nervous system, hypothalamic-pituitary-adrenal axis, and other body systems in cats with idiopathic cystitis. Histological changes, urothelial abnormalities, and decreased excretion of both total urinary GAG and a specific GAG, GP-51, have been identified in the bladders of cats with idiopathic cystitis. Histological changes generally are nonspecific, and may include an intact or damaged urothelium with submucosal edema, dilation of submucosal blood vessels with marginated neutrophils, submucosal hemorrhage, and sometimes increased mast cell infiltration. There is a paucity of neutrophilic infiltration, but there may be a minor increase in lymphoplasmacytic cells in the submucosa.

In the brain, a significant increase in tyrosine hydroxylase (TH) immunoreactivity (IR) has been in cats with idiopathic cystitis. Tyrosine hydroxylase is the rate-limiting enzyme of catecholamine synthesis. Chronic activation of the stress response system can increase TH activity in the LC, with accompanying increases in autonomic outflow. The increased THIR observed in the LC of cats with idiopathic cystitis may provide a clue to the observation that clinical signs follow a waxing and waning course in animals with this disease, and can be aggravated by environmental stressors. Increased plasma norepinephrine (NE) and CSF catecholamine concentrations and their metabolites have been documented in cats with idiopathic cystitis when measured during stressful situations.Increased noradrenergic outflow may alter urothelial permeability, increasing C-fiber activity, and activate local neurogenic inflammatory mechanisms. Increased epithelial permeability could permit constituents of urine to gain greater access to sensory afferent neurons in the bladder wall, which could result in increased sensory afferent firing and local inflammation.

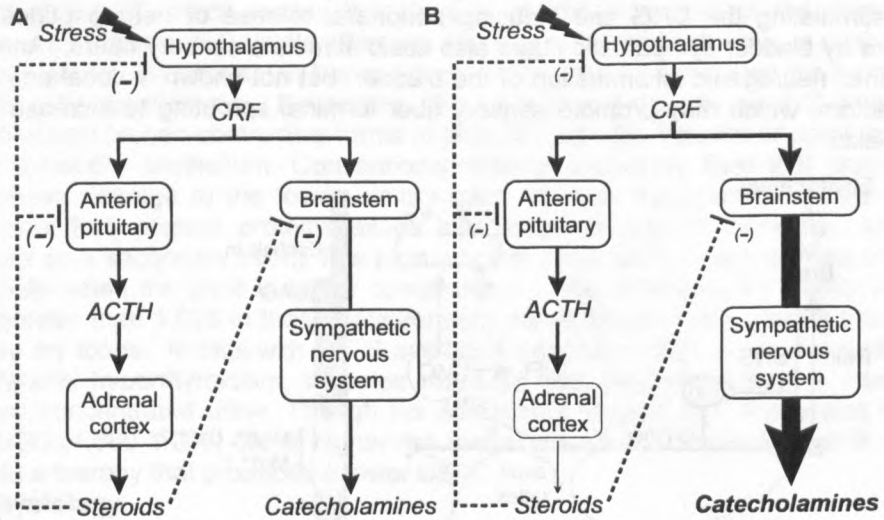
Neurogenic inflammation as it affects the urinary bladder in interstitial cystitis. Sensory neurons (C-Fiber) seem to play a central role in transmission of action potentials via the dorsal root ganglia (DRG) to the spinal cord (SC) and brain. These signals may be perceived as painful by the brain. Sensory fibers also can

propagate a local axon reflex without transmission of an axon potential. The axon reflex results in release of peptide neurotransmitters such as substance P (SP) by the nerve endings. Interaction of SP with receptors on vessel walls results in vascular leakage, which can be augmented by SP-induced release of histamine by mast cells. These actions may give rise to the submucosal petechial hemorrhages (glomerulations) observed at cystoscopy. Receptors for SP also occur on smooth muscle, which when activated stimulate muscle contraction. Also shown are the urothelium (epithelium) and the overlying glycosaminoglycan (GAG) layer adjacent to the bladder lumen. Damage or malfunction of either or both of these layers may permit constituents of the urine, such as protons, potassium ions, or hyperosmolar (>2,000 mOsm/L) fluid to activate the sensory fibers. The effects of stress on sensory fibers may be related to descending efferent sympathetic (SNS) signals stimulating the DRG and inducing peripheral release of neuropeptides. Local release of neurotransmitters by bladder sympathetic fibers also could stimulate sensory fibers. Another factor probably involved in chronic, neurogenic inflammation of the bladder, but not shown, is local and systemic release of nerve growth factors, which may promote sensory fiber terminal sprouting to increase the size of sensory fiber receptive fields.



Abnormalities in the hypothalamic-pituitary –adrenal axis (HPA) also have been observed in cats with idiopathic cystitis. Increased concentrations of corticotropin releasing factor (CRF) from the hypothalamus and ACTH from the anterior pituitary gland have been identified at times of decreased serum cortisol response to ACTH stimulation during periods of stress in cats with idiopathic cystitis, documenting the presence of reduced adrenocortical reserve in this population. CRF stimulates both the release of ACTH from the anterior pituitary and activation of the sympathetic nervous system in the brainstem. During chronic stress in cats with idiopathic cystitis, there appears to be a disproportionate activation of noradrenergic outflow in the absence of a parallel increase in outpouring of adrenocortical steroids (ACS). This phenomenon may be important since cortisol and other ACS normally restrain sympathetic nervous system outflow, and also inhibit their own release by feedback inhibition at the level of the anterior pituitary and hypothalamus to terminate the stress response. Decreased ACS activity may adversely affect epithelial permeability, as cortisol is known to enhance tight junction integrity to reduce permeability in other tissues. However, cats with idiopathic cystitis do not appear to experience long-term benefit from current glucocorticoid therapy regimens.

Imbalanced neuroendocrine system of cats with idiopathic cystitis. Excitatory sympathetic nervous system (SNS) outflow is inadequately restrained by cortisol and other adrenocortical steroids. This enhanced activity can increase tissue permeability, resulting in increased sensory afferent activity. Feedback inhibition at the level of the anterior pituitary and hypothalamus also is reduced, which tends to perpetuate corticotrophin releasing factor (CRF) output. Neurosteroid production by the adrenal cortex, which generally enhances central nervous system (CNS) inhibitory tone during chronic stress, also may be reduced. The bold solid arrows indicate stimulation, and the dotted arrows indicate. Line thickness is intended to indicate intensity of the signal.



Treatment

The waxing and waning natural history of cats with idiopathic cystitis has made it difficult to determine which treatments, if any, are effective. The goals of treatment are to decrease the severity and duration of signs during an acute episode (intra-episode), to increase the interval between episodes in those with recurrent idiopathic cystitis (inter-episode), and to decrease severity of signs in those with persistent idiopathic cystitis. Based on the pathophysiology described above, it is crucial to reduce the output of the sympathetic nervous system, since enhanced noradrenergic outflow appears to potentiate clinical signs by a variety of mechanisms. Based on the premise that cats with idiopathic cystitis are "sensitive cats in a provocative environment" one important objective of therapy is to identify and hopefully modify provocateurs (e.g., diet, water, indoor living with humans, sub-optimal husbandry, stress, and inactivity). Since chronic pain perception can amplify noradrenergic outflow, it is important to consider treatments that provide analgesia. Breaking the pain-inflammation cycle can be an important step in the management of some cats with chronic idiopathic cystitis. Providing analgesia systemically appears to be more important than analgesia within the bladder locally.

Treatment of a First Episode or an Infrequent Acute Flare

Resolution of clinical signs occurs in an estimated 85% of cats within one week, often without treatment, though the recurrence rate for clinical signs is high within the next 6 to 12 months with (or without) conventional treatment. Clinical signs for longer than 7 days are beyond the point of spontaneous resolution for most cats so specific recommendations are justified at that time.

Relief of bladder pain during acute episodes or flares of chronic idiopathic cystitis is recommended. Though not specifically studied, oral buprenorphine at 5 to 20 micrograms/kg BID to QID for 3 to 5 days has been helpful in providing relief to affected cats in our practice. Whether adequate provision of analgesia during acute episodes impacts development of future episodes currently is not known. The best regimen of analgesia for bladder pain (visceral) has yet to be determined.

Environmental Modification (EM) – Level 1

The overarching premise of EM is that some cats suffer adverse consequences of indoor housing, especially when cats are forced to spend nearly all of their time indoors in association with people and other animals. Ethological and behavioral studies demonstrate that captivity may elicit a

stress response in some cats. The indoor environment of some house cats may be monotonous and predictable, which could be stressful. If we are to continue to recommend indoor housing to reduce the risks of exposure to accidents and infectious agents, recommendations to improve the indoor environment from the cat's point of view should be developed. Many indoor-housed cats appear to survive adequately by accommodating to less than perfect surroundings. The neuroendocrine abnormalities in cats with recurrent idiopathic cystitis suggest a sensitized response to stress indicating that these cats may have greater needs for enriched surroundings than do healthy cats. Extensive indoor housing in unenriched environments does not create idiopathic cystitis, but it can contribute to its development and maintenance by unmasking the tendency of a particular cat to develop idiopathic cystitis in response to external risk factors.Successful EM may obviate the need for drug therapy in many instances. Based on uncontrolled prospective studies at our hospital, we estimate that 80% of cats with recurrent idiopathic cystitis will have clinically significant reductions in signs during the year following successful implementation of the first level of EM. Stressors in an individual cat can emanate from another cat, people, other aspects of environment, or combinations of these.

Enhanced management of the litter box is essential for cats with idiopathic cystitis, and for those with "toileting issues". The goal is to make the litter box a pristine place for the cat to eliminate. Nothing should discourage the cat from frequent trips to the litter box – anything that discourages use of the litter box also may encourage longer periods of retaining urine between urinations. This may have adverse effects on cats with idiopathic cystitis, since longer periods of urine retention may facilitate constituents of urine gaining access to the bladder wall. Litter tray numbers, locations, cleaning schedule, substrate type, and the nature of the tray are all important areas for client education.

Some cats with idiopathic cystitis have extremely concentrated urine based on specific gravity (1.060-1.080), especially if they eat nearly exclusively dry formulations of commercial cat food. Transitioning to the highest percentage of canned food that the cat will eat, or adding water to dry food or to semi-moist food pouches, may be one of the most powerful single treatment recommendations for prevention of recurrence of signs of idiopathic cystitis. Adding water to pouches of semi-moist foods forms a gravy that many cats will consume before they eat the solid portion. Cats with recurrent idiopathic cystitis that consumed canned formulations of a veterinary diet compared to a similar formulation of the dry product had far fewer recurrences during one year of therapy. The benefit from the canned formulation might have resulted from a substantially lower USG compared to that of cats fed the dry formulation. The target USG is 1.030 or less to attempt to decrease recurrence of clinical signs. It is difficult to impossible to achieve this low a specific gravity in cats that continue to consume mostly dry food. Even when the desired target zone cannot be achieved, any reduction in USG has the potential to be helpful.

Dietary modification should be recommended mostly to increase water intake and decrease the concentration of noxious substances in urine as described above. However, some cats and owners prefer dry foods, and may become stressed by forced transition to canned foods. Attempts to further acidify urine and minimize struvite crystalluria often are not indicated, since no evidence supports the notion that struvite crystalluria damages normal urothelium or worsens existing cystitis in non-obstructive forms of idiopathic cystitis. Perhaps more important is maintaining the constancy, consistency, and composition of the diet that is being fed.

Intercat conflict commonly is present when multiple cats are housed indoors together and health problems are present. Conflict among cats can develop because of threats to the cat's perception of their overall status in the home, from other animals in the home, or from outside cats. The goal is to reduce conflict to a more manageable level for the cats involved. Treatment for conflict between indoor cats involves providing a separate set of resources for each cat, preferably in locations where the cats can use them without being seen by other cats.

Environmental modification also involves providing resources and interactions with and for cats to simulate some of the activities that they encounter in the wild. Simulations of prey, including laser light pointers, lures, and feathered fishing pole toys can provide useful interactions for some cats. Cats often enjoy playing with toys, particularly those that are small, move, and that mimic prey characteristics. Use of containers or toys that intermittently release food during play may provide actions to simulate hunting behavior.

Cats generally prefer more space than the average house or apartment provides. Cats interact with both the physical structures and other animals, including humans, in their environment. The physical environment should include opportunities for scratching (both horizontal and vertical may be necessary),

climbing, hiding, and resting undisturbed. Cats seem to prefer to monitor their surroundings from elevated vantage points, so climbing frames, hammocks, platforms, raised walkways, shelves or window seats may appeal to them.

Synthetic feline facial pheromones are marketed to reduce urine marking or spraying behaviors in cats (Feliway; Ceva Sante Animale, Libourne, France). These pheromones reduce the vigilance of the cat so that the cat's need to mark or spray its territory is reduced. Since vigilance of cats is maintained largely by activity of the sympathetic nervous system, it is possible that use of these pheromones contributes to decreased adrenergic outflow from the brainstem in some cats. If so, they could be useful for treatment of chronic idiopathic cystitis in cats. A statistically significant effect could not be demonstrated in a study comparing facial pheromones and placebo in cats affected with idiopathic cystitis, though there appeared to be a positive trend. There appears to be a salutary effect of these pheromones in some cats (personal observations) and we continue to prescribe their use.

Further Environmental Modifications – Level 2

If implementation of EM at Level 1 does not adequately reduce signs of idiopathic cystitis, it is important to go back and review what was implemented and what was not, and why. Alternative approaches should be suggested for those that were not initially implemented based on collaboration with the client to address reasons for failure. Additional modifications also may be added at this time. Increased exposure to the outdoors can be helpful in the management of some cats.

Drug therapy is not attempted until analgesics have been administered and level -1 environmental modifications have been implemented without adequate resolution of clinical signs (including low-grade persistent signs, or frequent recurrence of clinical signs).

Tricyclic analgesics/antidepressants (TCA) can decrease clinical signs in some cats with recurrent idiopathic cystitis. Possible mechanisms include stabilization of mast cells (which may infiltrate the bladder wall during idiopathic cystitis), reduced contractions of detrusor muscle from anticholinergic effects, decreased sensory nerve pain fiber sensations from the bladder, effects on sodium, potassium, and glutamate channels, and downregulation of norepinephrine outflow from the brain. Two recent studies found no benefit of TCA for acute bouts of idiopathic cystitis; abrupt cessation of TCA administration after 7 days increased the severity of clinical signs and frequency of recurrence in one study. Prescription of amitriptyline was associated with resolution of clinical signs in 60 % of cats with severe recurrent idiopathic cystitis for one year during administration of 10 mg once daily by mouth at the owner's bedtime. Despite the decrease in clinical signs, no improvement in the cystoscopic appearance of the bladder mucosa was observed.. We prescribe TCA only when the EM treatments described above have not been sufficiently helpful. Cats may have a marked decrease in clinical signs of idiopathic cystitis during such treatment with amitriptyline, the TCA with which we have had the most experience. Despite the improvement in clinical signs, behavior of these cats may change, and weight gain and poor grooming may be noted by clients. We sometimes prescribe TCA while environmental modifications are being implemented. If EM is successful in reducing the cat's stress, it may be possible to taper the dose of TCA gradually and in some instances to stop this form of medication.Due to possible effects on liver enzymes or function during administration of TCA, we recommend a serum biochemical panel prior to starting the drug and again at 1,3 and 6 months during treatment. A complete blood count (CBC) is also recommended to ensure no adverse effects of chronic treatment are occurring (thrombocytopenia and neutropenia). TCA should be used cautiously if at all in cats with serious heart disease.

Studies to date have not shown a benefit of glucosamine or pentosan polysulfate (PPS) supplementation over that of placebo to cats with idiopathic cystitis. Whether GAG supplementation has a benefit in combination with other treatments, such as TCA or environmental modification, has not been investigated in cats. Diarrhea at routine doses and coagulopathy at high doses are possible side effects of GAG supplementation, but are rare.

References

Buffington CA, Westropp JL, Chew DJ, Bolus RR: Clinical evaluation of multimodal environmental modification (MEMO) in the management of cats with idiopathic cystitis. J Feline Med Surg 8(4): 261-268, 2006.

Buffington CA, Chew DJ, Woodworth BE: Feline interstitial cystitis. J Am Vet Med Assoc 215(5): 682-687, 1999.

Chew DJ, Buffington CA, Kendall MS, DiBartola SP, Woodworth BE: Amitriptyline treatment for severe recurrent idiopathic cystitis in cats. J Am Vet Med Assoc 213(9): 1282-1286, 1998.

Gunn-Moore DA, Shenoy CM: Oral glucosamine and the management of feline idiopathic cystitis. *J Feline Med Surg* 6(4): 219-225, 2004.

Gunn-Moore DA, Cameron ME: A pilot study using synthetic feline facial pheromone for the management of feline idiopathic cystitis. *J Feline Med Surg* 6(3): 133-138, 2004.

Kraijer M, Fink-Gremmels J, Nickel RF: The short-term clinical efficacy of amitriptyline in the management of idiopathic feline lower urinary tract disease: a controlled clinical study. *J Feline Med Surg* 5(3): 191-196, 2003.

Kruger JM, Conway TS, Kaneene JB, Perry RL, Hagenlocker E, Golombek A, Stuhler J: Randomized controlled trial of the efficacy of short-term amitriptyline administration for treatment of acute, nonobstructive, idiopathic lower urinary tract disease in cats. *J Am Vet Med Assoc* 222(6): 749-758, 2003.

Markwell PJ, Buffington CA, Chew DJ, Kendall MS, Harte JG, DiBartola SP: Clinical evaluation of commercially available urinary acidification diets in the management of idiopathic cystitis in cats. J Am Vet Med Assoc 214(3): 361-365, 1999.

Figure 1: A Normal bladder. Urine is repelled by the normal uroepithelium of the bladder and the glycosaminoglycan (GAG) layer. B: Chronic FIC showing increased bladder permeability. The GAG layer (1) or the GAG layer and the uroepithelium (2) have been damaged, allowing urine to permeate the bladder wall. Increased permeability in chronic FIC cats has been demonstrated even when cats were not showing signs of active inflammation. Infiltration with mast cells and increased numbers of sensory nerve fibers are a result (2).

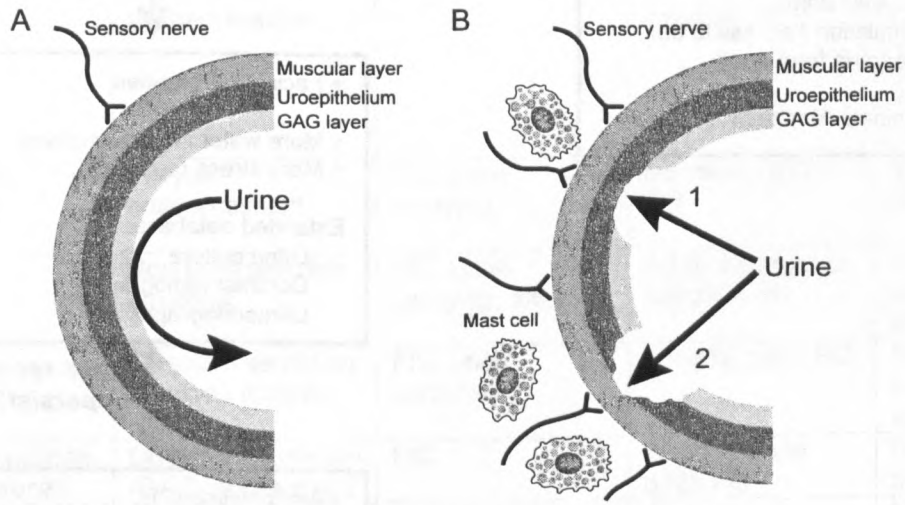


Figure 2. What do WE Do ? Step-wise approach to treatment of cats with idiopathic lower urinary tract signs. More diagnostics should be performed when cats fail to spontaneously clear of their initial lower urinary tract signs and when signs recur to ensure that the diagnosis is really idiopathic lower urinary tract disease. Properly controlled clinical trials may provide better approaches to treatment in the future, but this is what we do in the interim.

