FELINE GERIATRIC UPDATE: A NEW LOOK AT OLD CATS

Margie Scherk, DVM, Dip ABVP (feline practice)
Vancouver, B.C., Canada

The definition of "geriatric" has changed over the last decade, not just in cats, but in other species, as well. Our government, trying to find ways to prepare for the financial and social policy onslaught of creaking baby boomers is considering raising the retirement age. Life insurance companies have raised the age limits on coverage. These are reflections of greater longevity in our own species and the benefits of improved health care and nutrition. Cats are living longer than ever before: their life expectancy has risen, on *average*, to 14-15 years of age. The number of cats over a mere six years of age was reported as being 47% in 1996 whereas in 1983 it was only 24%. Many cats are living into their late “teens” and into their early twenties. Cats may be considered “mature” or “senior” after eight or nine years of age.

What does this mean to us, as practitioners, regarding our care of cats? A cat may *begin* to manifest serious age-related disorders, (e.g. renal insufficiency) on average, around 8 - 9 years of age. This does NOT make that individual old, or less treatable. With age come many interrelated cellular and molecular changes, which impact the wellbeing and health of our patients. Identified early, many of these changes can be corrected and blunted or managed to allow for comfortable, good quality and often, prolonged life. Therefore it is important to detect changes early through comprehensive physical assessment with appropriate diagnostic testing. This allows us to make medical and management recommendations based on the *individual* rather than their age.

Because the changes are usually so gradual, cats adapt to them and clients may view the changes, if they even notice them, as signs of: “just getting older”. One of the first, subtle changes common to older cats is progressive dehydration. The client may mention increased drinking or constipation. Less energy, “sleeping more” or lower activity level are signs of potentially reversible cellular changes. Muscle wasting may become obvious over time. Degenerative joint disease will contribute to “slowing down” and possibly to elimination outside of or away from the litter box. Weight loss, rather than weight gain, is the general rule in older cats, but rather than be alarmed, the client may be pleased with the new silhouette of a previously overweight cat or be proud of how alert and active their senior cat is.

There are "age-associated” or “age-appropriate” illnesses" we expect to see in older cats. These include a problems related to the urinary tract (chronic kidney disease (CKD), pyelonephritis, calcium oxalate ureteronephroliths, bacterial cystitis), endocrine system (hyperthyroidism, diabetes mellitus, hyperaldosteronemia), arthritis, dental diseases and neoplasia. Constipation may become an ongoing concern. Certain infectious diseases become more likely in the older individual (e.g., FIP). A decline in functioning of the special senses occurs frequently and behaviour changes suggestive of cognitive dysfunction may be seen in some individuals.

What are some of the impacts of aging on health? What practical implications do these have on veterinary care?
Vaccination frequency should be maintained in the older cat: as a cat ages, both the cell mediated immunity and humoral response decline. The number of T helper cells (CD4) decrease with thymic involution and the peripheral lymphoid population changes from a naïve, flexible, virgin one to a memory cell population. Some T cells lose their ability to progress through the cell cycle. The bone marrow, however, is unaffected by aging. Antigen processing and presentation are minimally affected. Aged macrophages are less responsive to chemotactic activating agents, such as interferon gamma. Clinically, this means that T cell lymphocytic processes are less regulated.

Mild-moderate dehydration becomes more difficult to assess. Age-related decline in collagen and elastin result in a delay in skin elasticity in many older cats. Assessing stool character, i.e., passing hard pellets rather than moist logs, is a helpful way to identify and monitor dehydration before signs of more serious deficit become apparent. Canned food, more water stations, water fountains, flavoured water should be considered. Daily subcutaneous (SQ) fluids are helpful for many cats: 60 ml/kg ideal weight/day are required to maintain hydration once rehydrated.

Constipation", for the most part, is a symptom of dehydration. Cellular water content has priority over fecal water content, thus primary treatment should be directed towards rehydration and the underlying cause(s) of that problem, rather than at the stool and its movement (e.g. with laxatives). Use of promotility agents, laxatives, osmotic agents and fiber-enriched diets should be used conservatively and only once rehydration has been addressed.

Oral health becomes particularly important as the risk of neoplasia and uremic ulcers is higher in this age-group. As at any age, tooth resorption, periodontal disease, gingivitis, stomatitis, tooth fractures, and eosinophilic granulomas may occur. Any of these diseases may result in oral discomfort, which may contribute to an acute or a progressive decline in food intake and less fastidious coat care. Systemic effects of periodontal infection have been disputed however the potential for bacterial seeding of the kidneys or heart exists. There may also be emotional deprivation should halitosis prevent the client from interacting with their companion in the ways the cat was accustomed to.

Concern regarding safety of performing anaesthesia in elderly cats should not be over-emphasized. The American Society of Anesthesiologists (ASA) characterizes risk using the following **physical status classification system** that is based on the physical status of the patient. Five categories are defined as follows:
• Class 1: Normal, healthy patient
• Class 2: A patient with a mild systemic disease
• Class 3: A patient with severe systemic disease
• Class 4: A patient with a severe systemic disease that is a constant threat to life
• Class 5: A moribund patient not expected to survive without the operation
Two studies have verified that in cats, as in people, age is not a risk factor and should not be a limiting factor in determining whether or not to undertake a medically beneficial procedure.

While we now recognize that degenerative joint disease (DJD) may be present in cats as young as a year of age, the prevalence of arthritis is certainly higher in older cats. The associated chronic pain is systemically debilitating from its inflammatory effects, its psychological and emotional impact as well as mechanically interfering with mobility. All of these contribute to decreased dietary intake as well as grooming, nail care, litter box use (or inappropriate elimination) and overall quality of life. Overgrowth of nails further contributes to the problem. We need to screen for joint and vertebral changes and prescribe analgesics along with offering recommendations for environmental modifications in the home.