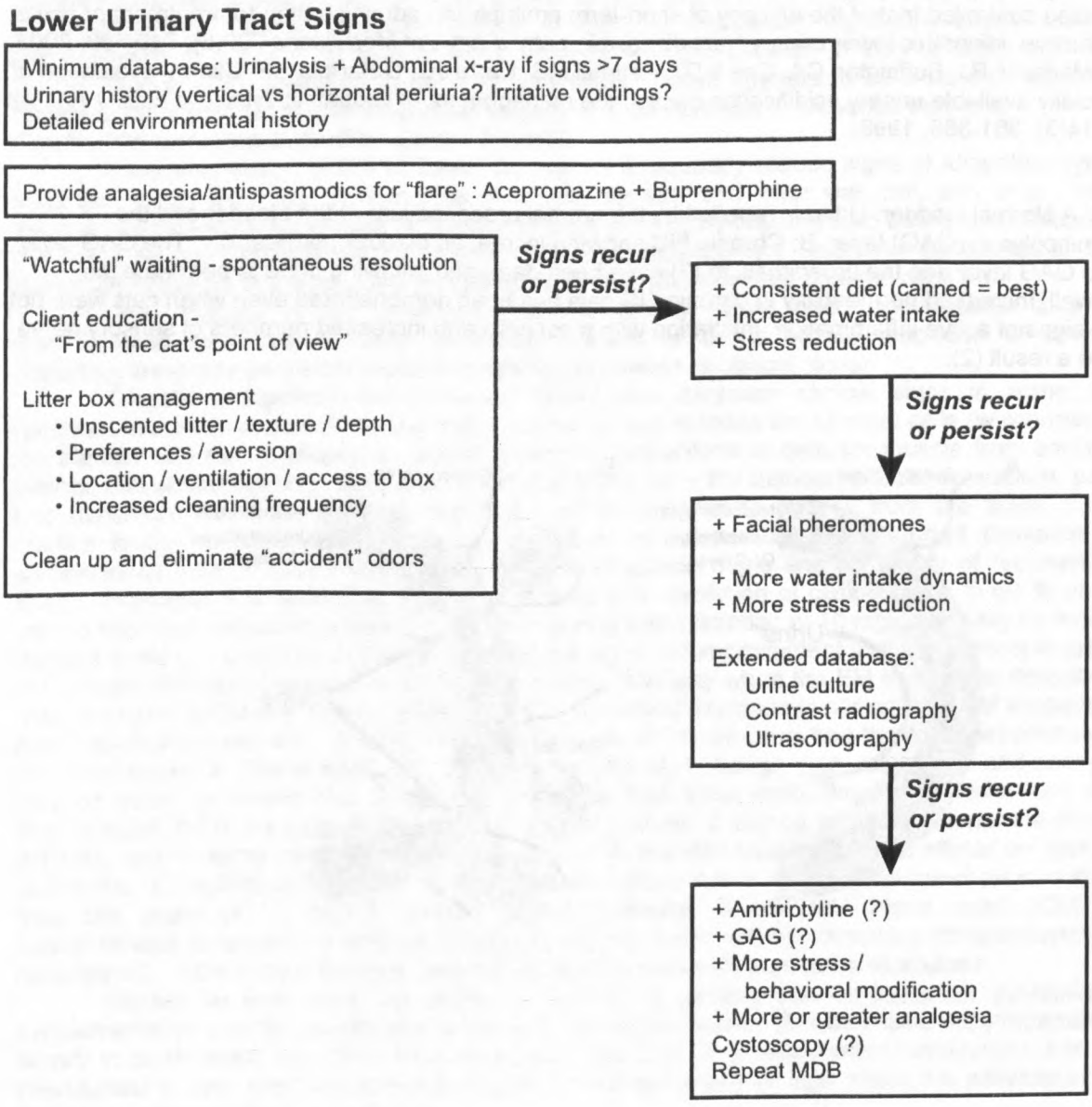


Table 1: Drugs used in the management of FIC

Acute therapy				
Drug	**Class**	**Indications**	**Dosage**	**Potential adverse effects**
Butorphanol (Torbugesic®)	Synthetic partial opioid agonist	Analgesia, acute episode	0.2-0.4 mg/kg q8h PO or SC	Sedation
Buprenorphine (Buprenex®)	Synthetic partial opioid agonist	Analgesia, acute episode	0.01-0.02 mg/kg q12h to q8h PO or SC	Sedation
Fentanyl (Duragesic®)	Opioid agonist	Analgesia, acute episode	25 µg/hr	Respiratory depression, bradycardia
Acepromazine (PromAce®)	Phenothiazine derivative	Sedation, anti-spasmodic	0.05 mg/kg q8h SC	Sedation, hypotension
Prazosin (Minipress®)	α1-adrenoceptor antagonist	Anti-spasmodic	0.5 mg per cat q12h PO	Sedation, hypotension
Phenoxybenzamine (Dibenzyline®)	α1-adrenoceptor antagonist	Anti-spasmodic	2.5 mg per cat q12h PO	Sedation, hypotension
Chronic therapy				
Drug	**Class**	**Indications**	**Dosage**	**Potential adverse effects**
Amitriptyline (Elavil®)	Tricyclic antidepressant	FIC	5 to 12.5 mg per cat q24h PO	Sedation, anti-cholinergic effects, weight gain, urine retention, urolith formation
Clomipramine (Clomicalm®, Anafranil®)	Tricyclic antidepressant	FIC, urine spraying	0.5 mg/kg q24h PO	Sedation, anti-cholinergic effects
Buspirone (BuSpar®)	Non-benzodiazine anxiolytic	FIC, urine spraying, anxiety	2.5 to 5.0 mg per cat q12h PO	Rare: sedation, other neurologic effects
Fluoxetine (Prozac®)	Selective serotonin reuptake inhibitor	FIC, urine spraying	1 mg/kg q24h PO	Rare: decreased food intake, vomiting, lethargy
Pentosan polysulfate sodium (Elmiron®)	Glycosaminoglycan (GAG) supplement	FIC	50 mg per cat q12h PO	Rare: vomiting, diarrhea
F3 fraction of feline facial pheromones (Feliway®)	Synthetic pheromone	Anxiety, FIC	1 spray in affected area q24h or room diffuser	None reported

How to think outside the litter box

Managing cats with nonobstructive idiopathic interstitial cystitis

Studies suggest that feline idiopathic cystitis results from complex interactions involving the bladder, nervous system, and adrenal glands and that husbandry practices and a cat's environment influence these interactions. These clinicians suggest identifying and reducing the stressors that may contribute to this disorder in cats.

Dennis Chew, DVM, DACVIM, and C.A. Tony Buffington, DVM, PhD, DACVN

A typical cat with idiopathic cystitis is 1 to 10 years old, lives indoors with people, uses a litter box, and consumes 75% or more of its diet in dry food. The cat may be unusually nervous or needy, overreactive to its environment, and often suffers from other medical conditions, such as obesity or upper and lower gastrointestinal, respiratory, and skin problems.[1]

Current evidence suggests that some cases of idiopathic cystitis represent a systemic disorder variably affecting the bladder and other organ systems rather than a primary bladder disease. Idiopathic cystitis may account for clinical signs related to the urinary system of irritative voiding (dysuria, stranguria, pollakiuria, gross hematuria, periuria) in up to 70% of cats that are less than 10 years old. In contrast, only about 5% of cats older than 10 years with such signs have idiopathic cystitis—instead, more than half of the cats in this age group have bacterial urinary tract infections with or without urolithiasis.[2]

Dennis Chew, DVM, DACVIM
C.A. Tony Buffington, DVM, PhD, DACVN
College of Veterinary Medicine
The Ohio State University
601 Vernon L. Tharp St.
Columbus, OH 43210

DIAGNOSIS

Abdominal palpation sometimes reveals pelvic organ pain, bladder wall thickening, and a small bladder. In cats with recurrent signs of lower urinary tract disease, we recommend survey abdominal radiography and double-contrast cystography or abdominal ultrasonography to rule out calculi and anatomic defects and identify bladder wall abnormalities.

Urinalysis in affected cats may reveal hematuria, proteinuria, crystalluria (which is likely secondary to sterile neurogenic inflammation that leads to proteinuria and increases urine pH so that struvite crystals precipitate), and high specific gravity. In cats with lower urinary tract signs and a urine specific gravity < 1.025, investigate a systemic problem such as renal disease, diabetes mellitus, or hyperthyroidism.

TREATMENT RATIONALE

Increased noradrenergic outflow (catecholamine secretion) in response to activation of the stress response system may increase epithelial permeability and activate local neurogenic inflammation in the bladder and elsewhere.[3] Thus, it is crucial to decrease noradrenergic outflow by identifying and reducing factors that may contribute to a cat's stress and epithelial compromise, such as living indoors with people, poor welfare, and inferior husbandry. In addition, providing systemic analgesia helps break the bladder pain-inflammation cycle.

TREATMENT

Clinical signs of a first or a recurrent episode of idiopathic cystitis usually resolve in about 85% of affected cats within a week with or without treatment, but about 50% of cats have another episode within a year. The signs of idiopathic cystitis are distressing to owners, and irritative voiding is presumably stressful for affected cats. Thus, we recommend the following treatment regimen.

We treat the distress and pain associated with acute flares of idiopathic cystitis with acepromazine and buprenorphine. The injectable form of acepromazine may be given orally (2.5 mg b.i.d. to t.i.d.), although some cats will exhibit hypersalivation. In these cats, the oral form may be used—¼ of a 10-mg tablet in a Greenies Pill Pocket (Nutro Products) or made up as a suspension and administered with an oral syringe. The injectable form of buprenorphine is given orally at 5 to 20 µg/kg two to four times a day for three to five days—buprenorphine is absorbed across the buccal mucosa.

We also recommend enriching the environment of indoor cats, because captivity and housing with people and other cats or other environmental challenges may elicit stress responses in some cats. Although extensive indoor housing in an unenriched environment doesn't

cause idiopathic cystitis, it may contribute to its development and ongoing occurrence. We have found that about 80% of cats with recurrent idiopathic cystitis respond to successful implementation of environmental modification.

Environmental modification

Environmental modification is an important aspect of treatment.[4,5] The litter box must be a clean, acceptable, and accessible place to encourage the cat to eliminate normally. Anything that hampers litter box use may increase the time the cat retains urine between eliminations. Prolonged exposure of the bladder wall to urine in cats with increased bladder wall permeability may increase access of "toxins" (*e.g.* acid, potassium, nitrogenous wastes) to suburothelial structures, which also may activate local inflammatory mechanisms. Litter box design, numbers, locations, obstacles, and cleaning schedules as well as litter type all influence a cat's litter box usage and should be discussed with clients.

Decreasing the cat's urine specific gravity below 1.030 is a treatment target and can be attempted by switching from dry to canned food or adding water to dry or semi-moist diet formulations, as long as the diet change or new diet is not aversive to the client or the cat. Owners also can encourage these cats to drink more water from their cats' preferred water sources such as a fresh-dispense bowl or even a running faucet in the sink, or by adding meat or fish-flavored ice cubes to their water if they like that. Acidifying the urine to minimize struvite crystalluria is usually not indicated.

Conflict between cats or other animals in the household or threats from outdoor cats can be a source of stress, so talk with owners about providing separate resources that each cat can use without interference from other animals.

Providing opportunities for owner-cat interaction and activity such as playing with toys that mimic prey motion or that intermittently release food are helpful. Methods to increase indoor space that the cat uses include providing vertical and horizontal scratching surfaces as well as objects to climb and areas in which to hide, perch, look outside, and rest undisturbed.

Based on our clinical experience, we also encourage owners to use synthetic feline facial pheromone products to augment other enrichment efforts. Feliway (Ceva Santé Animale) can be sprayed in the affected area of the enviornment or dispersed into larger areas by using an electric diffuser.

> Review the environmental modifications with the owner.

Additional environmental modification and medical management

If a cat continues to have signs of idiopathic cystitis, review the environmental modifications with the owners to find out what worked and what did not work and why. Suggest alternative or additional environmental modifications if needed, and consider including increased supervised exposure to the outdoors for some cats.

We sometimes prescribe amitriptyline (5 to 12.5 mg/cat orally once a day, always using the lowest possible dose) or another tricyclic antidepressant when environmental modifications as described above have not sufficiently reduced the cat's clinical signs. We taper the dose gradually and stop it whenever possible after at least three months of use, and we use the drug cautiously if at all in cats with heart disease. We also perform a complete blood count and serum chemistry profile to monitor the platelet and white blood cell counts and liver enzyme activities before and at one, three, and six months during therapy.

Additional medical therapy may include increasing the dose of buprenorphine. Unfortunately, glucosamine[6] and pentosan polysulfate[7] have been found to be ineffective therapy for feline idiopathic cystitis.

FOLLOW-UP

If a cat's clinical signs do not resolve or if the signs recur, you can perform additional diagnostic evaluation (repeat the complete blood count, serum chemistry profile, and urinalysis, and consider performing or referring the cat for cystoscopic evaluation) to rule out problems other than idiopathic cystitis.

Controlled clinical trials may provide additional information about the best approach to managing cats with idiopathic cystitis, but in the interim we have had success with the aforementioned environmental and medical management procedures.

REFERENCES

1. Buffington CA, Westropp JL, Chew DJ, et al. Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. *J Am Vet Med Assoc* 2006;228(5):722-725.
2. Westropp J, Buffington CAT, Chew DJ. Feline lower urinary tract diseases. In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine*. St. Louis, Mo.: Elsevier-Saunders, 2005;1828-1850.
3. Buffington CAT. Comorbidity of interstitial cystitis with other unexplained clinical conditions. *J Urol* 2004;172(4 Pt 1);1242-1248.
4. Westropp JL, Buffington CAT. Feline idiopathic cystitis: current understanding of pathophysiology and management. *Vet Clin North Am Small Anim Pract* 2004;34(4):1043-1055.
5. Buffington CAT, Westropp JL, Chew DJ, et al. Clinical evaluation of multimodal environmental modification (MEMO) in the management of cats with idiopathic cystitis. *J Feline Med Surg* 2006;8(4):261-268.
6. Gunn-Moore DA, Shenoy CM. Oral glucosamine and the management of feline idiopathic cystitis. *J Feline Med Surg* 2004;6(4):219-225.
7. Chew DJ, Bartges JW, Adams LG, et al. Randomized, placebo-controlled clinical trial of pentosan polysulfate sodium for treatment of feline interstitial (idiopathic) cystitis, in *Proceedings*. Am Coll Vet Intern Med, 2009.

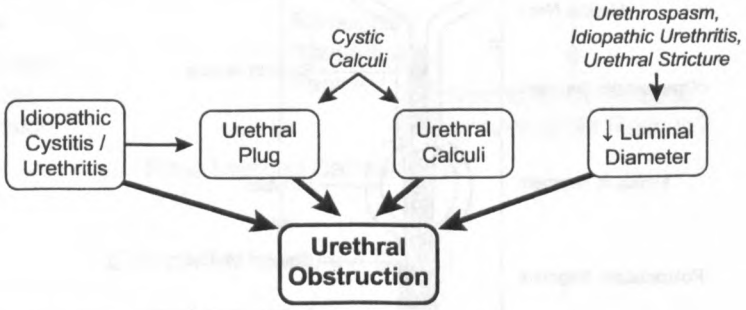
MANAGEMENT OF MALE CATS WITH URETHRAL OBSTRUCTION

Dennis J. Chew, DVM , Dip ACVIM and C.A. Tony Buffington , DVM PhD, Dip ACVN
The Ohio State University College of Veterinary Medicine, Columbus, Ohio

Pathophysiology of Urethral Obstruction

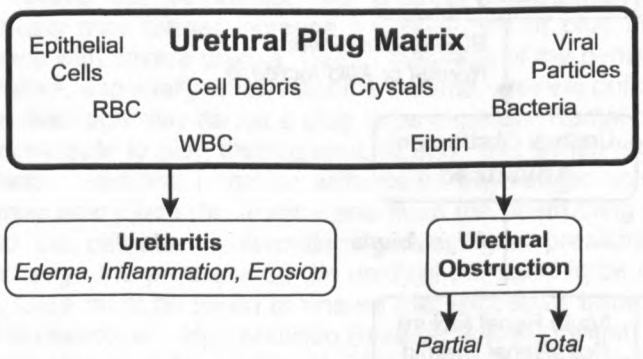
Urethral plugs are the most common cause of obstruction in male cats. In one series (Krueger 1991), urethral plugs occurred in 60%, no cause was found in 30%, uroliths alone were documented in 10% (struvite exclusively) and uroliths with bacterial urinary tract infection were observed in 2%. Occasionally stricture and rarely neoplasia are the causes of obstruction. Urethral obstruction due to calcium oxalate urethroliths is a phenomenon of the 1990's that was not encountered in the 1980's.

Figure 1) UNDERLYING CAUSES AND MECHANISMS OF URETHRAL OBSTRUCTION



Urethral plugs consist of proteins and embedded constituents of the urine in varying proportion. They contain little internal structure, and most commonly form in the penile urethra. Lower urinary tract inflammation, caused by either idiopathic cystitis/urethritis or bladder stones, precedes the formation of urethral plugs. Struvite still comprises the major crystal in plugs, despite the emergence of calcium oxalate crystalluria. Inflammatory exudates of white blood cells and proteins, red blood cells from hemorrhage, sloughed epithelial cells, fibrin, calcium oxalate crystals, and calici-like viral particles may also become trapped if present in urine at the time of plug formation.

Figure 2 – Possible contributors to formation of a urethral plugs and consequences of plug formation



In addition to intraluminal obstruction, lesions of the urethral wall may also contribute to obstruction. Edema, hemorrhage, and inflammation contribute to urethritis and can decrease the diameter of the urethral lumen. Functional decreases of the urethral lumen diameter also may result from inflammation and pain (see spasm below). Cats with chronic urethritis or recurrent urethral obstruction may become obstructed secondary to urethral stricture. Extramural causes (prostatic or urethral tumor) of urethral obstruction are exceedingly rare.

Most plugs cause obstruction within the penile urethra, but obstructions can also occur at more proximal sites. The predominant mineral composition in most plugs is magnesium ammonium phosphate (struvite). Secondary components can contribute to plug formation including inflammatory exudate (WBC and proteins), red blood cells, cellular debris, sloughed tissue (epithelial cells), struvite crystals and combinations. Virus-like particles resembling calicivirus and bacteria have also been observed within urethral plugs examined by transmission electron microscopy. Primary inflammatory changes (exudates, blood, and edema) or changes within the urethral wall secondary to intraluminal urethral plugs may contribute to the obstructive process. These changes may be magnified following instrumentation with catheters and back-flushing solutions used in therapeutic endeavors.

Figure 3 – Possible locations for intra-urethral plugs

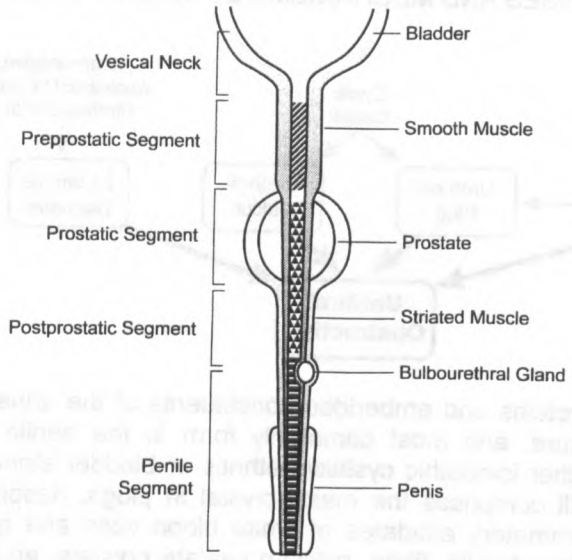
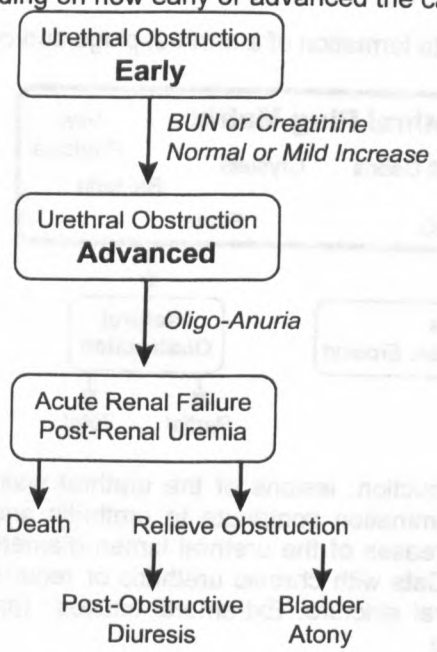


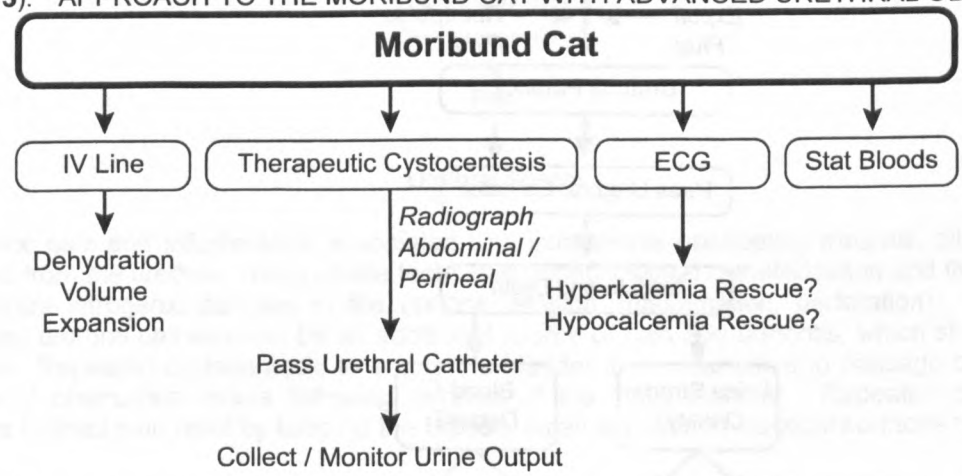
Figure 4- Possible outcomes depending on how early or advanced the case of UO



Diagnostics and Management

Urethral obstruction is diagnosed by the finding of an enlarged bladder in a male cat with signs of urinary urgency, difficulty in manually expressing urine, and by resistance encountered during the passage of a urethral catheter. It may not be obvious what is causing the urethral obstruction. Diagnostics and management of urethral obstruction are performed simultaneously. The degree of uremia, electrocardiographic stability, and the magnitude of bladder distension will dictate how quickly and in what order treatment must be performed. Those cats with uremic crisis and those with very large hard bladders are in need of prompt attention.

Figure 5). APPROACH TO THE MORIBUND CAT WITH ADVANCED URETHRAL OBSTRUCTION

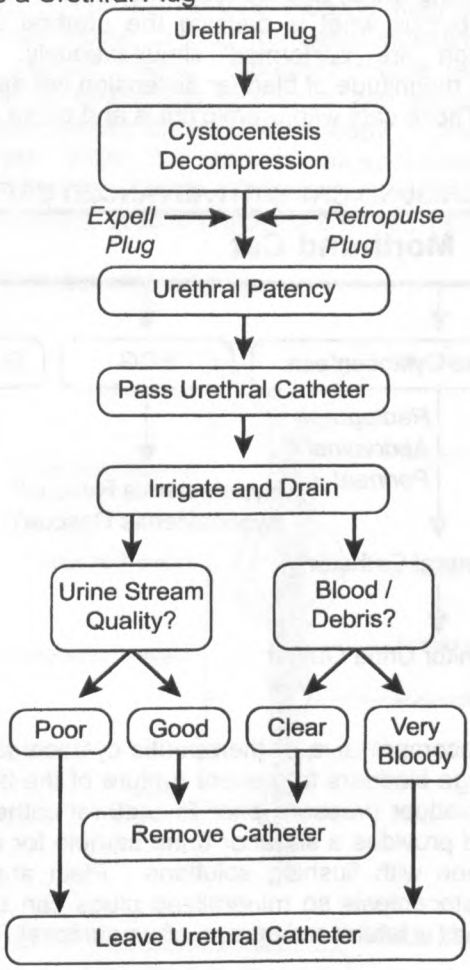


Relief of Obstruction Due to Plugs

Cystocentesis to drain the bladder(decompressive or therapeutic cystocentesis) should be performed as soon as possible in cats with very large bladders to prevent rupture of the bladder and to allow excretory renal function to resume. Relief of bladder pressure prior to urethral catheterization also may facilitate efforts to dislodge urethral plugs, and provides a superior urine sample for analysis prior to manipulation of the urinary tract and contamination with flushing solutions. Plain abdominal/perineal radiographs should follow the decompressive cystocentesis so mineralized plugs can be documented or that cystic and/or urethral calculi can be identified (a lateral radiograph often suffices).

Chemical restraint/anesthesia (isoflurane, low-dose IV ketamine, propofol) is often advisable to atraumatically relieve the obstruction via urethral catheterization. Urethral relaxation while under sedation/anesthesia may further increase the likelihood of plug dislodgment. Little or no sedation is indicated for those with severe uremia. Gentle massage of the penis may dislodge a urethral plug located in the penile urethra, especially when near the external urethral orifice. Gentle pulsatile bladder palpation following penile massage may cause a plug to be expelled. Rectal massage of the pelvic urethra may on occasion also contribute to plug dislodgment. Aseptic and gentle technique should be used while placing a urethral catheter. Urethral irrigation with sterile physiologic solutions (Lactated Ringer's solution or 0.9% saline) may now dilate the urethra and flush the obstructing plug distally out the external urethral opening around the catheter. Intermittent gentle digital pressure on the bladder following irrigation attempts may change the pressure on the urethral plug and force it to be expelled through the external urethral orifice. Care must be taken to ensure that excessive trauma or rupture of the bladder does not occur during this maneuver. Hydropulsion (reverse flushing) within the urethra may be attempted at this point if the obstruction is not yet relieved. The urethra is thoroughly flushed to make sure that all debris initially within the lumen has been back-flushed into the bladder or has been refluxed out the urethra. The urethral catheter can then usually be advanced into the bladder. Failure to adequately remove debris from the bladder and urethra is a major cause of rapid re-obstruction following catheter removal.

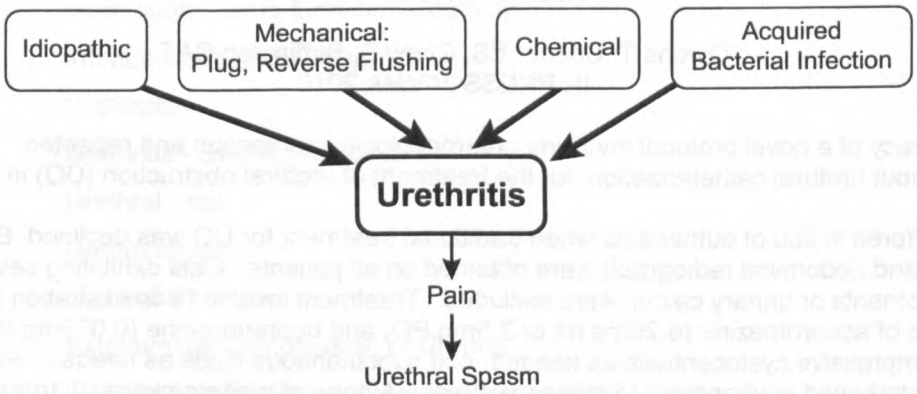
Figure 6). A Potential Decision-Making Algorithm - An Approach to Management of Urethral Obstruction in a Male Cat Due to a Urethral Plug



"Urethral spasm" refers to pathologic neurogenic or myogenic processes that contract the circular smooth and/or skeletal muscle of the urethra. The bladder and preprostatic segments of the urethra contain primarily smooth muscle, the prostatic and postprostatic segments contain both smooth and skeletal muscle, and the musculature of penile segment is predominantly circular skeletal muscle. Innervation of the urethra is provided by the sympathetic nervous system via the hypogastric nerve and the somatic nervous system via the pudendal nerve. Part of urethral tone maintained by the skeletal muscle (rhabdosphincter) is influenced by sympathetic innervation.

Stimulation of adrenoreceptors (particularly a-1) within the urethra increases urethral tone in normal cats. It is likely that both pain and stress associated with urethral obstruction increases sympathetic outflow from the central nervous system, favoring urethral spasm. Urethritis may exist prior to plug formation, or may be acquired secondary to trauma from the physical presence of intraluminal plugs or stones. Attempts to relieve obstruction with catheters, and indwelling urethral catheters also can result in urethritis. Urethritis may also be secondary to bacterial urinary tract infection (UTI) that is commonly acquired following placement of indwelling urinary catheters, even when a closed urinary collection system is employed. The use of antibacterial treatment does not prevent UTI.

Figure 7. Role of pain and urethritis in development and maintenance of urethral spasm.



To reduce pain and inflammation associated with intraluminal obstructing material, all material must be removed from the urethra. Using gentle technique during urethral catheterization and flushing is essential to minimize iatrogenic damage to the urethra (erosion, inflammation, perforation). Installation of an indwelling urethral catheter can be an additional source of pain and urethritis, which should be avoided if possible. Repeated cystocentesis to empty the bladder is an alternative to passage of another urethral catheter if obstruction recurs following removal of the initial catheter. Repeated cystocentesis also provides indirect pain relief by keeping the bladder small and painful mucosal surfaces non-distended.

Drugs recommended for the treatment of urethrospasm include analgesic, anti-inflammatory, antibacterial, and spasmolytic agents. Injection of diluted lidocaine solution through the urethral catheter at the time of its removal has been advocated by some to reduce urethral spasms, but this has not been critically evaluated. Also, the local effects of lidocaine on urothelial healing are unknown. If used, lidocaine should be diluted and injected slowly at low pressure – excessive amounts of systemically absorbed (> 0.5 mg/kg IV) lidocaine can cause seizures. Systemic treatment with a fentanyl (patch), low dose morphine (0.05-0.2 mg/kg IM), butorphanol (0.05-0.2 mg/kg IM), and/or low dose medetomidine (2-5 micrograms/kg IM ; centrally acting alpha-2 agonist that decreases sympathetic outflow) for relief of pain seems reasonable. It is possible that relief of pain will decrease urethral and bladder muscle spasms. Opioids increase urethral sphincter tone, increase bladder volume, and inhibit voiding initially but tolerance to these effects develops quickly. The central analgesic effects of opioids are most important. Butorphanol is a weak opioid that can be considered for use during the initial 12-24 hours. Unfortunately, patients develop tolerance to butorphanol rapidly. Butorphanol also has a ceiling effect in which increased doses provide no further analgesia. Finally, butorphanol produces agonist effects at kappa receptors and antagonist effects at mu receptors. This may decrease the effects of more potent mu opiods (morphine, oxymorphone, fentanyl) when needed. When additional analgesia is needed, combinations of drugs that act by different mechanisms should be considered. For example, morphine (opioid) and medetomidine (alpha 2 agonist) may be given every 6 to 12 hours as needed. Ketoprofen, tolfenamic acid, and carprofen are non-steroidal anti-inflammatory drugs (NSAID) that have been used in cats, but their effectiveness in decreasing lower urinary tract inflammation has not been substantiated. Adding an NSAID to this regimen might provide the most complete level of analgesia.

EFFICACY OF A NOVEL TREATMENT PROTOCOL IN MALE CATS WITH URETHRAL OBSTRUCTION

Owens T, Cooper ES. Chew D, Buffington CAT
IN PRESS JAVMA 2010

Objective
To determine efficacy of a novel protocol involving pharmacologic intervention and repeated cystocentesis without urethral catheterization, for the treatment of urethral obstruction (UO) in male cats.
Procedure
Enrollment was offered in lieu of euthanasia when traditional treatment for UO was declined Electrolytes, pH, renal values, and abdominal radiograph were obtained on all patients. Cats exhibiting severe metabolic derangements or urinary calculi were excluded. Treatment involved administration of a standardized dose of acepromazine (0.25mg IM or 2.5mg PO) and buprenorphine (0.075mg PO) three times daily, decompressive cystocentesis as needed, and subcutaneous fluids as needed. Patients were placed in a quite, darkened environment to minimize stress. A dose of medetomidine (0.1mg) was administered if urination did not occur within 24 hours. Treatment success was defined as spontaneous urination within 72 hours and discharge from the hospital.
Results
Twelve cats were treated with success in 67% of cases (8/12), Cats responsive to treatment tended to have spontaneous urination resume within 24 hours and were more likely to eat in hospital. Treatment failure occurred in 33% of cases (4/12). Three were euthanized for significant complications (uroabdomen or hemoabdomen). The fourth case survived but only urinated after urethral catheterization. Cats that experienced significant complications had higher renal values (though not statistically significant).
Conclusion
Pharmacologic therapy, in conjunction with a decompressive cystocentesis and a low stress environment, can result in spontaneous resolution of UO without the need for urethral catheterization. This protocol could offer an alternative to euthaniasia for patients which cannot receive traditional treatment.

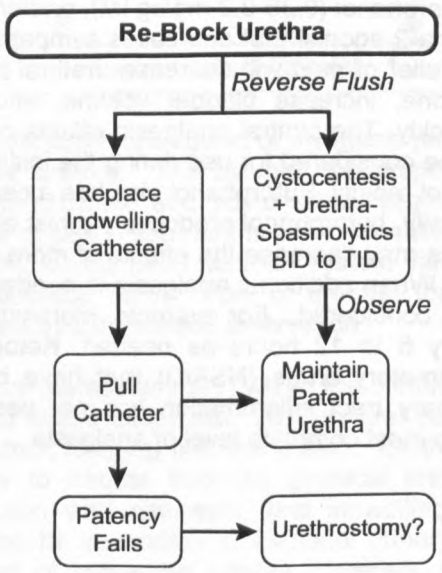


Table 1). RESISTANCE TO URETHRAL CATHETERIZATION

1. Inadequate Penile Extrusion Caudally
2. Intraluminal Urethral Plug
3. Urethrolith
4. Urethritis - Swollen/Erosions
5. Urethral Tear
6. Urethrospasm
7. Urethral Stricture
8. Extraluminal Compression of Urethra
9. Urethral Foreign Body - Catheter Fragment

TABLE 2). METHODS OF PLUG RETRIEVAL/DOCUMENTATION

1. Spontaneous Expulsion
2. Gentle Penile Massage
3. Gentle Bladder Massage
4. Cystocentesis and Gentle Bladder Massage
5. Rectal Massage of Urethra
6. Urethral Lavage - Gentle/Persistent
7. Urethral Catheter Aspiration
8. Plain Radiographs - pelvis/perineum/penis

Table 3) Complications Following/During Relief of Urethral Obstruction in Male Cats

A. Persistent Urethral Obstruction (Ongoing Episode Not Resolving)
B. Recurrent Episode of Urethral Obstruction (new)
C. Episodes of Cystitis/Urethritis - Idiopathic Non-Obstructive
D. Bacterial Urinary Tract Infection : Post Urethral Catheter
E. Urethral Trauma - Catheter-Associated ; Rupture-Iatrogenic
F. Bladder Trauma - Catheter-Associated ; Rupture -Spontaneous/Iatrogenic
G. Bladder Atony- Detrusor Overdistension
H. Urethral Stricture
I. Azotemia - Pre-Renal and Post-Renal Origin
I. Primary Renal Disease/ Failure - Pyelonephritis(Ascending), ATN (Uncommon)
J. Post-Obstructive Diuresis - Usually Reversible Within 2-5 Days

Table 4). **Inability of Cat to Evacuate Urine Following Urethral Catheter Removal**

1. New Urethral Plug Formation (RBC, protein, crystals)
2. Original Urethral Plug/Debris Not Adequately Cleared
3. Urethral Calculus Still There (Catheter Bypassed)
4. Urethritis
5. Urethrospasm
6. Atonic Bladder
7. Urethral Stricture
8. Bladder Outflow Obstruction -Intraluminal Hematoma

SELECTED REFERENCES

Osborne CA, Kruger JM, Lulich JP, Bartges JW, Polzin DJ: Medical management of feline urethral obstruction. Vet Clin North Am: Small Animal Practice 26(3):483-498, 1996.

Lees G: Use and misuse of indwelling urethral catheters. Vet Clin North Am: Small Animal Practice 26(3):499-505, 1996.

Lee JA, Drobatz KJ : Characterization of the clinical characteristics, electrolytes, acid-base, and renal parameters in male cats with urethral obstruction. J Vet Emerg Critical Care 13(4):227-233, 2003.

Lee JA, Drobatz KJ: Historical and physical parameters as predictors of severe hyperkalemia in male cats with urethral obstruction. Journal of veterinary emergency and critical care 16: 104-111, 2006.

Drobatz KJ, Hughes D. Concentration of ionized calcium in plasma from cats with urethral obstruction. J Am Vet Med Assoc. 1997; 211(11):1392-5.

Danuser H, Thor KB. Inhibition of central sympathetic and somatic outflow to the lower urinary tract of the cat by the alpha 1 adrenergic receptor antagonist prazosin. J Urol 1995; 153:1308-12.

Gerber B, Eichenberger S, Reusch CE: Guarded long-term prognosis in male cats with urethral obstruction. Journal of Feline Medicine and Surgery 10(1): 16-23, 2008.

Gerber B, Boretti FS, Kley S, Laluha P, Muller C, Sieber N, Unterer S, Wenger M, Fluckiger M, Glaus T, Reusch CE: Evaluation of clinical signs and causes of lower urinary tract disease in European cats. J Small Anim Pract 46(12): 571-577, 2005.

Strater-Knowlen IM, Marks SL: Use of muscle relaxants in feline obstructive lower urinary tract disease. Feline Practice 25(5-6), 26-33,1997.

Marks SL, Straeter-Knowlen IM, Moore M, et al. Effects of acepromazine maleate and phenoxybenzamine on urethral pressure profiles of anesthetized, healthy, sexually intact male cats. Am J Vet Res. 1996; 57(10):1497-500.

Straeter-Knowlen IM, Marks SL, Rishniw M, et al. Urethral pressure response to smooth and skeletal muscle relaxants in anesthetized, adult male cats with naturally acquired urethral obstruction. Am J Vet Res. 1995; 56(7):919-23.

Straeter-Knowlen IM, Marks SL, Rishniw M, et al. Urethral pressure response to smooth and skeletal muscle relaxants in anesthetized, adult male cats with naturally acquired urethral obstruction. Am J Vet Res. 1995; 56(7):919-23.

Straeter-Knowlen IM, Marks SL, Speth RC, et al. Effect of succinylcholine, diazepam, and dantrolene on the urethral pressure profile of anesthetized, healthy, sexually intact male cats. Am J Vet Res. 1994; 55(12):1739-44.

Barsanti JA, Shotts EB, Crowell WA, et al. Effect of therapy on susceptibility to urinary tract infection in male cats with indwelling urethral catheters. J Vet Intern Med. 1992; 6(2):64-70.

Burrows CF, Bovee KC. Characterization and treatment of acid-base and renal defects due to urethral obstruction in cats. J Am Vet Med Assoc. 1978; 172(7):801-5.

Finco DR, Cornelius LM. Characterization and treatment of water, electrolyte, and acid-base imbalances of induced urethral obstruction in the cat. Am J Vet Res. 1977; 38(6):823-30.

Schaer M. Hyperkalemia in cats with urethral obstruction. Electrocardiographic abnormalities and treatment. Vet Clin North Am. 1977; 7(2):407-14.

Making Errors: The Fundamentals

John Ludders

Medical Errors

- **Many terms, and often confusing:**
  - **Error**
  - **Mistake**
  - **Near miss** – an event that does not cause patient harm only because some intervention occurred before it affected the patient
  - **Incident** – any occurrence not consistent with either normal patient care or normal operation of a medical facility
  - **Adverse event** – occurs when a patient suffers unexpected harm as a result of some medical intervention
  - **Sentinel event** – adverse and unexpected event causing death or serious injury, or risk thereof

What Are Errors?

- Common definitions:
  - Performances that deviate from normal or from the ideal. {Allnutt, 1987}
  - All occasions in which a planned sequence of mental or physical activities fails to achieve its intended outcome. {Reason, 1990}
  - Use of a wrong plan to achieve an aim (i.e., error of planning), or failure of a planned action to be completed as intended (i.e., error of execution). {Leape, 2002}

Errors in Anesthesia

A Case in Point

Right Bottle, Wrong Drug!

- **Setting - The Practice**
  - Large successful multi-veterinarian mixed practice started in early 1950s
  - **To save money, distilled water was made by filtration at a central location; concentrates were added to the water to make a variety of IV fluids.**
    - Exception: LRS purchased in bags for use in small ruminants, foals, and small animal patients
  - Normal saline and potassium chloride, both made in-house, were distributed throughout the hospital in brown glass bottles which were labeled similarly as to each bottle's contents and date made.
  - **As per established policy, late afternoon on Mondays and Fridays shelves throughout the hospital were restocked with various supplies including fluids, by technicians working in various sections of the hospital.**

Right Bottle, Wrong Drug!