Muscle wasting is common in older cats. In part this is a result of a decreased ability to digest and absorb protein, in part due to muscle atrophy from inactivity (due to pain related or lack of environmental enrichment) and in part from inappropriate dietary recommendations. Along with regular body weight measurement, body condition scoring (BCS) and calculation of percentage weight change, muscle condition scoring should be included in physical exam protocols. If a decline in muscle condition is noticed, a diet with more protein, and more biologically available protein should be offered.

Renal function predictably declines. Most commonly tubulointerstitial nephritis is the underlying pathology, however other etiologies also occur. Pyelonephritis, ureteronephrolitiasis, amyloidosis, lymphoma, FIP, and glomerulonephropathies should not be overlooked. Rather than grouping all cats with CKD together and managing them with the same therapeutic protocol, attempts to identify cause are important. Use the International Renal Interest Society (IRIS) staging system and still monitor and adapt treatment to the individual. Approximately 15-30% of geriatric cats will develop CKD, and 30-65% of these cats will develop anemia as their renal disease worsens. (Chalhoub) This anemia is multifactorial in its pathogenesis but includes a decrease in erythropoeitin (epo) production. This decrease is not linear.

Anemia will result in weakness. It may be non regenerative as a result of chronic disease (iron sequestration), decreased epo production, iron deficiency, or decreased protein absorption. Blood loss associated with uremic gastritis may present as a regenerative or non-regenerative anemia depending on the degree of concurrent problems.

Blood pressure (BP) does not inherently increase with age, however, renal disease, hyperthyroidism and hyperaldosteronemia are more prevalent in older cats. Routine assessment of BP is justified especially as the clinical signs are invisible until retinal bleeding, detachment of a cerebrovascular accident occur.

There are significant nutritional changes that occur in cats as they age. Under 12 years of age, adult and senior cats tend to become overweight or obese as energy needs decrease without a concurrent decrease in energy intake. A significant reduction in lean body mass (LBM: skeletal muscle, bone, skin and organs) occurs just as it does in other species, with advancing age. As LBM is a primary driver of metabolism, decreased activity results in a reduction in MER. In the geriatric cat, energy requirements do not decrease as they do in dogs and humans. Diets should be extremely palatable as senior senses become compromised. Protein must not be restricted unless marked renal failure with uremia is present. Cats, as obligate carnivores, require approximately 23% protein (dry matter basis) regardless of aging, and if restricted, will acquire protein from body muscle to meet metabolic needs. This results in a negative nitrogen balance, protein: calorie malnutrition and deterioration of protective mechanisms impacting immunity, red cell hemoglobin content, muscle mass as well as tissue healing ability.

Studies in geriatric cats over 12 years of age show that fat digestibility decreases with age (Perez-Camargo). Additionally, approximately 20% of cats over 14 years of age have reduced protein digestion. This is clinically relevant when we try to design the optimal nutritional regime for older feline patients: protein and fat restriction may be *contra*indicated. Especially if underweight, older cats will benefit from a more energy-dense, highly digestible diet to help offset these age-related digestive and metabolic changes. It is essential to daily calculate caloric and protein requirements, just as one routinely calculates fluid needs as part of the therapeutic plan. [Calories: 50 kcal/kg ideal BW/day; 4 g protein/kg ideal BW/day].

Feeding tubes should not be considered only in patients with hepatic lipidosis or orofacial trauma, but rather be used to rehabilitate patients with catabolic conditions just as fluids are used for rehydrating a dehydrated individual.

A recent study (Yu) suggests that geriatric cats have a higher dietary vitamin B12 requirement; supplementation is warranted. Previously it has been shown that cats of any age with chronic small bowel pathology (Ruaux) or with pancreatitis (Simpson) should be supplemented and that hyperthyroid cats (Cook) may also be deficient in vitamin B12.

Potassium, folate and Vitamin K rapidly become deficient in an inappetant or anorectic cat. Hypokalemia is critical in cellular function and muscle strength; cardiac and all skeletal and smooth muscles are affected.

Changes in special senses occur. Ophthalmologic aging changes include iris atrophy, melanin deposition on the irises and lenticular sclerosis. While the former do not appear to affect vision, lenticular sclerosis results in a decreased acuity that would be expected to be most obvious in dim lighting. Impaired hearing is fairly common in older cats with selective frequencies being affected, similar to that which occurs in older humans.

Night-time yowling: The first strategy for dealing with this behaviour is to install nightlights throughout the home and to make deliberate auditory cues while performing pre-bedtime routines to help the kitty orient themselves. Other causes of this disturbing behaviour include hyperthyroidism or hypertension (both presumably resulting in agitation), unidentified pain and cognitive dysfunction. The first two conditions are readily identified through routine diagnostics of a screening program; Pain assessment should start with radiographic evaluation of joints (elbows, shoulders, stifles and hips) and the vertebral column. Should nothing be readily apparent, then test doses of an opioid (e.g., buprenorphine) should be given for several consecutive days to determine whether the yowling stops.

Cognitive dysfunction is a diagnosis of exclusion in the nighttime yowler. It may also present itself as disorientation, house soiling, altered memory or learning, changes in interactive behaviour, alterations in sleeping patterns or changes in activity.

Development of inappropriate elimination behaviour may have several age-associated causes. Pain from arthritis may make getting to the box or getting into the box difficult. Past experiences of discomfort from cystitis or difficult stool passage may result in aversion to use of the litter box. Urge incontinence (urinary or fecal) may result in the inability to get to the box in a timely fashion resulting in the development of an alternative location for eliminative behaviours. Hyperthyroidism may result in defecation of normal or diarrheic feces outside the litter box. While diagnosing the underlying cause is important, increasing the number of litter boxes and placing them in readily available locations is helpful.