- Setting - The Practice
  - Heparinized saline was made by adding heparin (1000 U/mL) to bottles containing 250 mL of normal saline (0.9% NaCl) to make heparinized saline (2 U/mL).
  - Another label would then be affixed to the bottle indicating that heparin had been added, the date, and by whom.

Right Bottle, Wrong Drug!

- **Setting – small animal anesthesia area**
  - The practice anesthetized between 12-19 small animal patients per day – 80% dogs, 15% cats, balance pocket pets
  - Anesthetic technique and drugs chosen for a patient undergoing anesthesia were selected based on the patient's health (physical status) and the procedure to be performed
  - **Induction and maintenance followed a set pattern:**
    - ✓ **Assessment of patient prior to premed**
    - ✓ **Assessment after premeds, and after catheterization before induction**
    - ✓ **Induced, intubated, attached to breathing circuit**
    - ✓ **Assessment of patient**

Right Bottle, Wrong Drug!

- **Scenario**
  - Tuesday morning
    - Young, healthy bitch weighing 7 kg anesthetized for OVH has a cardiac arrest after induction
      - Specifics: induction thiamylal, catheter flushed with heparinized saline, intubated, attached to a semi-closed circle system to which oxygen was delivered (no inhalant anesthetic). No peripheral pulse or heart sounds. CPR unsuccessful. No cause found at necropsy.
  - Wednesday
    - **Morning** - patients anesthetized without problems
    - **Early afternoon** - 13 kg dog scheduled for ophthalmic procedure has a cardiac arrest several minutes after induction. CPR ineffective.
      - Specifics: Drug doses and procedures followed were in accordance with the practice's SOPs. After this arrest and during the next 2 hours, two dogs and a cat were anesthetized uneventfully
    - **Two hours later**, another dog weighing 6 kg scheduled for abdominal exploratory has a cardiac arrest; CPR unsuccessful
      - Arrest occurred after IV catheter inserted (cephalic vein), capped and flushed with heparinized saline.

Right Bottle, Wrong Drug!

- Two 250 mL bottles of heparinized saline were being used in the induction area
- Both were labeled as heparinized saline
- Closer inspection revealed the heparinized saline label of one bottle was covering its original label indicating its contents as KCl (4mEq/mL)
- Who is to blame for this error?
- How should this error be dealt with?
- How can it be prevented in the future?

Some Insights to Errors

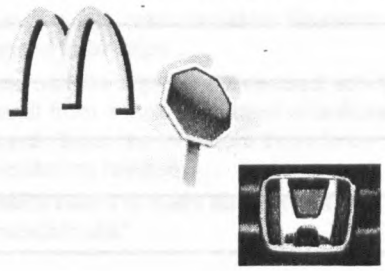
"Knowledge and error flow from the same mental sources, only success can tell the one from the other"
Ernst Mach, 1905

- Errors are…
  - actions that have gone wrong
  - actions are the results of decisions made
  - decisions made are windows through which we can observe the thought processes behind the action
- Need to look at cognitive processes underlying errors

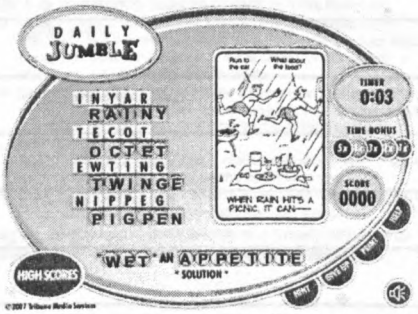
Errors and Cognition

- The human mind functions at two levels or in two modes {Leape, 1994; Reason, 1990}
  - **Schematic control mode** - an automatic, fast-response mode of cognition in which the mind has unconscious mental models composed of old knowledge **(schemata)** activated by very little conscious thought
  - **Attentional control mode** - a controlled, conscious, analytical mode of cognition that requires effort which is difficult to sustain, and that uses stored knowledge

Errors and Cognition



Humans Are Pattern Matchers



Cognition & Performance

- **Within this model of cognition there are three levels of performance:**
  - **Skill-based** (SB) level performance - governed by stored patterns of preprogrammed instructions (pattern recognition)
    - **Schemata**
      - largely **unconscious**
      - characterized as highly routinized
      - occur in **familiar circumstances**
    - Skill-based performance relates to technical performance and proper execution of tasks
  - **Rule-based** (RB) level performance - actions or solutions governed by **stored rules** of the type *if…then.*
    - Relates to supervision, training and qualifications, communications, and interpretations
  - **Knowledge-based** (KB) level performance - occurs when synthetic thought is used for novel situations
    - Requires conscious analytical processing and stored knowledge

Cognition & Errors

- We humans prefer pattern recognition over calculation to such a degree that we are strongly biased to search for a **prepackaged** solution before resorting to a more strenuous knowledge-based level of cognition.{Leape, 1994}

Cognitive Processes Underlying Actions

- Conceiving of and executing an action sequence involves…
  - **Planning**
  - **Storage** (memory)
    - Short-term memory is very labile
  - **Execution**
- Errors may occur within any one or all of these three stages

Types of Errors

- **General types of errors are** {Reason, 1990}…
- **Slips - actions occur not as planned and are usually observable (usually overt)**
- **Lapses - failures of memory that occur when one's attention is distracted or preoccupied; may only be apparent to the person who experiences them (usually covert)**
- **Mistakes – occur when a plan is inadequate to achieve its desired outcome even though the actions may run according to plan; mistakes occur at the planning stage of both RB and KB levels of performance; have been described as failures of higher level cognition**

Types of Errors

- Leape {Leape, 1994} considers Reason's lapses to be slips…
- And defines **slips** as unintended acts that result from a lack of a **timely attentional check**; thus, he considers them to be monitoring failures.
- **Weick refers to them as a lack of "mindfulness"**

Types of Errors: Leape & Reason

- **Slips or monitoring failures or lack of mindfulness:**
  - **Capture slip** – an example is a usual action sequence of ABCDEF, but if a new sequence is established such as ABCFG, conscious attention must be in force after C if the action sequence is to be completed properly.
  - **Description slip or error** – right action is performed on the wrong object. Example: an anesthetist reaches for the oxygen flowmeter control knob, but turns on the nitrous oxide flow control knob.
  - **Associative activation slip** – mental associations of ideas such as answering the phone when the doorbell rings.
  - **Loss of activation slip** – enter a room to do something but can't remember what it was (temporary memory loss).
- Again, these result from a lack of a timely attentional check often due to **attention diverting factors...**

Attention Diverting Factors

- **Physiological** – fatigue, sleep loss, alcohol or drug abuse, illness
- **Psychological** (internal or external of the individual) – other activity (busyness), emotional states such as boredom, frustration, fear, anxiety, or anger
- **Environmental** – noise, heat, cold, visual stimuli, odors, motion

Stress & Errors

- **Under conditions of stress certain cognitive processes lead to error generation:**
  - **Coning of attention** – under the stress of an emergency the tendency is to concentrate on one piece of information to the exclusion of other pieces of information which may be germane to the problem at hand.
  - **Reversion under stress** – recently learned behavior patterns are replaced by older, more familiar ones, even if inappropriate in the circumstances.

Mistakes

- Mistakes are subject to the same **attention diverting factors** as slips
  - **Rule-based errors (mistakes)**
    - wrong rule is chosen either because the situation was misinterpreted, or…
    - good rule (usually works, seems to fit situation) was misapplied.
  - **Knowledge-based errors (mistakes)**
    - complex in nature
    - a novel situation
      - operator does not possess pre-programmed solutions (no schemata; lacks knowledge)
      - or problem is misinterpreted

Knowledge-Based Mistakes

- **Knowledge-based errors (mistakes)**
  - Pattern matching is preferred, but sometimes the patterns do not match.
  - **The habits of thought (mindsets) that alter pattern matching and lead to mistakes are:**
    - **Biased memory** – familiar patterns are assumed to have universal applicability because they usually work.
    - **Availability heuristic** – the tendency to use the first information that comes to mind (*heuristic - self-educating techniques to aid learning through discovery or trial-and-error methods*).
    - **Confirmation bias** – the tendency to seek evidence that supports an early working hypothesis while ignoring data that contradict it.
    - **Overconfidence** – the tendency to believe in the validity of the chosen course of action and to focus on evidence that favors it.

People, Systems and Errors

- The majority of errors are due to people, not equipment…
- But the majority of us do not go to work intending to cause errors
- **Causes of errors often reside within the organization in which people work:**
  - **Active failures or conditions** - errors or violations (unsafe acts) committed by operators directly involved in the provision of care (e.g. drug administration error)
  - **Latent failures or conditions (aka root causes or resident pathogens)** - defensive gaps, weaknesses, or absences unwittingly created in a system as the result of earlier decisions made by the designers, builders, regulators, and managers of the system; correspond to systemic problems (eg, vials of similar shape, size and color but containing different drugs)

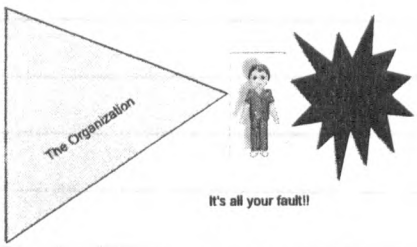
People, Systems and Errors

- Latent failures or conditions possess two important properties:
  1. Their effects are usually longer lasting than those created by active failures
  2. They are present within the system before an adverse event occurs and can be detected and repaired before they cause harm.{Reason, 2004}
- They are the primary targets of any rational safety management system.

How to Prevent Errors in Medicine

- **The Person Approach** (proximate cause analysis)
  - Errors are viewed as moral issues - bad things happen to bad people (just world hypothesis)
  - Blames the individual for aberrant mental processes such as:
    - forgetfulness, inattention, poor motivation, carelessness, negligence, recklessness, moral weakness
  - Solutions include naming, shaming and blaming

Proximate Cause Analysis

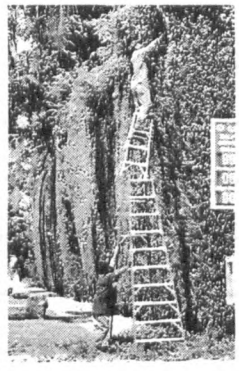


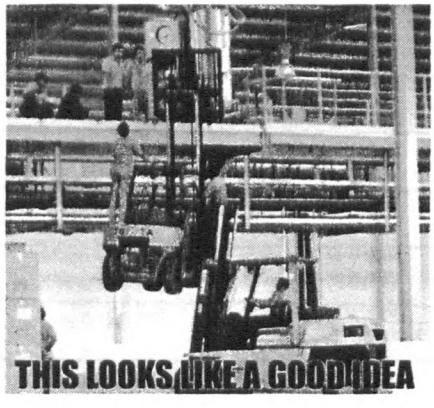
Preventing Errors in Medicine

- The Systems Approach
  - Recognizes two fundamental realities:
    1. "All human beings, without exception whatsoever, make errors and such errors are a completely normal and necessary part of human cognitive function" - Allnutt, 1987
    2. We cannot change the human condition—humans do and will continue to make errors—but we can change the conditions under which humans work – Reason, 2000
  - Approach is aimed at several different targets: **person, team, task, workplace, and institution as a whole**
  - Tries to build defenses to avert errors or mitigate their effects

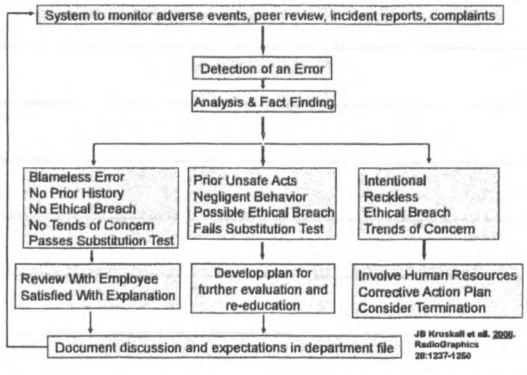
Error Vs Misconduct

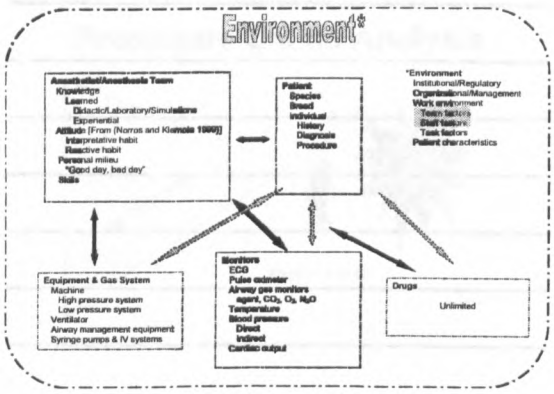
- **Fears about "blameless" medicine**
  - Error is confused with misconduct – Leape
    - **Misconduct is never to be tolerated!**
- The majority of errors are made by well-trained, well-meaning, conscientious people who are trying to do their job well, but who are caught in faulty systems that set them up to make mistakes and who become "second victims"



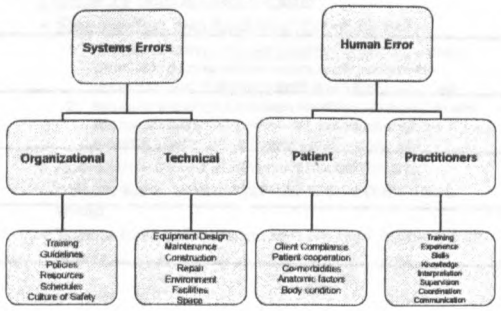


Model for Determining Accountability





A Taxonomy For Categorizing Errors – J. B. Kruskal, 2008



Right Bottle - Wrong Drug - Resolution -

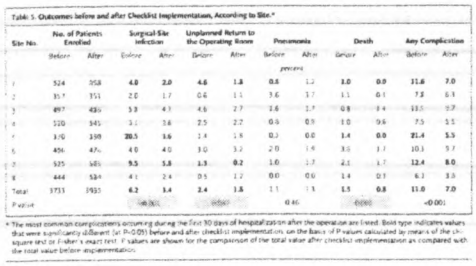
Questions asked:

- Who was to blame for the error?
- How was the error dealt with?
  - The technician
- How was a similar event prevented from occurring in the future?
  - Commercially manufactured KCl
  - Commercially manufactured fluids

Elements of the Surgical Safety Checklist

Haynes A et al. N Engl J Med 2009;10.1056/NEJMsa0810119

Outcomes Before and After Checklist Implementation



Haynes A et al. N Engl J Med 2009;10.1056/NEJMsa0810119

Part 2
Errors: Treasures of Practice (case examples)

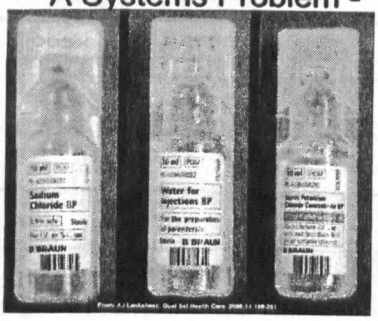
- **Cases**
  - Anesthesia of a Polar Bear: The Obvious Disguised as the Unusual
  - Out of Sight Cat!
  - Cool Cat!
  - Cat with Just an Eyelid Mass!

Team Behavior

"Authority with participation, assertiveness with respect"

D.M. Gaba, 1994, Crisis Management in Anesthesiology, Churchill Livingston, p 40

Right Bottle - Wrong Drug - A Systems Problem -



From A.J. Lanzafame, Qual Saf Health Care 2006;15:198-201

Feline Dermatology: Moving Pictures

Danny W. Scott, DVM, DACVD

Department of Clinical Sciences
College of Veterinary Medicine
Cornell University
Ithaca, NY 14853-6401

CETIRIZINE FOR CATS WITH ALLERGIC DERMATITIS

Antihistamines have been used for the control of pruritus in allergic cats since the 1980s.[1] They may be successful alone, act in synergy with omega-3/-6 fatty acids, or allow reduced doses of glucocorticoids.

First generation (traditional) H_1-antagonists, have antihistaminic, anticholinergic, sedative, and local anesthetic effects. Second generation (nonsedating) H_1-antagonists cause minimal side effects. Only four published clinical trials using antihistamines for the management of allergic pruritus in cats are available.[2-5] The antihistamines evaluated were all first generation: chlorpheniramine, clemastine, cyproheptadine, and oxatomide (not available in the U.S.) (Table 1).

Table 1 - Antihistamines Purported to be of Benefit in Allergic Cats*

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

*Peer-reviewed publication(s) demonstrate efficacy.

Responses to antihistamines are notoriously individualized and unpredictable.[1] Each antihistamine should be evaluated for at least two weeks. Antihistamines must be used with caution, if at all, in the presence of liver disease, glaucoma, urinary retention, gastrointestinal atony, seizures, pregnancy, and nursing queens.[1]

Cetirizine is a second generation antihistamine known to affect eosinophil function, and eosinophils are often prominent in skin-biopsy specimens from allergic cats. Some authors have suggested that cetirizine may be the antihistamine of choice for feline eosinophilic dermatoses.[6] A recent pharmacokinetic study of cetirizine in normal cats indicated that once-daily dosing (1 mg/kg) was appropriate, and side effects were not seen.[7]

We have recently completed a clinical trial with cetirizine in 32 cats with allergic skin disease: 14 with atopic dermatitis, 16 with allergic dermatitis of undetermined cause (atopic dermatitis and/or food allergy), 2 with atopic dermatitis and food allergy. Cutaneous reaction patterns included self-induced alopecia, nonlesional pruritus, and eosinophilic granuloma complex. In our study, 41% of the cats realized mild-to-marked reduction in pruritus which was repeatable and sustainable. There was no association between cutaneous reaction pattern, age, or severity of pruritus and response to cetirizine.

References

1. Scott DW, Miller WH. Antihistamines in the management of allergic pruritus in dogs and cats. J Small Anim Pract 40:359, 1999.
2. Miller WH, Scott DW. Efficacy of chlorpheniramine maleate for the management of pruritus in cats. J Am Vet Med Assoc 197:67, 1990.
3. Prost C. Les dermatoses allergiques du chat. Pract Méd Chir Anim Comp 28:151, 1992.
4. Miller WH, Scott DW. Clemastine fumarate as an antipruritic agent in pruritic cats: results of an open clinical trial. Can Vet J 35:502, 1994.
5. Scott DW, et al. Observations on the use of cyproheptadine hydrochloride as an antipruritic agent in allergic cats. Can Vet J 39:634, 1998.
6. Moriello KA. *British Small Animal Veterinary Association Manual of Small Animal Dermatology*, 2nd ed. Glouchestershire, 2003, p. 233.
7. Papich MG, et al. Pharmacokinetics of cetirizine in healthy cats. Am J Vet Res 69:670, 2008.

SEROLOGICAL DETECTION OF ALLERGEN-SPECIFIC IgE IN CATS

Atopic dermatitis (AD) is defined as a genetically-predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features, that is most commonly associated with IgE antibodies to environmental allergens.[1] Allergen may be absorbed transcutaneously and, perhaps, by inhalation or ingestion. A complex pathogenesis of immune dysregulation in association with genetic, environmental, anatomical, microbial, climactic, and physiological factors is envisioned in humans and dogs, but is only poorly studied in cats.

Reaction to house dust mites (*Dermatophagoides farinae* and *D. pteronyssinus*) and storage mites (*Acarus siro, Glycophagus domesticus, Lepidoglyphus destructor, Tyrophagus putrescentiae*) are the most common in feline AD.[1,2] House dust and storage mites are antigenically related to *Otodectes, Sarcoptes, Notoedres,* and *Cheyletiella* mites. Not surprisingly, false-positive reactions can occur in cats with these parasites. House dust mite-positive cat sera show a complex pattern of reactivity which is quite different than what is seen in dogs.

The diagnosis of feline AD is first and foremost **clinical**, and is based on compatible history, physical findings, elimination of other causes, and response to therapy.[1] "Allergy testing" (**NOT!**) is performed – **not** to establish a diagnosis – but to determine allergens to be considered for avoidance and allergen-specific immunotherapy protocols.[1]

In vitro serologic allergen-specific IgE tests have been available since 1985, and new companies and techniques continue to come on the scene. Regrettably, rarely is scientific information available on the methodologies, specificities, and utility of the tests.[1] Despite "refinements" and "improvements" in serological tests, false-positives, false-negatives, lack of correlation with intradermal tests, and inability to separate healthy from diseased cats persist.[1-6]

Manufacturers tout the benefits of their methodologies – ELISA, RAST, VARL, Heska – with little or no peer-reviewed science to back them. Serological tests results may be affected by systemic glucocorticoid therapy and season.

The keys to maximizing the success of **any** "allergy testing: are (1) patient selection (rule-outs, drug/bug withdrawal), (2) observing seasonal influences, and (3) correlating test results with patient.

References

1. Scott DW, et al. *Muller & Kirk's Small Animal Dermatology VI.* WB Saunders, 2001.
2. Noli C, et al. House dust mites and allergy. *Advances in Veterinary Dermatology IV.* Blackwell Science, 2002.
3. Taglinger K, et al. Measurement of serum immunoglobulin E (IgE) specific for house dust mite antigens in normal cats and cats with allergic skin disease. Vet Immunol Immunopathol 105:85, 2005.
4. Ordeix L, et al. Comparison of intradermal and serum testing for allergen-specific IgE using an Fcε RIα-based assay in allergic cats. Vet Dermatol 16:355, 2005.
5. Reinero CR. Feline immunoglobulin E: historical perspective, diagnostics and clinical relevance. Vet Immunol Immunopathol 132:13, 2009.
6. Diesel A, et al. Allergen-specific IgE in atopic and healthy cats – comparison of rapid screening immunoassay and complete-panel analysis. Vet Dermatol 20:216, 2009.

SKIN BIOPSY FINDINGS IN CATS WITH ALLERGIC DERMATITIS

Histopathologic findings in skin-biopsy specimens from allergic cats are somewhat controversial.[1,2] The significance of two histopathologic reaction patterns in cats with allergic dermatitis have been recently evaluated.

The prevalence of **infiltrative lymphocytic mural folliculitis** (ILMF) was evaluated in skin-biopsy specimens from 354 cats with various inflammatory dermatoses and from 33 cats with normal skin.[3] Although ILMF was present in 33/47 dermatoses studied, the prevalence of ILMF in allergic dermatoses was significantly greater than in nonallergic dermatoses. ILMF was not observed in normal skin.

The **depth of perivascular-to-interstitial inflammation** was evaluated in skin-biopsy specimens from cats with atopic dermatitis, food allergy, and flea-bite hypersensitivity.[4] Dermal inflammation was both superficial and deep in 93% of the cats. There was no difference in histopathologic reaction pattern based on clinical diagnosis or clinical cutaneous reaction pattern.

References

1. Scott DW, et al. *Muller & Kirk' Small Animal Dermatology VI.* WB Saunders, 2001.
2. Gross TL, et al. *Skin Diseases of the Dog and Cat II.* Blackwell Science, 2005.
3. Rosenberg AS, et al. Infiltrative lymphocytic mural folliculitis: a histopathological reaction pattern in skin-biopsy specimens from cats with allergic skin disease. J Feline Med Surg 12:80, 2009.
4. Scott DW. Superficial and deep dermal inflammation: a retrospective study of skin-biopsy specimens from cats with atopic dermatitis, food hypersensitivity, flea-bite hypersensitivity (in preparation).

Malassezia Dermatitis

Malassezia spp. (mostly *M. pachydermatis*) were demonstrated (ear canal, anus, claw fold, axilla, and groin were sampled) in 90% of Devon Rex, 50% of domestic shorthair, and 39% of Cornish Rex cats.[1] *M. slooffiae* (mostly clawbed) and *M. nana* (mostly ear canal) were occasionally isolated. Frequency of isolation and population sizes of *Malassezia* spp. (mostly *M. pachydermatis*) were greater in "seborrheic" Devon Rex and Sphynx cats than in healthy Devon Rex, Sphynx, or domestic shorthair cats.[2,87] The prevalence of *Malassezia* spp. in clawfolds was greater in Devon Rex (100%, 8.6/oil immersion) than nonDevon Rex (61%; 0.59/oil immersion).[3] The frequency of isolation and population sizes of *Malassezia* spp. were not significantly different in health cats and cats with diabetes mellitus, hyperthyroidism, and neoplasia.[4]

Results of a retrospective histopathological study suggested that the finding of *Malassezia* yeasts in surface keratin was often associated with the presence of systemic disease (e.g.,

thymoma, paraneoplastic alopecia).[5] *Malassezia* yeasts were demonstrated in allergic cats (atopic dermatitis, food allergy and treatment with itraconazole or ketoconazole resulted in reduced pruritus and dermatitis.[6] Itraconazole administration produced reduced *Malassezia* counts and dermatitis in "seborrheic" Devon Rex cats.[7]

References

1. Bond R, et al. Carriage of *Malassezia* spp. yeasts in Cornish Rex, Devon Rex, and domestic short-haired cats: a cross-sectional survey. Vet Dermatol 19:299, 2008.
2. Ahman S, et al. Carriage of *Malassezia* spp. yeasts in healthy and seborrheic Devon Rex cats. Med Mycol 45:449, 2007.
3. Colombo S, et al. Prevalence of *Malassezia* spp. yeasts in feline nail folds: a cytological and mycological study. Vet Dermatol 18:278, 2007.
4. Perrins N, et al. Carriage of *Malassezia* spp. yeasts in cats with diabetes mellitus, hyperthyroidism, and neoplasia. Med Mycol 45:541, 2007.
5. Mauldin EA, et al. Retrospective study: the presence of *Malassezia* in feline skin biopsies. A clinicopathological study. Vet Dermatol 13:7, 2002.
6. Ordeix L, et al. *Malassezia* spp. overgrowth in allergic cats. Vet Dermatol 18:316, 2007.
7. Ahman S, et al. Treatment of *Malassezia pachydermatis*-associated seborrheic dermatitis in Devon Rex cats with itraconazole – a pilot study. Vet Dermatol 18:171, 2007.
8. Ahman SE, et al. Cutaneous carriage of *Malassezia* species in healthy and seborrhoeic Sphynx cats and a comparison to carriage in Devon Rex cats. J Feline Med Surg 11:970, 2009.

Errors: Treasures of Practice (case examples)

John Ludders

Quick Review

"Knowledge and error flow from the same mental sources, only success can tell the one from the other"

Ernst Mach, 1905

- **Errors are…**
  - …actions that have gone wrong
  - …actions are the results of decisions made
  - …decisions made are windows through which we can observe the thought processes behind the action…
  - need to look at cognitive processes underlying errors

Errors and Cognition

- The human mind functions at two levels or in two modes {Leape, 1994; Reason, 1990}
  - **Schematic control mode** - mind uses unconscious mental models composed of old knowledge (**schemata**) activated by very little conscious thought
  - **Attentional control mode** - a controlled, conscious, analytical mode of cognition requiring effort which is difficult to sustain, and that uses stored knowledge

Cognition & Errors

- We humans prefer pattern recognition over calculation to such a degree that we are strongly biased to search for a prepackaged solution before resorting to a more strenuous knowledge-based level of cognition.{Leape, 1994}

Cognition & Performance

- **Cognitive model has three levels of performance:**
  - **Skill-based** - pattern recognition
    - **Schemata**
      - largely unconscious, **routinized**, occurs in familiar circumstances
  - **Rule-based (RB)** level performance - *if…then.*
  - **Knowledge-based (KB)** level performance - occurs when synthetic thought is used for novel situations
    - Requires conscious analytical processing and stored knowledge

Types of Errors

- James Reason - slips, lapses, mistakes
- Lucien Leape - slips are lack of a timely attentional check; monitoring failures
- Karl Weick – lack of "mindfulness"
- Often due to a lack of a timely attentional check because of **attention diverting factors…**

Attention Diverting Factors

- **Physiological** – fatigue, sleep loss, alcohol or drug abuse, illness
- **Psychological** (internal or external of the individual) – other activity (busyness), emotional states such as boredom, frustration, fear, anxiety, or anger
- **Environmental** – noise, heat, cold, visual stimuli, odors, motion

These factors can cause stress

Stress & Errors

- Under conditions of stress certain cognitive processes lead to error generation:
  - **Coning of attention**
  - **Reversion under stress**

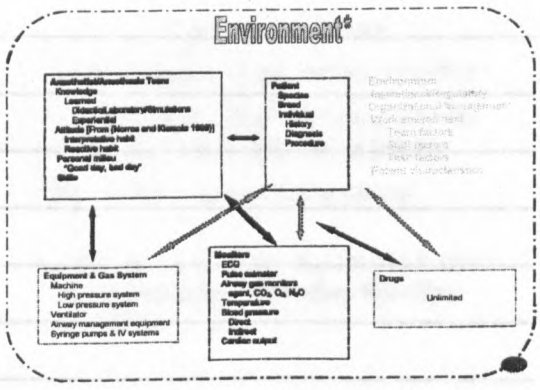
Mistakes

- Mistakes are subject to the same **attention diverting factors** as slips
  - **Rule-based errors (mistakes)**
    - wrong rule is chosen either because the situation was misinterpreted, or…
    - good rule (usually works, seems to fit situation) was misapplied.
  - **Knowledge-based errors (mistakes)**
    - complex in nature
    - a novel situation
      - operator does not possess pre-programmed solutions (no schemata; lacks knowledge)
      - or problem is misinterpreted

- **Knowledge-based errors (mistakes) occur when...**
  - habits of thought (mindsets) alter pattern matching and lead to mistakes; they are:
    - **Biased memory** – familiar patterns are assumed to have universal applicability because they usually work.
    - **Availability heuristic** – the tendency to use the first information that comes to mind
    - **Confirmation bias** – the tendency to seek evidence that supports an early working hypothesis while ignoring data that contradict it.
    - **Overconfidence** – some call it the macho syndrome

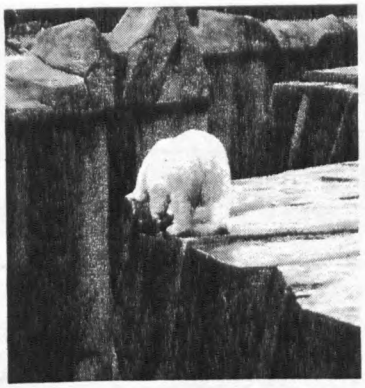
Preventing Errors

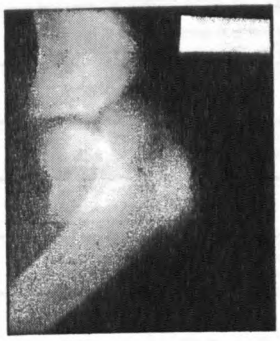
- **Systems Approach Vs Proximate Cause Approach**
  - Error Vs Misconduct – misconduct is never acceptable
- Most errors are made by well-trained, well-meaning, conscientious people who are trying to do their job well, but who are caught in faulty systems that set them up to make mistakes and who become "second victims"
- **Often the causes of errors reside within the organization in which people work.**
- **Active failures or conditions** - unsafe acts committed by operators directly involved in the provision of care (e.g. administration of the wrong drug, wrong dose, wrong route)
- **Latent failures or conditions** (aka **root causes or resident pathogens**) - defensive gaps, weaknesses, or absences unwittingly created in a system as the result of earlier decisions made by the designers, builders, regulators, managers, and trainers in the system



Anesthesia of a Polar Bear: The Obvious Disguised as the Unusual

http://www.alaskastock.com/preview.asp?imageCM0013D001 (5/24/2010)





Anesthesia of a Polar Bear: Losing Sight of the Obvious

- Scenario at zoo:
  - Remote examination of Ursus confirmed fractures, but he was alert, responsive and attentive
    - Closer exam was not possible
  - Zoo vet was concerned about about internal injuries. Assumed Ursus would not eat if there were significant internal injuries; offered an apple, a food item the bear was known to like, which he promptly ate indicating that he did not have internal injuries.
  - Ursus was scheduled for an orthopedic examination and possible surgery the following day at a tertiary care facility
- Scenario at hospital:
  - If fractures not reparable Ursus would be euthanized, and his carcass taken to a taxidermist and prepared for display at the zoo.
  - For this reason it was made clear that no part of Ursus's fur was to be shaved unless he was taken to surgery.
  - The press—print & TV—and public were keenly interested in Ursus's condition and how it was going to be managed.
  - Based on radiographs surgeons stated they could repair the fractures

Anesthesia of a Polar Bear: Or How to Lose Sight of the Obvious

- Anesthesia:
  - Pole-injected with etorphine (4 mg) and xylazine (10 mg), IM
  - Masked with 2% Hal in O2 at 10 L/ min
  - Intubated 18 mm ETT
  - IPPV 5 bpm
  - Question was asked about internal injuries
    - Ruled out in deference to zoo vet's experience and expertise
  - Comment was made about dense fur and risk of hyperthermia
- ECG – normal sinus tachycardia
- Lingual artery catheterized
- Hct 44%; TS 6.5g/dL
- Temp 103.1
- pH 7.40, PaCO2 49, PaO2 174, and base balance +5.2
- MAP ranged from initial high of 153 mmHg to a low of 72 mmHg; majority of readings between 100 to 110 mmHg.
- PaO2 range: 445 to 491 mmHg; PaCO2 average of 45 mmHg for 3 hrs, then average of 28 for fourth hour; base balance averaged 5.8 (range: 5.2 to 6.5).
- Temp increased to 106F then decreased to 104F with cooling
- Tachycardia assumed to be due to hyperthermia, and hyperthermia due to thick fur coat

Anesthesia of a Polar Bear: Or How to Lose Sight of the Obvious

- **Anesthesia**
  - During anesthesia the abdomen was noted to be "fluidy". No further observations were made or actions taken.
- What other interpretations might be made of the tachycardia and hyperthermia?
- Did members of the anesthesia & surgery team hold preconceptions or biases that affected their decision making? If so, what were they?
- Surgery was completed in 5 hours
- Banamine for post-op analgesia
- Ursus transferred to cage
- M50-50 given to reverse any remaining effects of etorphine
- Seemed to recover as expected
- Died one hour later while being transported back to the zoo

Anesthesia of a Polar Bear

- **Several factors prevented the entire team from correctly identifying the extent of Ursus's injuries:**
  - Failed to question a colleague's assessment of Ursus's condition.
    - Seemed uncollegial
      - Professional courtesy must not get in the way of checking colleagues' knowledge and experience. {Reason, 2004}
  - **Euthanasia was perceived as a sign of failure; not a "can do" attitude**
    - Public opinion
  - Assumption that tachycardia and hyperthermia were due to Ursus's dense fur
    - **Confirmation bias** – the tendency to seek evidence that supports an early working hypothesis while ignoring data that contradict it.
  - **Holding on to admonitions about how the bear was to be managed long after the justifications for those admonitions had passed.**
  - Failure to fully recognize that Ursus was a wild animal and the consequences of this fact for his behavior.

Anesthesia of a Polar Bear

- If barriers and biases had been identified and overcome, and a thorough examination performed under anesthesia, would Ursus have been "saved"?
  - No, but a correct diagnosis would have been made and…
  - he would have been humanely euthanized as he should have been.

Case Example

Out of Sight Cat!

The Practice and Anesthesia

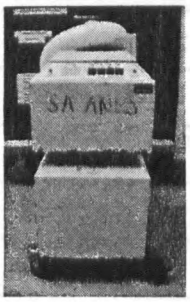
- **Background**
  - 2500 general anesthetics per year
  - Most frequent and persistent complication is hypothermia
    - Complications included…
      - Delayed recoveries
      - Respiratory arrest
      - Drug over doses
    - Made significant efforts to reduce this complication

Effects of Hypothermia

Respiratory	Blunted **response to CO2**
Blood	Increase in blood viscosity Impaired platelet function Impaired coagulation cascade
Immune system	Impaired neutrophil and macrophage function Delayed wound healing

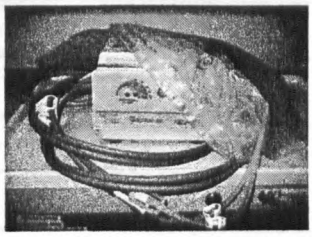
Techniques to Prevent Hypothermia

- Bair Hugger



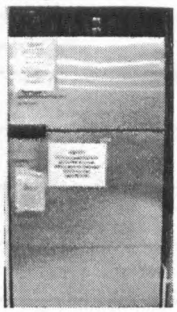
Techniques to Prevent Hypothermia

- Circulating warm water blankets



Techniques to Prevent Hypothermia

- Warm water bottles and warm water filled gloves



Techniques to Prevent Hypothermia

- Towels & Blankets

Out of Sight Cat!

- **Signalment:** 1year old cat
- **Hx:** 1.5 months of increased respiratory effort, especially after exercise
- mild asymmetry of the cardiac papillary muscles
- **PE:** Echocardiography and radiographs of the cat's thorax did not identify the cause of the cat's respiratory problem.
- **Diagnostic plan:** Under anesthesia, CT exam of the nasal passages/sinuses followed by bronchoscopy

- **Anesthetic plan:**
- **Premeds** - hydromorphone (0.1 mg/kg) + midazolam (0.2 mg/kg), SQ
- **Induction** – pre-O2; thiopental (6 mg/kg) + propofol (2.4 mg/kg), IV; oral exam then intubated 4mm ETT; pediatric circuit
- **Maintenance** - isoflurane in O2; mechanically ventilated (PIP=12cmH2O); **ETCO2 (28-32 mmHg)**
- **Monitoring** – ECG (NSR), NIBP (Doppler; low BP initially), SPO2 (100%); ETCO2

Out of Sight Cat!

- **CT exam:** no evidence of a space occupying lesion in
- nasal passages or sinuses
  - Cat allowed to breathe spontaneously

- **Endoscopy:**
- Sternal recumbency
- All monitoring devices were attached
- Two circulating warm water heating pads
  - one above the cat and one below
- Towel was then placed on top of uppermost heating pad leaving cat's head visible
- To better visualize the endoscopy monitor, the room lights were turned off

Out of Sight Cat!

- **Endoscopy:**
- Numbers…
  - SP02 100%
  - ETCO2 45 mmHg
  - Systolic BP 110 mmHg
  - ECG NSR
  - Fluids - 10ml/kg/hr.

- **Endoscopic exam:**
- cat was extubated for airway exam and propofol infusion (0.1 mg/kg/min) was started
- fresh gas hose of anesthesia machine was attached to endoscope port
  - fresh gas flow was started at 3 L/min, then increased to 8 L/min

Out of Sight Cat!

- Endoscopic exam:
- As scope was advanced into trachea systolic BP decreased from 92 mmHg to 83 mmHg so dopamine CRI was started.
- cat also seemed light so propofol bolus (10 mg) was injected IV.

- Endoscopic exam:
- 10 minutes later the bronchopulmonary lavage was started
- At same time, anesthetist attempted to measure blood pressure
  - Inflated BP cuff to >200 mmHg and could still hear the arterial pulse on the Doppler.
- Following events occurred rapidly:
  - Checked cuff placement and it seemed OK
  - Noted that fluids were not flowing and propofol injected earlier was flowing up IV line

Out of Sight Cat!

- **Endoscopic exam:**
- Following events occurred rapidly:
  - Catheter was flushed but fluids did not start to flow
  - ECG clip fell off cat
  - SPO2 decreased to 77% but increased to 83% as the endoscopist quickly removed scope

- Endoscopic exam:
  - Anesthetist attempted to intubate cat but could not because of severe oropharyngeal swelling
  - Decision made to perform a tracheostomy at which point the room lights were turned on and the cat was uncovered
  - Cat had severe sub-cutaneous emphysema
  - CPR was unsuccessful
  - Cause: insufflated oxygen ruptured through tracheal wall and caused pneumomediastinum, pneumothorax and subcutaneous emphysema.

Out of Sight Cat!

- What errors were made?
  - Systemic errors (latent conditions)
    - ♦Turning lights off was common and considered inconsequential
    - ♦Endoscopic monitor was a distraction
    - ♦Setting put the cat out of sight

Out of Sight Cat!

- What errors were made?
  - **Active failures or conditions**
    - ♦Unforeseen local triggers
      - ❖High O2 flow
        - ►No forcing mechanism
      - ❖Scope occluding trachea
      - ❖Defect in trachea [redacted]
    - ♦Atypical events came together and caused this cat's demise
    - ♦Lack of "mindfulness"
      - ❖**The best of intentions can and do go awry**

A Cool Cat!

A Cool Cat!