Normal radiographic changes seen in the older feline patient include an increase in sternal contact of the heart. A decrease in bone density may be seen in very elderly individuals. Some minor calcific changes may occur in the pulmonary parenchyma of normally aging cats. Spondylosis should be looked for especially of the lumbar vertebrae, but bony changes may be seen in any part of the spinal column as well as degenerative, proliferative or lytic changes of the joints. Calcifications may be noted in the kidneys: these are often insignificant, representing calcification of old clots. Differentiation from nephroliths can be made with aid of ultrasound. Similarly, adrenal calcification should not me over-interpreted in cats, as it may be a normal, age-related change.

Pain is common with increasing age and need for analgesia MUST be considered as part of any treatment plan for the older cat. Common procedures including blood collection, intravenous catheter placement, restraint of a thin or arthritic patient may be uncomfortable. In addition, there are numerous potentially chronic painful conditions. Bacterial cystitis and pyelonephritis are more frequent in older cats while the incidence of interstitial/sterile cystitis or inflammatory bowel disease is not different than in cats of younger age groups. The likelihood of neoplasia increases with increasing age. Oral diseases and DJD are potentially painful.

Caring for the elderly cat

Older feline patients have particular therapeutic and nursing needs. It is important to restrict the hospital stay to as short as possible, as the older cat is less tolerant of the hospital environment and is more prone to depression and pining. This applies to Siamese cats of any age. Many of the conditions, which these special individuals develop, require ongoing home care, such as subcutaneous fluid administration, frequent medication administration and dietary manipulation. Problems may be masked and even undetectable with careful and thorough examination, yet make their presence known when the patient is stressed. Slow, gentle persistence with acute and *empathic* observation are our best tools in the care and handling of older cats.

Screening programs for the older cat are an excellent management tool. Offering such programs, as part of a Wellness Program approach, provide the best preventive medical care as well as giving the clinic a more predictable income base. An example of a Mature Cat Program consists of a comprehensive physical examination and consultation, a urinalysis, blood pressure determination and a blood panel consisting of a CBC with differential, biochemical screen including a basal serum T4, amylase, lipase and electrolytes. This should be recommended annually for all cats from the age of 8 years onwards, and twice annually for cats over 14 years of age or once abnormalities have been detected to assist in the management of these problems.

The most important therapeutic tools that must be incorporated in every patient, especially those who are geriatric, are optimizing comfort (through analgesia), hydration and nutrition.

Updates from the recent literature

Hyperaldosteronism *(Conn's Syndrome)*
Primary hyperaldosteronism is probably the most common adrenocortical disorder in cats. It is caused by a unilateral neoplasm of the adrenal cortex producing excess mineralocorticoids. Cats present with systemic hypertension, muscle weakness from hypokalemia, and polyuria. Usually seen in geriatric cats, it can be mistaken for renal insufficiency. Treatment consists of potassium supplementation and control of hypertension. Some cats require very high doses of IV and oral K supplementation to resolve the hypokalemia. Doses as high as 60-80 mEq of KCl/liter of fluids may be required in some cats. The first clinical clue to the hypertension may be retinal detachment. Blood pressures are in 200-280 systolic range. Amlodipine is indicated to reduce the hypertension and doses are titrated to effect. The ratio of plasma aldosterone concentration to plasma renin activity (aldosterone:renin ratio) is currently the best screening test for feline primary hyperaldosteronism. repeated sampling for the ARR may be required, as a single ARR within the reference interval does not exclude primary hyperaldosteronism in cats. On ultrasound, a unilateral adrenal mass is found. These tumours are usually benign and surgery can be curative. If surgery is declined, then amlodipine and potassium supplementation will help to control the clinical signs. Spironolactone, a potassium-sparing diuretic works by antagonizing aldosterone receptors (2-4 mg/kg/d). Interestingly, almost all of the cats have had other endocrine disorders (esp. hyperthyroidism). It has also been seen with insulinoma, so this may be a feline example of multiple endocrine neoplasia.

Acromegaly
Acromegaly has been studied in the last several years with an increased level of interest as it has been discovered that ¼-1/3 of cats with diabetes may have unrecognized acromegaly. This condition is usually caused by an adenoma in the pars distalis of the anterior pituitary gland that secretes excessive growth hormone (GH). Less commonly, pituitary hyperplasia is suspected to result in acromegaly. Insulin-like growth factor 1 (IGF-1) is produced in the liver in response to the GH. GH has catabolic and diabetogenic effects, while IGF-1 has anabolic effects.

The characteristic signs of acromegaly are insulin resistance, believed to be caused by a GH-induced post-receptor defect in the tissues. Most are middle-aged to older, neutered male mixed breed cats. Physical changes consisti of prognathism and a broad face, large thickened limbs with clubbed paws and organomegaly may be subtle. Upper respiratory stridor associated with structural changes may be seen. Organomegaly is common as hypertrophic cardiomyopathy and renomegaly. In addition, arthropathies occur and, in some cases, there may be neurological signs from intracranial tumour expansion.

Classic signs of diabetes: PU/PD with polyphagia are present despite increasing doses of insulin. Uncharacteristic of diabetes, however, is concurrent weight gain. There are two populations of acromegalic cats: those who have been diabetic for some time and then deteriorate while the second group consists of those cats who appear to be acromegalic from the beginning of their diabetes.

Other differentials for an insulin resistant or uncontrolled diabetic include treatment failure of compliance or comprehension, inappropriate insulin handling, resistance associated with concurrent, uncontrolled inflammatory or infectious conditions, hyperprogesteronemia or hyperadrenocorticism.