- **Signalment:** 10 year old, F/S, DLH cat
- **Hx:** acute unilateral retinal detachment

FeLV positive

- **PE, Blood work & Imaging:** blind but BAR
- Blood work normal except T4 0.10 ug/dL (normal: 1.5-4); FT4d 0.37 ng/dl (normal: 1.5-4); total T3 0.7 (normal: 0.3-0.9)
- Chest rads were read as unremarkable.
- **Surgical plan:** Retinal aspiration

- **Anesthetic plan:**
- **Premeds:** hydromorphone (0.1 mg/kg) + midazolam (0.4 mg/kg), SQ
- **Induction:** pre-O2; thiopental (6 mg/kg) + propofol (2.4 mg/kg), IV; pediatric circuit
- **Maintenance:** isoflurane in O2;
- **Monitoring:** ECG – sinus bradycardia (110); NIBP (Doppler; low BP responded to decreasing iso); SPO2 (100%); ETCO2 (44-46mmHg)

A Cool Cat!

- Retinal aspiration
  - Performed uneventfully
- Bone marrow aspirate
  - Uneventful
- Recovery
  - Recovered as expected
  - Temperature was low (95F)
    - Decision was made to keep cat under warm water pad and Bair Hugger until temperature was 97F
    - When temp was 97 a decision was made to continue warming the cat in the recovery cage with the Bair Hugger

- **Recovery**
  - Operational logistics
    - Ophthalmology student extern assigned to this patient was requested to go to the OR and assist with another surgery
    - The anesthesia schedule was very busy, and the anesthetist assigned to this cat had to start another case,
    - It was agreed that in a few minutes someone would check the cat's temperature.
  - Two-and-a-half hours latter the cat was found dead in its cage with the Bair Hugger still running

A Cool Cat!

- **Case Analysis**
  - Chest rads – initially read as unremarkable
    - Subsequently changed to mild, diffuse airway lung pattern due to inflammatory or immune-mediated airway disease, cardiogenic or non-cardiogenic pulmonary edema, or possibly infiltrative neoplasia; negative for cardiomegaly.
- **Necropsy**
  - Mild hypertrophic cardiomyopathy
  - Lymphocytic optic neuritis

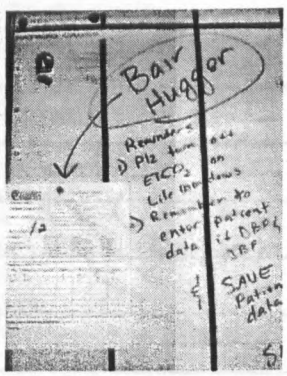
A Cool Cat!

- Lessons learned
  - Follow up on patient depended on short-term memory, the most labile of human memory.
    - No memory jogging clues
    - No one person clearly identified to check on the patient
  - A busy schedule is a source of distractors

Cool Cat

Solutions implemented

- Visual reminders
- Check list for recovery:
  - Time
  - Temperature
  - Consciousness
  - Activity
  - Pain
  - Total score
  - Initials



Just an Eyelid Mass

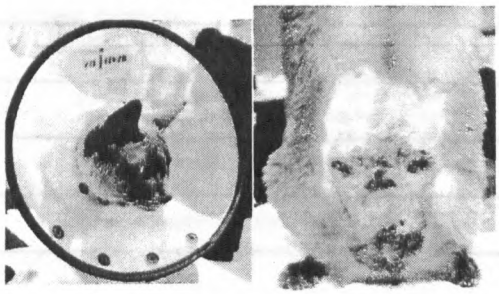
Just an Eyelid Mass

- **Signalment:** 12 year old, F/S Siamese, 5.4kg
- **Hx:** 5mmx3mmx3mm mass on lower left eyelid diagnosed as a mast cell tumor
- **PE & Diagnostics:** Blood work unremarkable; US exam - chronic unilateral nephropathy; small pancreas; chest rads - no pulmonary metastases
- **Surgical plan:** surgical excision of mass
- **Anesthesia plan:**
- **Premeds:** hydromorphone (0.1 mg/kg) + midazolam (0.2 mg/kg), SQ; 32 minutes later dexmedetomidine (3ug/kg), IM. diphenhydramine (10mg); femotidine (2.7mg)
- **Induction:** pre-O2; etomidate (8.4mg)
- **Maintenance:** isoflurane in O2; pediatric circuit
- **Monitoring:** ECG – sinus rhythm (135-185); NIBP (Cardel); SPO2 (96-97%);
- Total anesthesia time 60 minutes
- Cat recovered uneventfully except for hematuria (late stream) in recovery.
- **Discharged from hospital**

Just an Eyelid Mass

- The saga continues:
- 9 days later the owners return with the cat
  - Complaint: cat developed burn-like lesions on its abdomen that required medical/surgical treatment (debridement) at their local practice.
  - Examination revealed bacteria-filled pustules on the abdomen, necrotic tissue, and wound pattern very much like a burn.

Just an Eyelid Mass

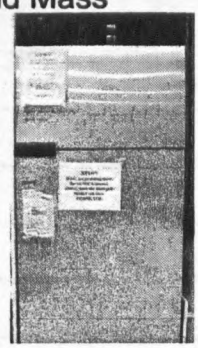


Just an Eyelid Mass

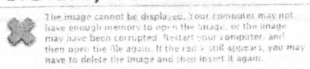
- **Actions taken:**
  - A letter of concern and apology that outlined how the injury occurred was sent to the owners
- **Analysis of the problem…**

Just an Eyelid Mass

- **A tech acknowledged that a water-filled fluid bag had been used to keep the cat warm**
- **Checked fluid warmer**
  - Working OK, but…
  - many felt that bottles and bags were not effectively warming patients, so…
  - over time thermostat setting was increased to 124F (51C).
  - Bag temperatures were at least 106F (41.3C)



Temperature, Contact Time & Burns



Actions Taken

- Thermostat was reset to 110F
- Problem was made known throughout the practice
- If bags are used to warm a patient, cloth towel must be placed between bag and patient

Techniques to Prevent Hypothermia

- Prevention strategies…
  - were viewed as relatively harmless (except gloves and water-filled bags)
  - were viewed as positive, implemented with the patient's best interest at heart
  - developed over time in an *ad hoc* manner
  - technique used varied from individual to individual

Hypothermia

- **Systemic errors (latent conditions)**
  - Everyone assumed that warming efforts were relatively harmless, with few exceptions…
    - Hot water bottles or gloves
    - Electric heating pads
  - viewed as positive, implemented with the patient's best interest at heart…
  - developed over time in an *ad hoc* manner (without forethought)…
  - technique used varied from individual to individual

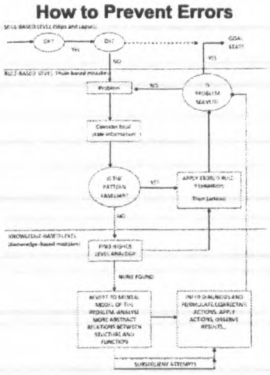
How to Prevent Errors

- These three cases have taught us a great deal as to why and how specific errors and mistakes occur in our practice…
  - but the lessons were learned over 4 years…
  - and were learned at great expense to our patients and clients.
    - **There has to be a better—safer, more efficient—way to learn how to prevent errors**
- **Near misses and Learning Organizations**

How to Prevent Errors

Mnemonic	Definition
C	Circulatory Capnograph Color
O	Oxygen supply Oxygen Analyzer
V	Ventilation Vaporizer
E	Endotracheal tube Eliminate the anesthesia machine
R	Review monitors Review equipment

How to Prevent Errors



How to Prevent Errors

- **Near misses**
  - **If you find yourself saying…**
    - Whoa, I didn't know that could happen!!
    - Oops, that was a close call!!
    - Whew, we pulled that one out of the fire!!
    - Good catch!!
  - **These responses may be prompted by near misses that are worthy of our attention.**

    - They are educational gems! -

Selected Readings

- James Reason. Human Error. Cambridge University Press, Cambridge, UK; 1990
- James Reason. The Human Contribution: Unsafe Acts, Accidents and Heroic Recoveries. Farnham, England; Ashgate Publishing Co. 2008
- David M. Gaba, Kevin J. Fish, Steven K. Howard. Crisis Management in Anesthesiology. Philadelphia, PA USA; Churchill Livingstone. 1994
- Catherine Marcucci, Norman A. Cohen, David G. Metro, Jeffrey R. Kirsch, Editors. Avoiding Common Anesthesia Errors. Philadelphia, PA USA; Lippincott Williams & Wilkins. 2008.

The End!

The Functions of an Anesthetist

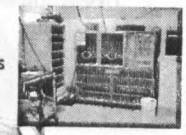
- There are four:
  - Manage the patient's airway
  - Anticipate, identify or control for elements (Reason's "bad stuff") that place a patient at increased risk of morbidity or mortality in the peri-anesthetic period
  - Respond to the patient's response to both anesthesia (drugs and techniques) and the procedure it is undergoing.
  - For each patient develop an anesthetic plan that provides an adequate plane of anesthesia and analgesia for the procedure being performed.
- These functions are learned!

THE EMERGENCY CLINICIAN'S APPROACH TO THE FELINE RESPIRATORY DISTRESS PATIENT

Gretchen Lee Schoeffler, DVM, DACVECC
Emergency & Critical Care

Overview

- Definitions
- The 5 causes of hypoxemia
- The 8 causes of respiratory distress
- The dyspneic cat
- Case examples
- Summary



Definitions

- Symptom
  - Subjective evidence of disease or physical disturbance observed by the patient
- Clinical sign
  - An objective evidence of disease as observed and interpreted by the physician (or vet!) rather than by the patient or lay observer
- Dyspnea
  - Symptom
  - Patient's perception of difficult or labored breathing
- Respiratory distress
  - Clinical sign
  - Our perception of difficult or labored breathing

Medline Plus Medical Dictionary, Merriam-Webster

Respiratory Function

- Ventilation - ability to move air into and out of the alveoli
  - Reflected in the partial pressure of carbon dioxide dissolved in arterial blood ($PaCO_2$) as measured on a blood gas
- Oxygenation - ability to get oxygen into the blood
  - Reflected in the partial pressure of oxygen dissolved in arterial blood (PaO_2) as measured on a blood gas
  - Reflected in the percent saturation of arterial hemoglobin with oxygen SaO_2 (SpO_2)

PaO_2	SaO_2	Implication
100+	98+	Normal
80	95	Below is hypoxemia
60	90	Warrants aggressive therapy
40	75	Imminently life threatening

5 Causes of Hypoxemia

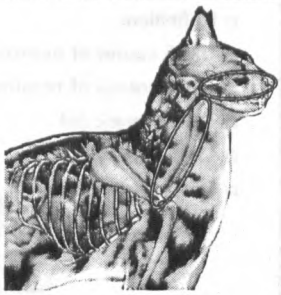
- Decreased FiO_2
  - Anesthesia
- Hypoventilation
  - Neurologic
  - Anesthesia/sedation
  - Obstruction
  - Airway disease
- Diffusion Impairment
  - Pulmonary fibrosis
  - Interstitial disease (edema/hemorrhage)
- V/Q Mismatch
  - Alveolar disease
  - Pulmonary hypertension
- Shunt (V/Q = ZERO)
  - Atelectasis
  - Severe alveolar disease
  - No response to O_2 supplementation

Respiratory Distress - Signs

- Increased respiratory rate and/or effort
- Abnormal posture (orthopnea)
- Pallor
  - Vasoconstriction due to catecholamine
  - Anemia
- Cyanosis
  - 3-5 g/dl of deoxygenated hemoglobin
  - With normal HCT, SpO_2 = 73-78%, PaO_2 = 39-44 mmHg
  - With LOW HCT, SpO_2 is even LOWER
- If due to respiratory disease
  - Hypoxemia: PaO_2 < 60 mmHg
  - Hypercapnia: $PaCO_2$ > 50 mmHg

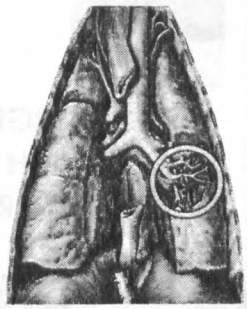
8 Causes of Respiratory Distress

1. Upper airway



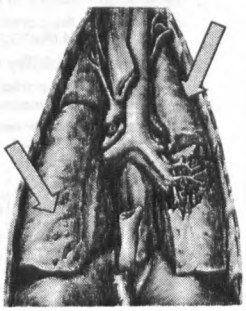
8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway



8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway
3. Pulmonary parenchyma

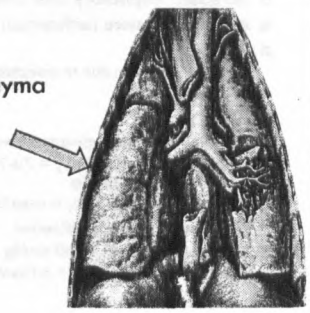


8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway
3. Pulmonary parenchyma
4. Pleural space

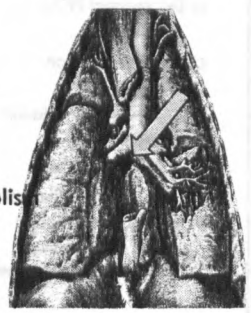
8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway
3. Pulmonary parenchyma
4. Pleural space
5. Chest wall



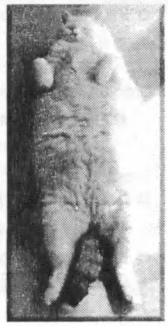
8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway
3. Pulmonary parenchyma
4. Pleural space
5. Chest wall
6. Pulmonary thromboembolism



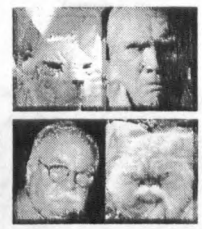
8 Causes of Respiratory Distress

1. Upper airway
2. Lower airway
3. Pulmonary parenchyma
4. Pleural space
5. Chest wall
6. Pulmonary thromboembolism
7. Abdominal distension



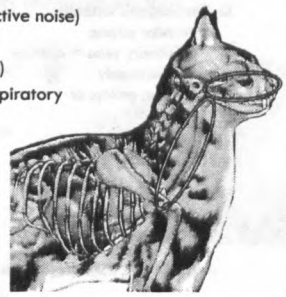
8 Causes of Respiratory Distress

1. Upper Airway
2. Lower airway
3. Pulmonary parenchyma
4. Pleural space
5. Chest wall
6. Pulmonary thromboembolism
7. Abdominal distension
8. Look-alikes



1. Upper Airway

- Characteristic Findings
  - Stridor (laryngeal obstructive noise)
  - Stertor (snoring)
  - Cough (trachea / bronchi)
  - May be inspiratory or expiratory
- Cause of Distress
  - Obstruction of air flow
  - Hypoventilation
- Blood Gas
  - Hypercarbia
  - ±Hypoxemia



1. Upper Airway - DDx

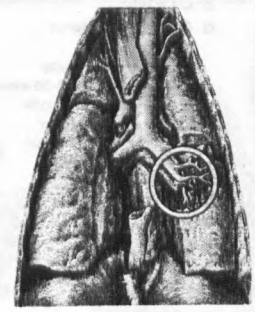
- Degenerative
  - Laryngeal paralysis
  - Collapsing trachea
- Anomalous
  - Brachycephalic airway syndrome
- Metabolic
  - ?
- Neoplasia
  - Primary
  - Metastatic
- Infectious / inflammatory
  - Sterile laryngitis
  - Abscess / granuloma
  - Foreign body
- Trauma
  - Hematoma
  - Swelling
  - Fracture
- Vascular
  - Coagulopathy

1. Upper Airway - Treatment

- Relieve the obstruction!
  - Sedation
    - Butorphanol 0.3 mg/kg combined with one of the following:
      - Diazepam 0.2 mg/kg
      - Midazolam 0.2 mg/kg
      - Acepromazine 0.01 mg/kg
    - Propofol 1-2 mg/kg boluses to effect
  - Intubation
  - Tracheostomy
- Treat hyperthermia
  - Active cooling until T < 104°F
  - IV fluids

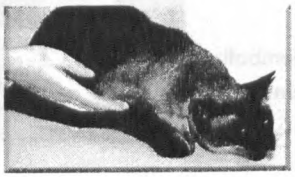
2. Lower Airway

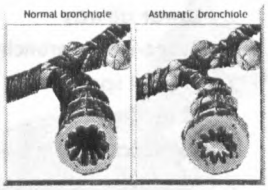
- Characteristic findings
  - Wheezes on auscultation
  - Coughing
  - Expiratory dyspnea
- Cause of distress
  - Obstruction of expiration
  - Air trapping
  - Hypoventilation
- Blood gas
  - Hypercarbia
  - ±Hypoxemia



2. Lower Airway - DDx

- Cats
  - Asthma!





2. Lower Airway - Treatment

- Bronchodilators
  - B_2 agonists – best choice
    - Terbutaline, 0.01 mg/kg IM
    - Albuterol inhaler
  - Phosphodiesterase Inhibitors
    - Aminophylline 5-10 mg/kg IM
    - Theophylline – oral only
- Corticosteroids
  - Dexamethasone 0.1 mg/kg IM
- Put in an O_2 cage and LEAVE ALONE!

3. Pulmonary Parenchymal

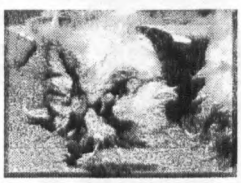
- Characteristic Findings
  - Crackles on auscultation
  - May be areas with dull sounds
  - Most commonly inspiratory distress
- Cause of Distress
  - Hypoxemia
  - Hypoventilation less common
- Blood Gas
  - Hypoxemia
  - ±Hypercarbia in SEVERE cases or fatigued animals (young)

3. Pulmonary Parenchymal - DDx

- Water
  - Cardiogenic edema
    - Perihilar edema
    - Pulmonary veins > arteries
    - Cardiomegaly
    - Murmur, gallop, or arrhythmia
    - Hypothermia
  - Non-cardiogenic edema
    - Caudodorsal edema
    - Normal heart and vessel size
    - History of strangulation, electrocution, seizures, near-drowning
- Blood
  - Contusion – hx of trauma
    - Patchy, variable distribution
  - Coagulopathy
- Soft Tissue
  - Neoplasia
- Interstitial
  - Pulmonary fibrosis
- Pus
  - Pneumonia
    - Cranioventral or patchy alveolar pattern
    - Fever

3. Pulmonary Parenchymal - Tx

- OXYGEN!
- Cardiogenic Edema
  - Lasix!
    - 2-4 mg/kg initially
    - 1-2 mg/kg q 15-30 minutes
    - CRI 0.7-1.4 mg/kg/hr
  - Vasodilator Therapy
    - Nitroglycerine topical
    - Nitroprusside CRI
  - NO FLUIDS!
- Non-Cardiogenic Edema
  - Time
  - Lasix?
- Pulmonary contusion
  - Oxygen
  - Conservative IVF therapy



4. Pleural Space

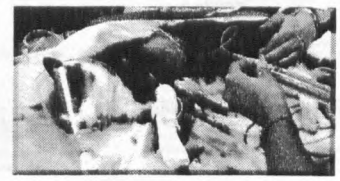
- Characteristic Findings
  - Dull to normal lung sounds
  - Rapid, shallow respirations (restrictive pattern)
- Cause of Distress
  - Hypoventilation
  - Inability to expand lungs
- Blood Gas
  - Hypercarbia
  - ±Hypoxemia

4. Pleural Space - DDx

- Air (pneumothorax)
  - COMMON in trauma
  - Doesn't always sound dull
- Water (hydrothorax)
  - Congestive heart failure
  - Hypoproteinemia
- Pus (pyothorax)
  - External wound may have already healed
  - Pulmonary abscess
- Other exudate
  - FIP
- Blood (hemothorax)
  - Trauma
  - Coagulopathy
- Chyle (chylothorax)
  - Idiopathic
  - Heart disease
  - Neoplasia
  - Heartworm disease

4. Pleural Space - Tx

- Thoracocentesis is a "twofer"
  - Therapeutic
  - Diagnostic
- Options
  - Needle
  - Catheter
  - Butterfly

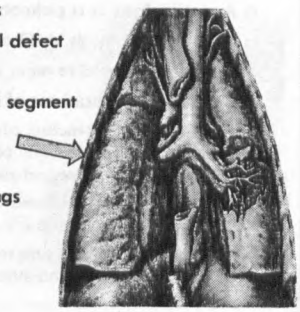


4. Pleural Space - Tx

- Indications for emergency thoracostomy tube
  - Tension pneumothorax
    - Disruption of lung
    - Tissue acting as "ball valve"
    - Air enters thorax on each inspiration
  - Continuous pneumothorax
    - Hole in lung open to pleural space
    - Hole in chest open to pleural space
  - Pyothorax
    - Risk of sepsis
    - Evacuate abscess, just as if it were in some other location
- Once stable, place in O_2

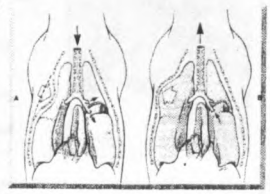
5. Chest Wall

- Characteristic Findings
  - Palpation of chest wall defect
  - Pain on palpation
  - Identification of a flail segment
- Cause of Distress
  - Hypoventilation
  - Inability to expand lungs
- Blood Gas
  - Hypercarbia
  - ±Hypoxemia



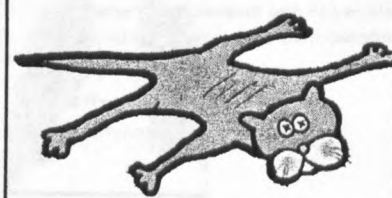
5. Chest Wall - DDx

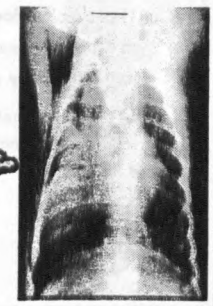
- Flail segment is the only chest wall disease that can cause respiratory distress
  - Penetrating chest wound = pleural space
  - Rib fracture = look alike (pain)
- Two fractures on same rib
- Compromises ventilation



5. Chest Wall - Diagnosis

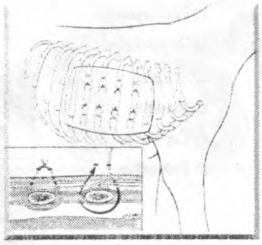
- Radiographs
- Visualization





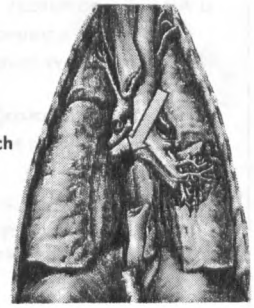
5. Chest Wall - Tx

- Put affected side down
  - Up lung ventilates better
  - Fractures stabilized
- ANALGESIA!!
  - Opiates
- Place bandage
- Consider surgical stabilization



6. PTE

- Characteristic Findings
  - Hypoxemia
    - Often unresponsive to O_2
- Cause of Distress
  - Hypoxemia
  - Presence of V/Q mismatch and SHUNT
- Blood Gas
  - Hypoxemia
  - Hypocapnia



6. PTE - Pathophysiology

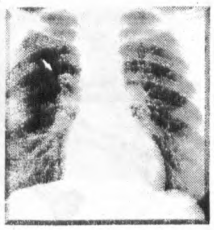
- A clot lodges in a pulmonary vessel
- This causes a high V/Q condition
  - Blood is shunted to other areas of lung
- Proposed mechanisms of hypoxemia
  1. Decreased surfactant production in affected area, alveoli collapse, leads to low V/Q when reperfused
  2. Production of inflammatory mediators leads to lung injury and low V/Q
  3. Increased PA pressure may increase intrapulmonary and intracardiac shunt

6. PTE - Diagnosis

- Diagnosis of exclusion
- Look for reason for hypercoagulability
  - Sepsis / SIRS
  - PLN, PLE
  - Immune mediated disease
  - Cardiac disease
  - Heartworm disease
  - Endothelial damage

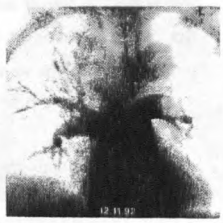
6. PTE - Diagnosis

- Thoracic radiographs
  - Commonly unremarkable
  - Occasionally note blunted vessels



6. PTE - Diagnosis

- Thoracic radiographs
  - Commonly unremarkable
  - Occasionally note blunted vessels
- Pulmonary angiography

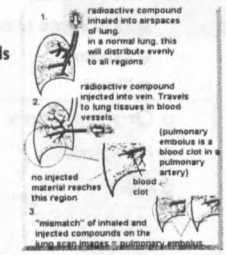


6. PTE - Diagnosis

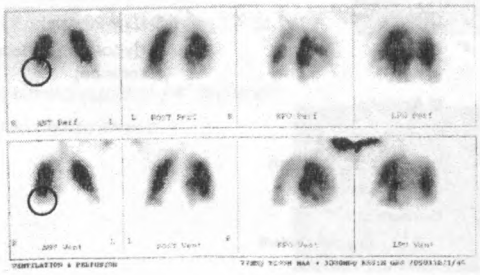
- Thoracic radiographs
  - Commonly unremarkable
  - Occasionally note blunted vessels
- Pulmonary angiography
- Contrast CT
  - Angiogram sometimes successful
  - Often unremarkable

6. PTE - Diagnosis

- Thoracic radiographs
  - Commonly unremarkable
  - Occasionally note blunted vessels
- Pulmonary angiography
- Contrast CT
  - Angiogram sometimes successful
  - Often unremarkable
- V/Q Scan



6. PTE - Diagnosis

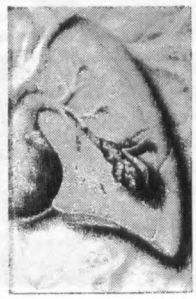


6. PTE - Diagnosis

- Thoracic radiographs
  - Commonly unremarkable
  - Occasionally note blunted vessels
- Pulmonary angiography
- Contrast CT
  - Angiogram sometimes successful
  - Often unremarkable
- V/Q Scan
- Ultrasound

6. PTE - Treatment

- Supportive care
- Heparin
  - Does not BREAK DOWN clot
  - Decrease growth of clot or new clot formation
  - Dosing is a CHALLENGE!
  - Monitor PTT, shoot for 150% of normal
- Thrombolytic therapy
  - All convert plasminogen to plasmin, which breaks down clots
  - Streptokinase
    - Not specifically active at clot sites => risk of bleeding
  - Tissue plasminogen activator (tPA)
    - Increased activity when bound to fibrin (clot)
    - Can still cause bleeding at high doses
  - VERY limited experience with dogs and cats
  - $$$$$$$

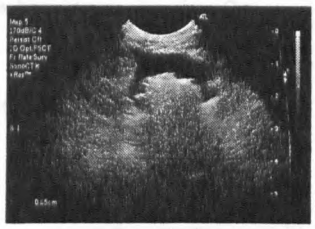


7. Abdominal Distension

- Characteristic findings
  - Abdominal distension on palpation
- Cause of Distress
  - Hypoventilation
  - Sometimes combined with Pickwickian Syndrome (decreased chest compliance)
- Blood Gas
  - Hypercapnia
  - ±Hypoxemia

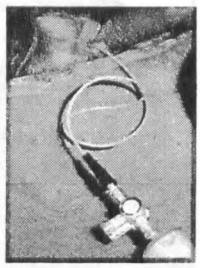
7. Abdominal Distension - DDx

- Fluid (ascites)
  - Transudate (±modified)
  - Exudate
  - Blood
- Organomegaly
- Neoplasia
- Fat



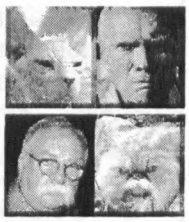
6. Abdominal Distension - Tx

- Most commonly due to ascites when acute
- Abdominocentesis
  - Only enough to relieve distress
  - Removing large volumes can lead to fluid shifts
    - Hemodynamic effects
    - Electrolyte effects



8. Look Alikes

- Characteristic findings
  - Rule out other causes
- Cause of distress
  - Neither hypoxemia nor hypercapnia
  - A non-respiratory problem that makes the patient appear to be in respiratory distress
- Blood gas
  - Hypocapnia
  - Normoxemia

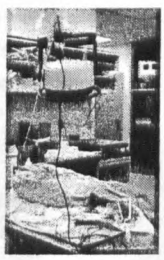


8. Look Alikes - DDx

- Behavioral
  - Stress
  - Fear
  - Pain
  - Anxiety
- Metabolic
  - Metabolic acidosis
    - Compensatory
  - Anemia
    - Low oxygen content
- Environmental
  - Hyperthermia
  - Hypothermia (less common)

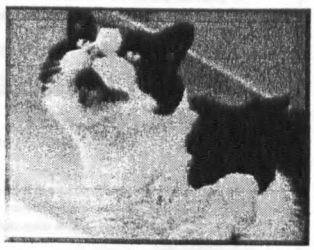
8. Look Alikes - Treatment

- Behavioral
  - Anxiolytics
  - Analgesics
- Metabolic acidosis
  - Treat underlying cause
  - Sodium bicarbonate
    - Bicarb deficit = 0.3 * BW[kg] * BE
    - NEVER give more than 1/3 – 1/2 of that dose
    - ONLY give if severe acidemia and patient can ventilate!
- Anemia
  - Transfuse if symptomatic
  - 1 ml/kg of pRBCs raises PCV by 1%
  - General guideline, 10-15 ml/kg



The Dyspneic Cat

- You auscult and you hear…
- Hmmm, was there a crackle? A wheeze?
- Top three differentials
  - CHF with pulmonary edema
  - Pleural space disease
  - Asthma
- How do you treat?
  - Put in an O_2 cage
  - Lasix IM (2-4 mg/kg)
  - LEAVE ALONE!
  - Diagnostic / therapeutic thoracocentesis
  - Last resort….
    - 2 mg/kg lasix
    - 0.1 mg/kg dexamethasone SP
    - 0.01 mg/kg terbutaline

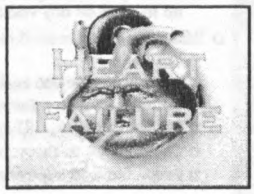


Blanche

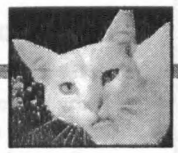
- Sig: 2 yr SF DSH cat – 3.5 kg
- Hx:
  - Previously healthy
  - < 24 hr history of tachypnea and lethargy
  - Indoor cat that lives with 3 other cats, and is up to date on her vaccinations including FeLV
- PE:
  - General:
    - T = 99.6, HR 200 bpm, RR = 140
    - Overt respiratory distress
  - EENT: mildly cyanotic, CRT ~ 2 seconds
  - CV: IV/VI left sided systolic murmur, gallop rhythm
  - Resp: marked tachypnea and effort, minimal BV sounds

Blanche's Problem List

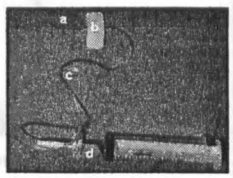
- Cyanosis
- Respiratory distress
  - Minimal lung sounds
  - Restrictive pattern
- Heart murmur and gallop
- Hypothermia



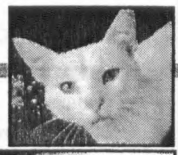
Emergency Stabilization

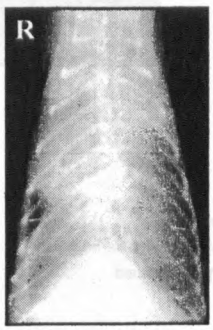


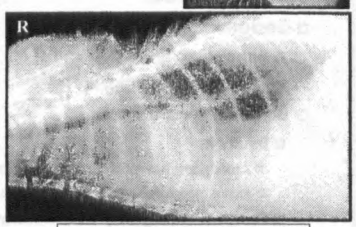
- Thoracocentesis!!!!
- Furosemide (2 mg/kg IM or IV)
- Oxygen
- Nitroglycerin (1/4" inguinal)
- Minimize stress!



Radiographs

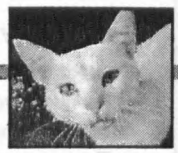






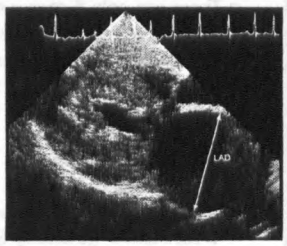
Too MUCH Fluid!!!!

Echocardiography

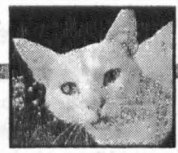


- What's your diagnosis?

FELINE HYPERTROPHIC CARDIOMYOPATHY WITH CONGESTIVE HEART FAILURE



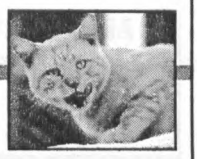
Can We Stabilize Blanche?



- After our second thoracocentesis Blanche is MUCH more stable
- Principles of management of CHF:
  - Improve oxygen delivery
    - Supplement!!
  - Reduce formation of edema and congestion
    - Lasix PRN!!
  - Increase cardiac output
    - Consider:
      - β-adrenergic blocker (atenolol)
      - Calcium channel blocker (diltiazem)
      - ACE inhibitor (enalapril)

O_2

Bixby

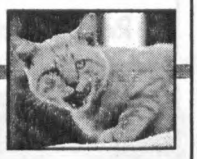


- Sig: 7 yr CM DSH cat – 5 kg
- Hx:
  - 5 day progressive stridor
  - < 24 hr history of tachypnea and lethargy
  - Indoor / outdoor cat that lives with 1 other cat, neither are up to date on any vaccinations
- PE:
  - General:
    - T = 103.6, HR 200 bpm, RR = 36
    - Overt respiratory distress
  - EENT: pale pink, CRT ~ 1.5 seconds
  - CV: difficult to assess heart due to referred stridor
  - Resp: marked inspiratory effort and stridor

Bixby's Problem List

- Respiratory distress with stridor
- Elevated rectal temperature
- Lesion localization – upper airway
- Differential diagnoses:
  - Sterile laryngitis
  - Neoplasia
  - Abscess / granuloma
  - Trauma
  - Laryngeal paralysis
  - Foreign body

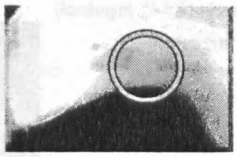
Emergency Stabilization



- Oxygen
- Minimize stress!
- Sedation!!!!
  - Butorphanol (0.3 mg/kg IV)
  - Diazepam (0.2 mg/kg IV)
- Be prepared to:
  - Intubate
    - Anticipate narrowed airway (small tube)
    - Have propofol available for possible emergent induction
  - Perform emergency tracheotomy if needed
  - Perform upper airway exam

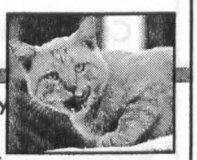
Radiographs

- Bixby improves and is sedate enough for a lateral cervical radiograph

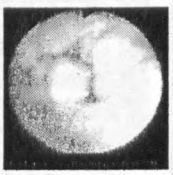


Severe laryngeal soft-tissue swelling

Diagnosis and Therapy



- Upper airway exam and laryngoscopy
  - Severe proliferative changes
- Histopathology reveals granulomatous laryngitis



- Treatment
  - Temporary tracheotomy
  - Dexamethasone SP (0.2 mg/kg/day) pending bx results
  - Oral amoxicillin with clavulanic acid 25 mg/kg PO q 12 hrs x 2 weeks
  - Oral prednisolone (1 mg/kg PO q 12 hrs) x 4 weeks past resolution of clinical signs

Summary

- Provide oxygen
- Minimize stress
- There are only 8 causes of respiratory distress!
  - Upper airway: stridor and or stertor
  - Lower airway: wheezes and or whistles
  - Pulmonary parenchymal: ± crackles
  - Pleural space: restrictive breathing pattern, ±dull or muffled lung sounds
  - Chest wall: palpate
  - PTE: exclusion
  - Abdominal distension: palpate
  - Look alikes: go looking!

After a thorough PE, there will only be 2 or 3!

Questions?

Suggested Reading

- Textbook of Respiratory Disease in Dogs and Cats
  - Lesley King
- Small Animal Critical Care Medicine
  - Deborah Silverstein and Kate Hopper
- Manual of Small Animal Emergency and Critical Care Medicine
  - Douglass Macintire, Kenneth Drobatz, Steve Haskins and William D. Saxon
- Kirk's Current Veterinary Therapy XIV
  - John Bonagura and David Twedt
- Consultations in Feline Internal Medicine, Volume 6
  - John R. August

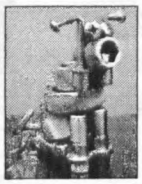
Practicing Feline CPCR An Interactive, Case-Based Simulation with Audience Participation

Gretchen Lee Schoeffler DVM, DACVECC
Daniel Fletcher DVM, PhD, DACVECC
CASS Rogers DVM, DACVECC

The Faculty of the Cornell University College of Veterinary Medicine's Companion Animal Hospital Section of Emergency and Critical Care Medicine

- **Cardiopulmonary cerebral resuscitation (CPCR) is an important technique to put into practice when patients suffer unexpected cardiac arrest.**
- **Simulation based training is gaining more recognition in human healthcare as a method of training that combines adult learning theory with real-time clinical situations.**
- **Debriefing and group discussion will allow the audience an opportunity to reinforce critical thinking and problem solving skills while enhancing collaboration and communication in the CPCR scenario.**
- **The following brief presentation will be followed by real time simulations.**

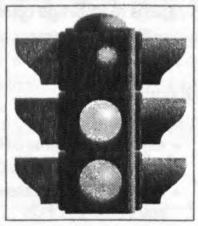
CPCR




THE NUTS AND BOLTS

Is the patient in cardiac arrest?

- Check for heart beat
- Check for pulses
- Code status
  - Red
  - Yellow
  - Green
- Owner's wishes?
- Cost?

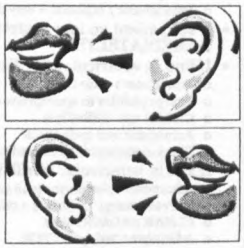


Members of the Team

- Leader
  - The individual running / directing the arrest
- Compressor
  - The person performing the chest compressions
  - If adequate personnel rotate compressor every 2 minutes
- Breather
  - Get control of the airway and breathe for the patient
- Drug pusher
  - Estimates patient weight and confirms estimate with leader
  - Readies appropriate doses of drugs and fluids
  - Anticipates needs....
- Recorder
  - Writes everything that is done down with a time stamp
  - Keeps the team appraised of time
- Owner advocate and communicator
  - Runs between the arrest and the owner – supports the owner through the decisions that must be made

Communication

- Closed loop communication
  - The practice of repeating back information when one member the team member makes a request of another



Basic Life Support = C - A - B

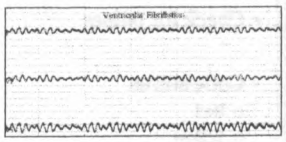
- Compressions = circulation
  - 100-120 compressions / minute
  - Hand placement
    - Directly over heart (smaller)
    - Over widest portion of chest (larger)
  - Achieve 30% compression of thorax
  - 1:1 duty cycle
  - Provide for adequate recoil
- 1 compression cycle = 2 minutes
  - Switch compressors every cycle (if possible)
- **MINIMIZE interruptions to compressions!**

Basic Life Support = C - A - B

- Airway – get control!
  - Intubate
  - Tracheostomy
  - Mouth to snout
- Breathe
  - 6-10 breaths / minute
  - Achieve normal chest rise
  - Supplement oxygen when possible

Advanced Life Support - Monitoring

- Subjective
  - Mucus membrane color
  - Capillary refill time
  - +/- pulse quality
- Objective
  - Electrocardiogram
    - Asystole: continue CPCR
    - Pulseless electrical activity (PEA): continue CPCR
    - Ventricular fibrillation: electrical counter-shock (defibrillation) and continue CPCR
  - End tidal CO_2
    - Is high or low good...?