Insulin growth factor-1 is the screening test with confirmation of diagnosis by imaging the pituitary gland. If possible, GH measurements should be measured. No single antemortem test is 100% reliable as there may be false positives and negatives. Because GH is secreted in a pulsatile fashion, there may be false negatives, i.e., normal GH values in an acroegalic cat. IGF-1 is secreted continuously and is, therefore, theoretically more reliable. Contrast enhanced CT or MRI studies are used for diagnosis as well as for treatment planning, should radiation or stereotactic radiosurgery be a consideration.

There are several therapeutic options. Conservative treatment with high doses of insulin as needed may be used, however the risk is that iatrogenic hypoglycemia may occur if the insulin dose is too

high for the GH surge at the time. Thus, should this form of treatment be the one chosen, the client and veterinary team needs to work closely together to ensure that the client is able to assess blood glucose levels and trends.

Medical therapeutic options for people are of three kinds:
1. Somatotropin analogues control GH and IGF-1 secretion in about 50% of humans. Octreotride was effective in treating a small number of cats but did not result in normalization of GH after a single IV injection in one study.
2. Pegvisomant is a GH-receptor antagonist that is used in humans but does not appear to be effective in cats.
3. 70% of humans respond to dopamine antagonists such as bromocriptine and L-deprenyl (Selegiline). These have not been properly evaluated in cats.

Currently the best treatment option is radiation therapy: by reducing the bulk and function of the pituitary mass, neurological signs associated with mass as well as insulin resistance improve. Adjustment of insulin doses is not straightforward as resolution of insulin resistance can occur immediately or months after radiotherapy. Hepatic IGF-1 hyperproduction does not always resolve, so while diabetic management may become significantly easier or diabetes may resolve, the anabolic effects (polyphagia, bone growth, organomegaly, etc.) may still cause problems.

Stereotactic radiosurgery using a gamma knife to reduce the tumour mass is being investigated at Colorado State University. Another technique, transsphenoidal cryohypophysectomy has been attempted in two cats with favourable long-term results in one cat.
Because there are chronic, ongoing changes associated with the effects of the IGF-1, namely possible arthropathy, HCM, renal insufficiency and hypertension, these, along with quality of life must be addressed regardless of form of therapy.

Hyperthyroidism
Hyperthyroidism is the most common endocrine disorder in the cat. Since being first recognized in 1977, the incidence has increased steadily. This is, no doubt partly due to greater awareness and early screening, but certainly also due to a real increase in occurrence of this disease. The **etiology and pathogenesis** are not certain, but numerous epidemiological surveys have shown an increased incidence of this disease is seen in cats fed > 50% canned food in their diet, especially containing fish, living strictly indoors, using litter.

The disease has been reported in North America, Europe, Australia and New Zealand, but less frequently, or not at all, in other parts of the world. These risk factors implicate environmental, nutritional and genetic factors. It is also logical to assume, however, that cats who are well cared for and thus live longer, will be exposed to litter and canned foods.

Some of the goitrogens that have been studied include iodine and phyhalates (common in cat foods), resorcinol, polyphenols and PCBs, all of which may also be in diets, especially those containing fish, or in the environment. In the 1970's because the units for iodine supplementation were changed from amount/animal to amount/kg of diet, a wide variation exists in the amount of iodine a cat ingests. In addition, the variability in the bioavailaibility of different iodine sources compounds the problem further. As a result, it is possible that cats have been chronically iodine deficient for several decades. Another theory considers that nodular goiter development may be a normal age-related condition. (Edinboro)

Most recently, attention has been directed towards brominated-flame retardants also introduced into household consumer products in the 1970-80's. Pet cats in the U.S. have been found to have high PBDE serum levels, which could be a result of exposure in cats living strictly indoors. Further, because cats groom their fur they may ingest any volatilized PBDE-like material or PBDE-laden dust that deposits on it.

Hyperthyroidism and chronic kidney disease:

Concurrent renal dysfunction is also fairly common in untreated hyperthyroid cats, and may be masked due to increased cardiac output and renal blood flow. Therefore, it is essential to continue to monitor these renal parameters during therapy. It is well recognized that amelioration of the hyperthyroid state by any method (i.e. medical therapy, 131I treatment or surgery) can result in decreased GFR, elevations in BUN and creatinine, and, in some cases, overt azotemia. The decline in GFR stabilizes by approximately four weeks.

Numerous studies have attempted to identify predictive parameters. GFR can be measured using plasma clearance of exogenous creatinine exo-iohexol or endo-iohexol; N-acetyl-beta-D-glucosaminidase index and retinol-binding protein have been assessed as possible biomarkers. Of the common clinical measures, cats with hypertension and/or an increase urine protein: creatinine ratio are more likely to develop problems while cats with elevated plasma globulins, a high usg and PCV are less likely to.

A practical approach is to treat cats with methimazole until the serum T4 is adequately controlled when the effect of permanent therapy can be assessed. If renal failure does become overt after definitive correction of hyperthyroidism, exogenous thyroid hormone can be supplemented to support the kidneys. A balance must then be struck between creating iatrogenic hyperthyroidism and maintaining renal function as iatrogenic hypothyroidism appears to contribute to azotemia and decreased survival.

Nutritional therapy of hyperthyroidism:
Dietary therapy (Hill's y/d) has recently become available and operates on the premise that a reduction in iodine as a substrate for thyroid hormone production corrects the hyperthyroid state. The diet was tested on cats with minimal clinical signs of hyperthyroidism so how well it will work in cats with concurrent cardiac or hypertensive complications is unknown. Cats being treated with this diet may not have any other food or treat. The manufacturer recommends that medical therapy be reduced by 50% one week after the cat has been transitioned completely onto y/d, that the medication be discontinued after one week at this lower dose and that the T4 levels should be checked 3-4 weeks after a complete transition onto the diet to verify euthyroidism and compliance.

Concerns regarding this diet that Mark Peterson has written eloquently about (www.endocrinevet.blogspot.com/2011/09/treating-hyperthyroid-cats-with-iodine.html) include it's low protein content and the potential (theoretical, at least) for development of toxic nodular goiter.
TSH was not studied in any of the studies that Hills has performed.
a. all of the cats (or at least the vast majority), in the same studies, were cats very early in disease progression with no cardiac effects or hypertension
b. none of the cats had significant decline in renal function.
The suggested protocol for tapering methimazole therapy after introducing the diet is somewhat speculative as it was developed on the aforementioned cats.

Chronic Kidney Disease
There is evidence in cats suggesting that the use of a phosphate-restricted diet in IRIS stage 2-3 disease has a beneficial effect on clinical outcome. However, despite the fact that intestinal phosphate binders are commonly used in veterinary practice for patients with CKD, there have been few published reports focusing on the safety and efficacy of these products in veterinary medicine. No phosphorus binders are licensed as medications for dogs or cats. This article draws on data from clinical trials in humans and studies in cats to discuss treatment goals and options for phosphate retention and hyperphosphatemia in feline CKD. With careful monitoring of serum phosphate and parathyroid hormone, and implementation of phosphate-restricted dietary management and intestinal phosphate binders, progression of CKD and the degree of hyperparathyroidism in cats may be reduced. (Kidder)

Diabetes
In a study published in 2010, clinical remission of diabetes was evaluated. Ninety cats with newly diagnosed diabetes were followed until death or remission. Remission was defined as normoglycemia without insulin for $\geq$ 4 weeks. Likelihood of remission was found to be greater in older cats and in

cats with higher body weight. Remission was less likely in cats with increased serum cholesterol and was of shorter duration when serum glucose was higher, i.e., less well regulated. (Zini, Nov 2010)

Good glycemic control soon after diagnosis is associated with increased probability of remission and should be the goal of insulin therapy. (Roomp, Marshall)

Glucometers:
In a study comparing AlphaTRAK, Ascensia ELITE and reference hexokinase methods for determining serum glucose, the AlphaTRAK meter results did not differ from the reference method, however results from the Ascensia ELITE were significantly lower. The superior performance of the AlphaTRAK meter supports its use to monitor blood glucose levels in cats. (Zini, 2009)

In a UK study: (Dobromylskyj), six portable blood glucose monitors (PBGM) were compared to the reference method.
Percentage of acceptable readings (unacceptable readings would result in a inappropriate clinical decision)
Meter 1: Accu-Chek Active (Roche): 95.3% (81 samples)
Meter 2: Ascensia Breeze (Bayer): 81.2% (69 samples)
Meter 3: Accu-Chek Compact (Roche): 96.5% (82 samples)
Meter 4: One-Touch Ultra (LifeScan): 85.9% (73 samples)
Meter 5: Supreme Plus (Hypoguard): 95.3% (81 samples)
Meter 6: Freestyle (TheraSense): 92.7% (77 samples)

Percentage of readings in zone where PBGM indicates opposite of reference, i.e., PBGM says hypoglycemic when reference says hyperglycemic (for instance, PBGM = 3.5 mmol/l; reference = 10 mmol/l) or PBGM says hyperglycemic when reference says hypoglycemic (for instance, PBGM = 14.5 mmol/l; reference = 2 mmol/l)
Accu-Chek Active (Roche): 2.4%
Ascensia Breeze (Bayer): 3.5%
Accu-Chek Compact (Roche): 2.4%
One-Touch Ultra (LifeScan): 3.5%
Supreme Plus (Hypoguard): 1.2%
Freestyle (TheraSense): 2.4%
Meter 3 had the smallest mean differences overall, together with the highest percentage of clinically acceptable readings.

Urine ketone measurement is routinely performed in cats with diabetes mellitus to identify impending or established ketoacidosis. The urinary ketone dipstick test has a low sensitivity as it quantifies the less abundant ketone acetoacetate. Beta-hydroxybutyrate (beta-OHB) is the predominant serum ketone. Determination of plasma beta-OHB concentration was shown to be a useful method to distinguish between diabetic and non-diabetic sick cats. (Zeugswetter)

Feline diabetes shares several similarities with the disease in humans. Impaired beta-cell function, decreased beta-cell mass, insulin resistance that is often related to obesity, and pancreatic amyloid deposition, are among these common features. (Zini March 2010)
Inflammation is another recognized predisposing factor for susceptible individuals to develop diabetes. Franchini has shown at a molecular level that the inflammation induced by bacterial or viral infection can, via molecules recognized by toll gate receptors, damage endocrine pancreatic tissue.

Neoplasia: lymphoma
Owners 'perception of their cats' quality of life (QoL) during COP chemotherapy for lymphoma was surveyed. (Tzannes) The QoL scores during chemotherapy were, not surprisingly, significantly lower than prior to the onset of cancer, but significantly higher during treatment than prior to starting treatment. Adverse effects were experienced by 87% of the cats during the course of chemotherapy. Eighty-three percent of clients were happy that they had treated their cat and 87% of the owners said that they would treat another cat. The results suggest that COP chemotherapy is perceived by owners to be tolerated by cats.