Advanced Life Support - Drugs

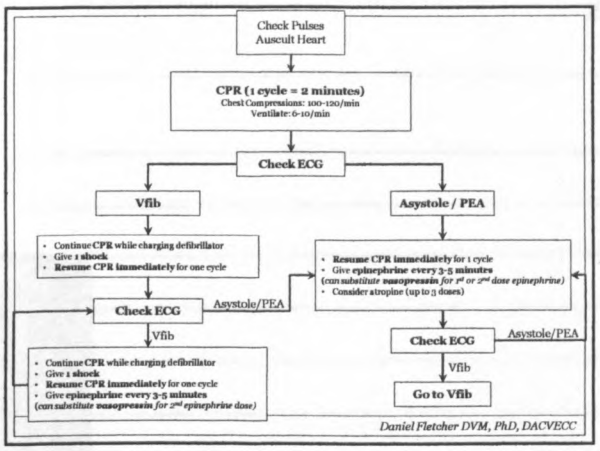
- Intravenous or intraosseous access
- Good time to get some POS tests
  - QATs, blood gas, electrolytes, other...
- Epinephrine (available in 2 different concentrations)
  - Low dose – high dose (0.01 – 0.1 mg/kg)
  - Redose every 3-5 minutes
- Vasopressin (20 U/ml)
  - 0.8 U/kg
  - Can be used instead of 1st or 2nd dose of epinephrine (1x only)
- Atropine (0.54 mg/ml)
  - 0.04 mg/kg
- Fluids
  - Generally isotonic to the patient
  - Dose dependent on underlying disease and condition

Advanced Life Support - Defibrillation

- Know your defibrillator!
  - Monophasic / biphasic = very different energy doses
- If see patient go into ventricular fibrillation – defibrillate IMMEDIATELY!!!
- If find in ventricular fibrillation
  - Administer 1 cycle CPCR
  - Charge paddles to appropriate energy (see dosing chart)
  - **CLEAR** and defibrillate
  - Administer 2nd cycle CPCR
  - Check electrocardiogram and patient
- If still in ventricular fibrillation
  - Administer epinephrine (can substitute vasopressin for 2nd dose of epinephrine)
  - Increase energy by 50% (1 x only)
  - **CLEAR** and defibrillate
  - Administer 2nd cycle CPCR
  - Check electrocardiogram and patient
- Repeat as necessary

Key Points

- MINIMIZE interruptions to compressions!
- Make sure ALL personnel are CLEAR prior to defibrillation!
- Practice direct closed loop communication with the team!



CPCR Emergency Drug Chart

CPCR Emergency Drugs and Doses

		Weight (kg)	2.5	5	10	15	20	25	30	35	40	45	50
		Weight (lb)	5	10	20	30	40	50	60	70	80	90	100
	DRUG	DOSE	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml
Arrest	Epi Low (1:10000)	0.01 mg/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Arrest	Epi High (1:1000)	0.1 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Arrest	Vasopressin (20 U/ml)	0.8 U/kg	0.1	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
Arrest	Atropine (0.54 mg/ml)	0.05 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Naloxone (0.4 mg/ml)	0.04 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Flumazenil (0.1 mg/ml)	0.01 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Atipamezole (5 mg/ml)	50 ug/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Defib	External Defib (J)	2-10 J/kg	6	15	30	50	75	75	100	150	150	150	150
Defib	Internal Defib (J)	0.2-1 J/kg	1	2	3	5	6	8	9	10	15	15	15

Daniel Fletcher DVM, PhD, DACVECC

Monophasic Defibrillator Dosing Chart

CPCR Emergency Drugs and Doses

		Weight (kg)	2.5	5	10	15	20	25	30	35	40	45	50
		Weight (lb)	5	10	20	30	40	50	60	70	80	90	100
	DRUG	DOSE	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml
Arrest	Epi Low (1:10000)	0.01 mg/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Arrest	Epi High (1:1000)	0.1 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Arrest	Vasopressin (20 U/ml)	0.8 U/kg	0.1	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
Arrest	Atropine (0.54 mg/ml)	0.05 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Naloxone (0.4 mg/ml)	0.04 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Flumazenil (0.1 mg/ml)	0.01 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Atipamezole (5 mg/ml)	50 ug/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Defib	External Defib (J)	2-10 J/kg	6	15	30	50	75	75	100	150	150	150	150
Defib	Internal Defib (J)	0.2-1 J/kg	1	2	3	5	6	8	9	10	15	15	15

Daniel Fletcher DVM, PhD, DACVECC

Biphasic Defibrillator Dosing Chart

CPCR Emergency Drugs and Doses

		Weight (kg)	2.5	5	10	15	20	25	30	35	40	45	50
		Weight (lb)	5	10	20	30	40	50	60	70	80	90	100
	DRUG	DOSE	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml	ml
Arrest	Epi Low (1:10000)	0.01 mg/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Arrest	Epi High (1:1000)	0.1 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Arrest	Vasopressin (20 U/ml)	0.8 U/kg	0.1	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
Arrest	Atropine (0.54 mg/ml)	0.05 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Naloxone (0.4 mg/ml)	0.04 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Flumazenil (0.1 mg/ml)	0.01 mg/kg	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Atipamezole (5 mg/ml)	50 ug/kg	0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Defib	External Defib (J)	2-10 J/kg	20	30	50	100	200	200	200	300	300	300	360
Defib	Internal Defib (J)	0.2-1 J/kg	2	3	5	10	20	20	20	30	30	30	50

Daniel Fletcher DVM, PhD, DACVECC

References

- **2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care**
  - **Circulation - vol. 112 (24), supplement; Dec 13, 2005**
- **Kirk's Current Veterinary Therapy XIV**
  - **John Bonagura and David Twedt, editors**
- **Small Animal Critical Care Medicine**
  - **Deborah Silverstein and Kate Hopper**
- **Manual of Small Animal Emergency and Critical Care Medicine**
  - **Douglass Macintire, Kenneth Drobatz, Steve Haskins and William D. Saxon**




22nd Annual Fred Scott Feline Symposium

July 23–25, 2010

Veterinary Education Center
Cornell University
Ithaca, New York

Welcome

Continuing in the tradition of providing the most up-to-date information on feline health issues, this year's 22nd Annual Fred Scott Feline Symposium draws on the knowledge of recognized experts in feline medicine. Speakers from The Ohio State University and Washington State University, plus faculty members from the College of Veterinary Medicine at Cornell University, will offer participants in-depth learning opportunities in feline medicine. Topics include urology, cardiology, critical care, dermatology and feline anesthesiology.

Elizabeth, the Feline Health Center mascot.

The symposium will be held in the Veterinary Education Center on Cornell University's Ithaca campus, and is presented by the Cornell Feline Health Center, Cornell University College of Veterinary Medicine, and our corporate sponsors. This symposium has been submitted (but not yet approved) for 17 hours of continuing education credit in jurisdictions which recognize AAVSB RACE approval; however participants should be aware that some boards have limitations on the number of hours accepted in certain categories and/or restrictions on certain methods of delivery of continuing education. Call Amanda Mott at 607.253.3200 for further information.

This year's symposium features the James R. Richards Memorial Feline Lecture presented by renowned veterinary urologist/nephrologist, Dr. Dennis Chew. This will be the latest in a lecture series established to honor the late Dr. Richards, and to remember his efforts to improve the health and well-being of cats everywhere.

The Finger Lakes region of upstate New York is beautiful in the summertime. We look forward to seeing you at the Feline Symposium, the annual Friday evening picnic and, new this year, the Saturday evening Wine and Cheese Reception.

The Feline Continuing Education Committee

Christine A. Bellezza, DVM, Acting Co-Director of the Feline Health Center

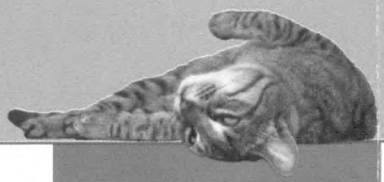
Bruce G. Kornreich, DVM, PhD

Paul S. Maza, DVM, PhD, Acting Co-Director of the Feline Health Center

Carolyn M. McDaniel, VMD

Kenneth W. Simpson, BVM&S, PhD

SCHEDULE



Friday, July 23

7:30–8:00 a.m. **Registration and Continental Breakfast**
Sponsored by Fallon Wellness Pharmacy

8:00–8:15 a.m. **Welcome**

8:15–9:15 a.m. **Chronic Kidney Disease (CKD) - Staging Renal Disease and Updates on Treatment**
We will briefly discuss the IRIS staging system based on creatinine, blood pressure, and urinary protein levels. Methods to make the diagnosis of CKD at early stages will be considered. The reasons that renal diseases progressively worsen will be reviewed, as this information is necessary to prescribe rational therapy.
Dennis Chew

9:15–9:30 a.m. **Break**

9:30–10:30 a.m. **Chronic Kidney Disease (CKD) - Staging Renal Disease and Updates on Treatment** *(continued)*
This session will emphasize treatment strategies that include dietary intervention with emphasis on phosphorus restriction. The use of intestinal phosphorous binders will be featured along with methods to best control renal secondary hyperparathyroidism and blunt RAAS system activity that are beneficial for preserving renal function and extending the expected life span of the cat. *Dennis Chew*

10:30–10:45 a.m. **Break**

10:45–11:45 a.m. **James R. Richards, Jr. Memorial Feline Lecture**
Feline Idiopathic Hypercalcemia
Updates on the diagnosis and treatment strategies for IHC will be detailed. We will discuss relatively new information on the use of bisphosphonates for treatment. Theories on the possible causes of this enigmatic syndrome will be presented. *Dennis Chew*

11:45-1:00 p.m. **Lunch**

1:00–2:00 p.m. **Hot Topics in Feline Cardiology**
Updates on biomarkers, identification of CHF, echocardiography, and Feline Heartworm Disease will be presented. *Mark Rishniw*

2:00–2:15 p.m. **Break**

2:15–3:15 p.m. **Clinical Use of Genetic Testing for Feline Hypertrophic Cardiomyopathy**
In this session we will discuss the inherited aspects of hypertrophic cardiomyopathy emphasizing the use of the available genetic tests for Maine Coon and Ragdoll cats and how to use the information to provide guidance to cat breeders. We will also discuss what is known about inherited hypertrophic cardiomyopathy in other breeds of cats as well. *Kathryn Meurs*

3:15–3:30 p.m. **Break**

3:30–4:30 p.m. **Feline Cardiomyopathy-Clinical Diagnosis and Management**
We will discuss controversies in the diagnosis of feline cardiomyopathy including use of BNP and assessment of diastolic parameters. Medical management including when and how to treat will also be discussed. *Kathryn Meurs*

4:30-5:30 p.m. **Feline Clinical Cardiology Rounds**
Sponsored by Paris Hill Animal Hospital
An interactive discussion of feline cardiology cases outlining principles of physiology, pathophysiology, diagnosis, and therapy. *Bruce Kornreich*

6:30–9 p.m. **Annual Picnic—Six Mile Creek Winery**

Speakers

Dennis Chew, DVM, Diplomate ACVIM (Internal Medicine), The Ohio State University

Daniel Fletcher, DVM, PhD, Diplomate ACVECC, Cornell University

Bruce Kornreich, DVM, PhD, Diplomate ACVIM (Cardiology), Cornell University

John Ludders, DVM, Diplomate ACVA, Cornell University

Kathryn Meurs, DVM, PhD, Diplomate ACVIM (Cardiology), Washington State University

Mark Rishniw, BVSc, MS, PhD, Diplomate ACVIM (Cardiology & Internal Medicine), Cornell University

Catherine Rogers, DVM Diplomate ACVECC, Cornell University

Gretchen L. Schoeffler, DVM, Diplomate ACVECC, Cornell University

Danny Scott, DVM, Diplomate ACVD, Cornell University

Saturday, July 24

7:30–8:00 a.m.	**Continental Breakfast** *Sponsored by Fallon Wellness Pharmacy*
8:00–9:00 a.m.	**Feline Idiopathic/Interstital Cystitis (FIC)** Updates on diagnosis and our proposed theories for the pathophysiology of FIC. *Dennis Chew*
9:00–9:15 a.m.	**Break**
9:15–10:15 a.m.	**Feline Idiopathic/Interstital Cystitis (FIC)** *(continued)* Treatment strategies for management of FIC emphasizing implementation of environmental enrichment (MEMO). Drug therapy will be mentioned, but this will be not be emphasized since MEMO works well without drugs. *Dennis Chew*
10:15–10:30 a.m.	**Break**
10:30–11:30 a.m.	**Urethral Obstruction in Cats - Standard and Novel Approaches** The causes for urethral obstruction in male cats will be reviewed. Rescue from the metabolic ravages secondary to urethral obstruction will be addressed. Standard methods to relieve urethral obstruction will be presented and a novel approach hat does not use instrumentation of the urinary tract will be introduced. *Dennis Chew*
11:30 a.m.–12:30 p.m.	**Making Errors: The Fundamentals** As the Institute of Medicine made clear in its publication, To Err Is Human: Building a Safer Health System (2000), highly trained and well- intentioned professionals make errors. Why and how do we make errors? This presentation presents some of the basic concepts underlying error generation and sets the stage for the second presentation. *John Ludders*
12:30–1:30 p.m.	**Lunch** *Sponsored by Intervet Schering-Plough Animal Health*
1:30–2:30 p.m.	**Feline Dermatology: Moving Pictures** These lectures will capture snapshots of selected topics in feline dermatology: serological allergy testing, cetirizine, histopathologic findings in allergic skin diseases, Malassezia, and a cool unknown. *Danny Scott*
2:30–2:45 p.m.	**Break**
2:45–3:45 p.m.	**Feline Dermatology: Moving Pictures** *(continued)* *Danny Scott*
3:45–4 p.m.	**Break**
4:00–5:00 p.m.	**Errors: Treasures of Practice (case examples)** Using the basic concepts presented in the first presentation, the case examples of this presentation demonstrate how and why errors occur, specifically during anesthesia, and how we can turn these unimaginable errors into educational gems. *John Ludders*
5:00-6:00	**Wine and cheese reception** *Sponsored by Merial*

Hotels and Lodging

Participants are responsible for making their own hotel reservations.

*Room blocks are being held until June 22, 2010

***Best Western University Inn**
East Hill Plaza, 607.272.6100

Comfort Inn Ithaca
356 Elmira Road (Rt. 13S), 607.272.0100

***Courtyard by Marriott**
29 Thornwood Drive, 607.330.3762

EconoLodge Ithaca
2303 N. Triphammer Road, 607.257.1400

Holiday Inn Ithaca
222 S. Cayuga Street, 607.272.1000

Homewood Suites
36 Cinema Drive, 607.266.0000

***Ramada Inn**
2310 N. Triphammer Road (Rt. 13N)
607.257.3100

Super 8 Motel
400 S. Meadow Street (Rt. 13S)
607.273.8088

For more information please contact:

College of
Veterinary Medicine
Office of
Continuing Education
Cornell University
S2 169 Veterinary Education Center, Box 52
Ithaca, NY 14853-6401
Phone: 607.253.3200
Fax: 607.253.3198
Email: amm36@cornell.edu

www.vet.cornell.edu/education/ConEd.htm

Sunday, July 25

8:00–8:30 a.m. **Continental breakfast**

8:30–10:00 a.m. **The Emergency Clinician's Approach to the Feline Respiratory Distress Patient**

As an emergency clinician it is imperative to be able to rapidly differentiate upper and lower airway disease from parenchymal and pleural space disease in cats with respiratory distress. Real world cases will be used to illustrate how to best determine the underlying etiology of these extremely fragile patients in an effort to better optimize treatment and outcome. *Gretchen L. Schoeffler*

10:00–10:15 a.m. **Break**

10:15–11:45 a.m. **Practicing Feline CPR–An Interactive, Case-Based Simulation with Audience Participation**

Cardiopulmonary resuscitation (CPR) is an important technique to put into practice when our patients suffer unexpected cardiac arrest. Simulation based training is gaining more recognition in human healthcare as a method of training that combines adult learning theory with real-time clinical situations. Debriefing and group discussion will allow the audience an opportunity to reinforce critical thinking and problem solving skills while enhancing collaboration and communication in the CPR scenario. *Gretchen L. Schoeffler, Catherine Rogers, and Daniel Fletcher*

SPONSORS

Intervet Schering-Plough Animal Health

MERIAL

Fallon Wellness Pharmacy

ProLabs™

Nate's PHARMACY AND SURGICAL SUPPLIES

Paris Hill Cat Hospital

Feline Health Center Professional Membership

Veterinarians registering by June 24, 2010 will receive a one-year complimentary Cornell Feline Health Center membership. Veterinarians who are already members of the center will have their membership extended for another year at no additional charge.

Special Events

Friday

Friday Lunch Tour—Register to take a 30-minute tour of the Cornell University Hospital for Animals during lunch hour on Friday *(space is limited).*

Friday lunch with Dr. Dennis Chew

$20—Join a small group of seven others for an informal lunch with a speaker *(space is limited).*

Annual Picnic

Join us on Friday evening for our annual symposium picnic at the Six Mile Creek Winery. This year we will enjoy chicken, ribs, grilled veggies and lasagna from Tucker's Catering; and music by Jorge Cuevas & The Caribe Jazz Allstars. The picnic price is included in the symposium registration fee but you must pre-register. Guests are also welcome for a fee.

Saturday

Saturday lunch with Dr. Kathryn Meurs

$20—Join a small group of seven others for an informal lunch with a speaker *(space is limited).*

Wine and Cheese Reception

The Wine and Cheese Reception is new this year and will provide a chance to relax and socialize with others following Saturday's lectures. A shuttle service will be provided to the Ithaca Commons after the Reception, giving conference attendees an opportunity to explore the shops and restaurants downtown. *Sponsored by Merial.*

Photos by Alexis Wenski-Roberts and Dr. Mark N. Frolick.

Printed on recycled paper.
5/10 3.3M FLP

Registration Form

Registration deadline: July 2, 2010

Register online at www.vet.cornell.edu/education/ConEd.htm

Full Name (for name badge) DVM, VMD, Other (please specify)

Practice Name

Type of Practice

Mailing Address ❑ Home ❑ Office

City State Zip

Telephone (weekday)

Email

College Attended Year of Graduation

Special Needs: Please advise us of any dietary, mobility, or other special needs you may have. _____

❑ Registration received **on or before June 24, 2010** **$400**

❑ Registration received **after June 24, 2010** **$450**

I would like to:

❑ lunch with Dr. Dennis Chew on Friday @ $20 (space is limited)

❑ lunch with Dr. Kathryn Meurs on Saturday @ $20 (space is limited)

❑ tour Cornell University Hospital for Animals during lunch on

____ Friday (space is limited)

❑ I will ❑ will not attend the Friday evening picnic (included in registration fee)

_____ Number of guests coming to the Friday evening picnic @ $40 each

Guest name(s) _____

❑ I am driving and will need a parking permit (necessary on Friday only)

❑ I am unable to attend the symposium, but would like to have a copy of the symposium proceedings mailed to me at $60 each. Your order must reach us before June 24, 2010. Proceedings will not be available for sale after June 24. The fee includes shipping and handling.

REGISTRATION

Registration deadline: July 2, 2010

You may register online at www.vet.cornell.edu/education/ConEd.htm or by completing this conference registration form and submitting by:

1) Fax: 607.253.3198 with a credit card

2) Phone: 607.253.3200 with a credit card

3) Mail: Send check payable to **Cornell University** or provide credit-card information below to:

College of Veterinary Medicine
Office of Continuing Education
S2 169 Veterinary Education Center, Box 52
Cornell University
Ithaca, NY 14853-6401

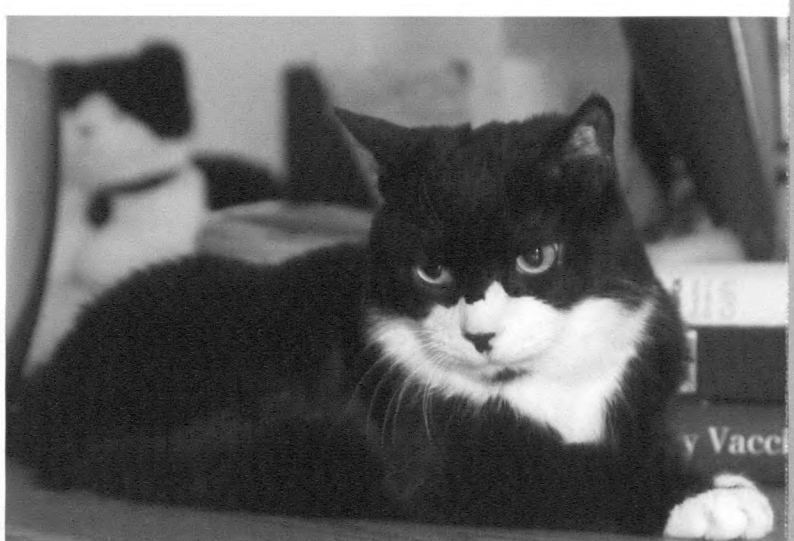
Charge to my: ❑ Visa ❑ MasterCard ❑ Discover ❑ American Express

Card Number: _____

Expiration Date: _____ CVV Code: _____

Signature: _____

Cancellation Policy: To cancel your registration, call 607.253.3200. Your fee, less a $100 processing charge, will be refunded for cancellations made on or before **July 2.** No refund will be issued after July 2, 2010, or for failure to attend.



Cornell University
College of Veterinary Medicine

Office of Continuing Education, Box 52
Ithaca, NY 14853-6401