Treatment outcomes
Twenty-three cats received a cyclic combination of l-asparaginase, vincristine, cyclophosphamide, doxorubicin, methotrexate, and prednisolone with a planned total treatment time of 122 weeks. The complete remission (CR) rate was 74% with the median duration of first CR of 264 days (range, 45-2,485 days); Six-month, 1-, and 2-5-year remission rates were 75, 50, and 34%, respectively. The median survival in cats with CR was 296 days (range, 50-2,520 days). Six-month, 1-, 2-, and 3-5-year survival rates in cats with CR were 82, 47, 34, and 27%, respectively. (Simon)

Ninety-seven cats with nasal lymphoma received one of three protocols. RT + chemotherapy (n = 60), RT alone (n = 19), or chemotherapy alone (n = 18). There were no significant differences in survival times among the 3 treatment groups but these results suggest that the addition of higher doses of RT to a cat's treatment protocol may control local disease and therefore influence survival. (Hane)

The response to chemotherapy and survival in 110 cats with extranodal lymphoma was reported. (Taylor) Sixty-nine cats had nasal lymphoma, 35 renal, 15 central nervous system, 11 laryngeal and 19 miscellaneous locations. Sixty-six cats received cyclophosphamide, vincristine, prednisolone, 25 Wisconsin-Madison doxorubicin-containing multi-agent protocol, 10 prednisolone alone and nine other combinations. The response rate for the 110 treated cats was 85.5 per cent. Of cyclophosphamide, vincristine, prednisolone treated cats 72.7 per cent achieved complete remission, median survival 239 days. Sixty-four per cent of Wisconsin-Madison treated cats achieved complete remission, median survival 563 days. Cats with nasal lymphoma achieving complete remission had the longest survival (749 days) and cats with central nervous system lymphoma the shortest (70 days). Corticosteroid pretreatment reduced survival time in cats achieving complete remission.

Low-grade alimentary lymphoma (LGAL) was diagnosed by histological and immunohistochemical evaluation of full-thickness biopsies from multiple regions of the gastrointestinal tract collected during exploratory laparotomy in 17 cats. (Lingard) The most common ultrasonographic finding was normal or increased intestinal wall thickness with preservation of layering. Ultrasound-guided fine-needle aspirates of mesenteric lymph nodes (n=9) were incorrectly identified as benign lymphoid hyperplasia in eight cats, in which the histological diagnosis from biopsies was lymphoma. There was neoplastic infiltration of more than one anatomic region of the gastrointestinal tract in 16/17 cats. The jejunum (15/15 cats) and ileum (13/14 cats), followed by the duodenum (10/12 cats), were the most frequently affected sites.
Twelve cats were treated with oral prednisolone and high-dose pulse chlorambucil, two with a modified Madison-Wisconsin multiagent protocol and three with a combination of both protocols. Thirteen of the 17 cats (76%) had complete clinical remission with a median remission time of 18.9 months. The prognosis for cats with LGAL treated with oral prednisolone in combination with high-dose pulse chlorambucil is good to excellent.

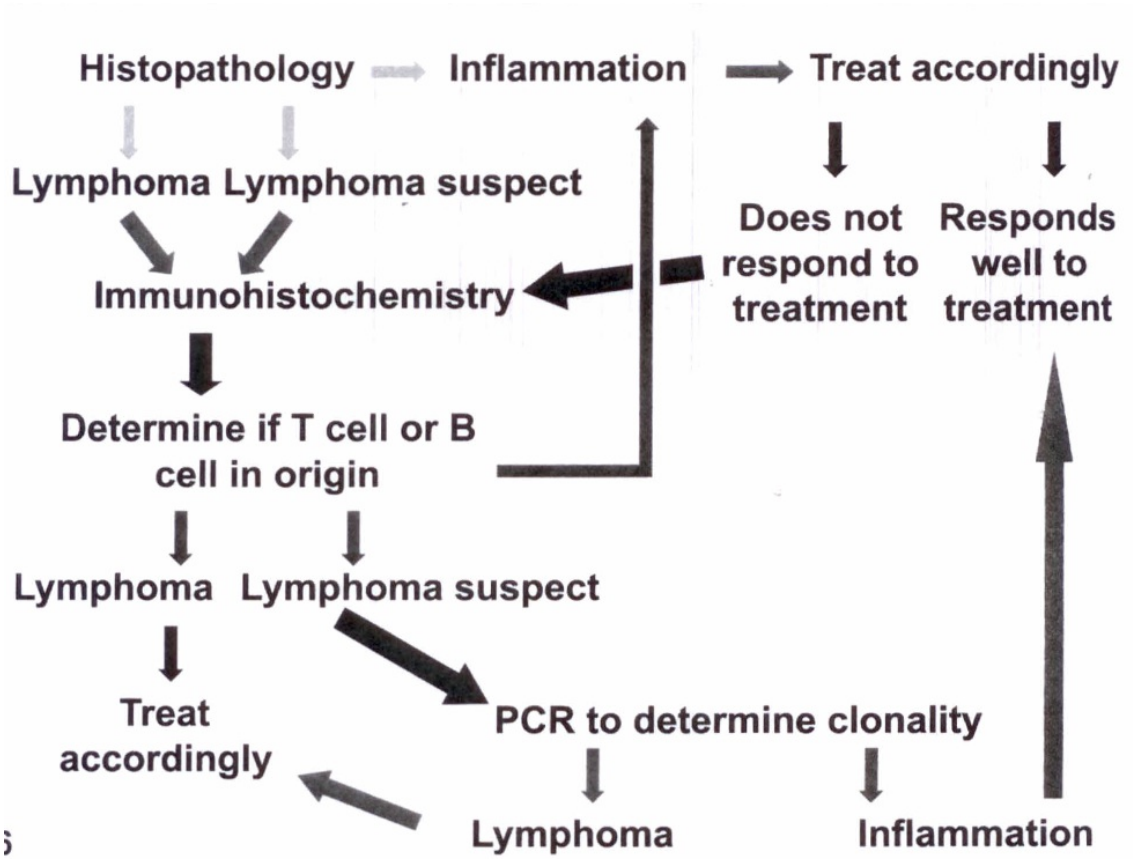
The efficacy of treating feline gastrointestinal small-cell lymphoma with chlorambucil and glucocorticoids was re-evaluated by Stein. The overall clinical response rate was 96%, with a median clinical remission duration of 786 days. Follow-up identified seven cats with relapsed disease-all of which were treated with a rescue protocol of cyclophosphamide and glucocorticoids; the response rate was 100%.

Treatment of lymphoma is most effective when tailored to the specific cell type, hence numerous studies have been performed to attempt to determine the best ways to identify the cells. Pohlman examined 50 cases of feline gastrointestinal lymphoma. Tissue sections were stained with HE, phosphotungstic acid hematoxylin, and immunohistochemical stains (anti-CD3, anti-CD79a, and anti-BLA.36). Small intestinal lymphoma was the most common form found, with 74% of cats affected: T-cell tumors comprised 52%; 38% were B-cell tumors. Gastric tumors were diagnosed in 24% and 18% were present only in the stomach. All gastric lymphomas were of B-cell lineage. Of the 8 cats (16%) that had lymphoma of the large intestine, 88% had B-cell tumors and 12% had T-cell tumors. The strongest association between gastrointestinal lymphoma immunophenotype, histologic classification, and location occurred in the stomach, where there was a predominance of diffuse large

B-cell lymphoma of immunoblastic nuclear type.

Low-grade alimentary lymphoma (LGAL) is a recently described entity displaying many microscopical features similar to lymphoplasmacytic enteritis (LPE). Evaluating 53 cases of these conditions, Briscoe reviewed the histopathological and immunohistochemical features of LPE and LGAL to determine if specific features are useful in distinguishing between these disorders.
There were 24 cases of LPE, 12 were mild, seven were moderate and five were marked in severity. The ileum and jejunum were the most common sites affected for both LGAL and LPE (70-90% of cases). Involvement of the stomach was more common with LPE (29%) than LGAL (7%). Complicating matters further, 12 cases of LGAL (41%) had evidence of concurrent LPE. Microscopic features significantly associated with LGAL were epitheliotropism, involvement of the muscularis propria and/or serosa, more severe infiltration and more severe changes to the villus and crypt architecture. In contrast, plasma cell infiltration within the mucosa was a feature of LPE.

Evaluating surgical and endoscopic intestinal biopsy specimens from 63 cats with a history of chronic diarrhea or vomiting or weight loss, Kiupel developed a diagnostic algorithm that begins with histologic assessment, followed by immunophenotyping and then applies PCR to determine the clonality of the lymphocytes, to more accurately differentiate between intestinal lymphoma and inflammatory bowel disease (IBD). A diagnosis of lymphoma or inflammation was based on microscopic examination of hematoxylin and eosin (HE)-stained sections alone, HE-stained sections plus results of immunohistochemical labeling (IHC) for CD3e and CD79a, and HE staining, immunophenotyping, and polymerase chain reaction (PCR) results for B and/or T cell clonality. Important histologic features that differentiated intestinal lymphoma from IBD included lymphoid infiltration of the intestinal wall beyond the mucosa, epitheliotropism (especially intraepithelial nests and plaques), heterogeneity, and lymphocyte nuclear size.



Tests for clonality: PARR assay is a PCR assay in which DNA is being amplified. The results determine whether the majority of cells in the sample are derived from the same original clone (most consistent with neoplasia), or from multiple clones (most consistent with a reactive process). The limitations of PARR in feline lymphoma are a low sensitivity, i.e., there are approximately 35% false negatives. The tests complement each other and both should be run together. Both tests can be run on blood; PARR can be run on stained slides but not on formalin fixed, paraffin embedded samples or cover-slipped slides.

With flow cytometry live cells are stained with labeled antibodies that bind to proteins expressed on the cell surface. Different types of lymphocytes express different protein (for example T cells express the protein CD3, and B cells express the protein CD21). The cells are analyzed on a flow cytometer, which tells us how many cells of each type are present. This information allows us to determine the lineage of the cells present, and whether they are homogeneous (more consistent with neoplasia) or heterogeneous (more consistent with a reactive process).
(www.cvmbs.colostate.edu/ns/departments/mip/cilab/which_test.aspx)

The Bcl-2 gene is a member of the rapidly expanding Bcl-2 family of genes that regulate apoptosis. Bcl-2 has been shown to repress cell death triggered by a diverse array of stimuli, including chemotherapy and gamma irradiation. Kano et al confirmed the expression of Bcl-2 in T-cell lymphoma cell lines using an immunoblot assay. Their conclusion was that pending further evaluation, Bcl-2 expression might be useful in the differential diagnosis of feline tumors.

Useful client resources:

- The WellCat log of the Feline Advisory Bureau (fabcats.org/publications/index.php)
- AAFP-AAHA Feline Life-Stage Guidelines (catvets.com/professionals/guidelines/publications)
- The Cat Friendly Practice Program (www.catfriendlypractice.catvets.com)
- Morris Animal Foundation Happy Healthy Cat (www.research4cats.org/mystery/is-your-cat-at-risk.html)

From Veterinary Cancer Society website: (www.vetcancersociety.org)
Ten Common Signs of Cancer in Small Animals
Abnormal swellings that persist or continue to grow.
Sores that do not heal.
Weight loss.
Loss of appetite.
Bleeding or discharge from any body opening.
Offensive odor.
Difficulty eating or swallowing.
Hesitation to exercise or loss of stamina.
Persistent lameness or stiffness.
Difficulty breathing, urinating, or defecating.

References

- Briscoe KA, Krockenberger M, Beatty JA, et al. Histopathological and immunohistochemical evaluation of 53 cases of feline lymphoplasmacytic enteritis and low-grade alimentary lymphoma. J Comp Pathol. 2011 Aug-Oct;145(2-3):187-98.
- Brodbelt DC, Pfeiffer DU, Young LE, et al. Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into perioperative small animal fatalities (CEPSAF). British Journal of Anaesthesia published online on September 19, 2007.
- Chalhoub S, Langston C, Eatroff A. Anemia of renal disease: what it is, what to do and what's new. J Feline Med Surg. September 2011;13(9):629-40.
- Cook AK, Suchodolski JS, Steiner JM, et al. The prevalence of hypocobalaminaemia in cats with spontaneous hyperthyroidism. J Small Anim Pract. February 2011: 52 (2): 101-6.
- Dobromylskyj MJ, Sparkes AH.Assessing portable blood glucose meters for clinical use in cats in the United Kingdom. Vet Rec. September 2010;167(12):438-42.

- Edinboro CH, Scott-Moncrieff JC, Glickman LT. Feline hyperthyroidism: potential relationship with iodine supplement requirements of commercial cat foods. J Feline Med Surg. 2010 Sep;12(9):672-9.
- Franchini M, Zini E, Osto M, et al. Feline pancreatic islet-like clusters and insulin producing cells express functional Toll-like receptors (TLRs) Vet Immunol Immunopathol. November 2010;138(1-2):70-8.
- Hane SM, Beaver L, Turrel J, et al. Survival analysis of 97 cats with nasal lymphoma: a multi-institutional retrospective study (1986-2006) J Vet Intern Med. 2009 Mar-Apr;23(2):287-94.
- Hosgood G, Scholl DT. Evaluation of Age and American Society of Anestheiologists (ASA) Physical Status as Risk Factors for Perianesthetic Morbidity and Mortality in the Cat. J Vet Emerg Crit Care. 2002; 12 (1): 9-15.
- Kano R, Sato E, Okamura T, et al. Expression of Bcl-2 in feline lymphoma cell lines Vet Clin Pathol. March 2008;37(1):57-60.
- Kidder AC, Chew D. Treatment options for hyperphosphatemia in feline CKD: what's out there? J Feline Med Surg. November 2009;11(11):913-24.
- Kiupel M, Smedley RC, Pfent C, et al. Diagnostic algorithm to differentiate lymphoma from inflammation in feline small intestinal biopsy samples. Vet Pathol. January 2011;48(1):212-22.
- Lingard AE, Briscoe K, Beatty JA, et al. Low-grade alimentary lymphoma: clinicopathological findings and response to treatment in 17 cases J Feline Med Surg. August 2009;11(8):692-700.
- Marshall RD, Rand JS, J M Morton JM. Treatment of newly diagnosed diabetic cats with glargine insulin improves glycaemic control and results in higher probability of remission than protamine zinc and lente insulins. J Feline Med Surg. August 2009;11(8):683-91.
- Perez-Camargo G. Cat Nutrition: what's new in the old? Compend Contin Edu Pract Vet 2004; 26 (Suppl 2A): 5-10.
- Pohlman LM, Higginbotham ML, Welles EG, et al. Immunophenotypic and histologic classification of 50 cases of feline gastrointestinal lymphoma. Vet Pathol. March 2009;46(2):259-68.
- Ruaux CG, Steiner JM, Williams DA. Early biochemical and clinical responses to cobalamin supplementation in cats with signs of gastrointestinal disease and severe hypocobalaminemia. J Vet Intern Med. 2005 Mar-Apr;19(2):155-60.
- Roomp K, Rand J. Intensive blood glucose control is safe and effective in diabetic cats using home monitoring and treatment with glargine. J Feline Med Surg. August 2009;11(8):668-82.
- Simpson KW, Fyfe J, Cornetta A, et al. Subnormal Concentrations of Serum Cobalamin (Vitamin B12) in Cats with Gastrointestinal Disease. J Vet Intern Med 2001;15:26–32
- Simon D, Eberle N, Laacke-Singer L, et al. Combination chemotherapy in feline lymphoma: treatment outcome, tolerability, and duration in 23 cats. J Vet Intern Med. 2008 Mar-Apr;22(2):394-400.
- Stein TJ, Pellin M, Steinberg H. Treatment of feline gastrointestinal small-cell lymphoma with chlorambucil and glucocorticoids. J Am Anim Hosp Assoc. 2010 Nov-Dec;46(6):413-7.
- Taylor SS, Goodfello MR, Browne WJ, et al Feline extranodal lymphoma: response to chemotherapy and survival in 110 cats. J Small Anim Pract. November 2009;50(11):584-92.
- Tzannes S, Hammond MF, Murphy S, et al. Owners 'perception of their cats' quality of life during COP chemotherapy for lymphoma J Feline Med Surg. February 2008;10(1):73-81.
- Yu S, Melendez L, Ahle N, et al. Dietary Supplementation of Vitamin B12 Improves Vitamin B12 Status in Geriatric Cats ACVIM Forum 2011
- Zeugswetter F, Handl S, Ibe C, et al. Efficacy of plasma beta-hydroxybutyrate concentration as a marker for diabetes mellitus in acutely sick cats J Feline Med Surg. April 2010;12(4):300-5.
- Zini E, Moretti S, Tschuor F, et al. Evaluation of a new portable glucose meter designed for the use in cats. Schweiz Arch Tierheilkd. September 2009;151(9):448-51.
- Zini E, Franchini M, Osto M, et al. Quantitative real-time PCR detection of insulin signalling-related genes in pancreatic islets isolated from healthy cats. Vet J. March 2010;183(3):287-93.
- Zini E, Hafner M, Osto M, et al. Predictors of clinical remission in cats with diabetes mellitus J Vet Intern Med. 2010 Nov-Dec;24(6):1314-21.