

Feline Hyperthyroidism: Management and Options for Treatment

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Hyperthyroidism is recognized as the most common endocrinopathy of older cats. Despite worldwide occurrence, the pathogenesis of feline hyperthyroidism remains unclear. Traditional methods of managing feline hyperthyroidism include thyroidectomy, anti-thyroid medications, and radioactive iodine. Recent studies document that another option now exists for hyperthyroid cats; feeding a limited-iodine food normalizes thyroid hormone concentrations and alleviates clinical signs of hyperthyroidism. Surgery and radioactive iodine are designed to provide permanent solutions, whereas, oral anti-thyroid drugs and nutritional management control hyperthyroidism and are needed daily to achieve/maintain their effect. All management options are effective and each has its pros and cons. It's important to discuss all options with pet owners so the appropriate management can be selected for each hyperthyroid cat.

Diagnosis

Diagnosis most often is based on the presence of one or more typical clinical signs and increased serum total thyroxine (T_4) concentration. However, up to 10% of all hyperthyroid cats and 40% of those with mild disease have serum T_4 values within reference range.^{1,2} The diagnosis of hyperthyroidism should not be excluded on the basis of a single normal serum T_4 value, especially in a cat with typical clinical signs, a palpable thyroid nodule and serum T_4 in the upper half of the normal range.³ In these cases, serum free T_4 (fT_4), measured by equilibrium dialysis, may provide an alternative means of diagnosing hyperthyroidism in cats with normal serum total T_4 values. Studies document that up to 20% of sick euthyroid cats can have increased fT_4 concentration.⁴ Therefore, it is most appropriate and reliable to interpret the two values together. Mid-to-high reference range total T_4 and increased fT_4 concentration is consistent with hyperthyroidism. In contrast, low total T_4 and increased fT_4 values are usually associated with non-thyroidal illness.

Management options

Once hyperthyroidism has been diagnosed, all management options (thyroidectomy, radioactive iodine, anti-thyroid drugs, nutritional management) should be discussed with pet owners. All options can be $\geq 90\%$ effective for controlling hyperthyroidism when used appropriately. The selected management option will differ for each cat based on several considerations (**Table 1**). Radioactive iodine therapy is considered the gold standard for treatment of hyperthyroidism; however, most pet owners currently opt for medical management. Until recently, this included oral or transdermal anti-thyroid drugs. Now nutritional management using a limited-iodine food is another option for cats with hyperthyroidism.

Radioactive iodine

Radioiodine treatment is often considered the best option for many hyperthyroid cats because:

- It has the potential to eliminate a benign thyroid tumor or abnormal thyroid tissue with a single treatment
- It treats extra-thyroidal thyroid tissue, which may occur in 10 to 20% of hyperthyroid cats
- No general anesthesia is required
- Reported side effects are minimal

Cats should be stable prior to radioiodine therapy; those with clinically significant cardiovascular, renal, gastrointestinal, or endocrine (e.g., diabetes mellitus) disease may not be very good candidates, especially because of the time necessary for boarding after treatment.⁵

After administration, radioactive iodine is actively concentrated by the thyroid gland and has a half-life of 8 days. It emits both β -particles and γ -radiation; the β -particles are responsible for the majority of tissue destruction, but are only locally destructive, traveling a maximum of 2 mm. Therefore, no significant damage to adjacent parathyroid tissue, atrophic thyroid tissue, or other cervical structures is expected. The main limitation to widespread use of radioactive iodine is the requirement for special licensing and the isolation of the cat for variable periods after treatment. This can range from several days to several weeks depending on state or local radiation regulations and the dose administered.⁶

The goal of treatment is to restore euthyroidism with the smallest possible single dose of radioactive iodine, while avoiding development of hypothyroidism.⁶ Controversy exists as to the best method of calculating the optimum dose for individual cats.^{5,6} Based on the majority of reported cases, post-treatment hypothyroidism is transient and generally uncommon (2 to 7% of cases); even fewer cats have clinical signs or appear to require thyroid hormone replacement.⁷⁻¹¹ However, up to 30% (50 of 165 cats) were hypothyroid 3 months after radioactive iodine therapy in one study; of these, 56% (19 of 34 hypothyroid cats with available information) had clinical signs of hypothyroidism and 52% (23 of 44 cats) were given thyroid hormone supplementation.¹² Thyroid hormone replacement may be needed in some cats, especially those with concurrent kidney disease, since hypothyroidism has been

associated with azotemia and decreased survival time in previously hyperthyroid cats.¹³ Owners should be advised of this possibility, particularly if their motivation is to avoid long-term oral medication.

Anti-thyroid drugs

Anti-thyroid drugs (e.g., methimazole, carbimazole) are commonly used for treatment of hyperthyroidism in cats.¹⁴⁻²¹ If administered appropriately, they reliably inhibit the synthesis of thyroid hormones and thereby lower serum thyroid hormone concentrations. These drugs do not affect the thyroid gland's ability to trap inorganic iodide or release preformed hormones. They are widely recommended to stabilize hyperthyroid cats prior to surgery and are the only drugs that can be used chronically for management of hyperthyroidism.⁶ Almost all cats are potential candidates unless thyroid carcinoma is suspected.

Anti-thyroid drugs used most often in cats include methimazole and carbimazole; both can be given orally or formulated for transdermal application. Custom formulation of transdermal products may increase expense of therapy and stability of the product is not guaranteed. Results of a recent prospective study conducted in New Zealand showed that once daily treatment for 12 weeks with transdermal methimazole in a novel lipophilic vehicle was as effective as twice-daily carbimazole administered orally.¹⁴

While many cats have been successfully managed long-term with anti-thyroid drugs, it's important to monitor for potential side effects that have been associated with their use.^{15,18,19,21} In the study with the largest number of cats, 18% had side effects associated with methimazole; a more recent study revealed that 44% of 39 cats had side effects.^{15,19} In 44 cats receiving carbimazole for 1 year, 44% had associated side effects with gastrointestinal signs (decreased appetite, vomiting, diarrhea) being most common. In another study, 13% of 39 cats treated with carbimazole experienced side effects.¹⁸ It's difficult to determine what % of side effects are caused by the drug versus something else such as concurrent disease.²¹

Most adverse reactions occur within the first few weeks to months after beginning therapy and include depression, inappetence, vomiting, and self-induced excoriations of the head and neck (facial pruritus). Gastrointestinal signs are less common with transdermal administration of methimazole.¹⁶ Mild to serious hematological complications, including agranulocytosis and thrombocytopenia either alone or concurrently, and more rarely immune-mediated hemolytic anemia may also occur. Hepatic toxicity with marked increases in bilirubin concentration and hepatic enzyme activities has been described in less than 2% of cats treated with methimazole. Cessation of therapy is required if either serious hematologic or hepatic reactions develop. Serum antinuclear antibodies develop in approximately 50% of cats treated with methimazole for longer than 6 months, usually in cats on high-dose therapy (> 15 mg/day). Although clinical signs of a lupus-like syndrome have not been reported, decreasing the daily dosage is recommended.⁶

Nutritional management

Production of thyroid hormone requires uptake by the thyroid gland of sufficient amounts of iodine, which is provided by dietary intake. The only function for ingested iodine is for thyroid hormone synthesis.⁵ This observation led to the hypothesis that limiting dietary iodine intake could be used to control thyroid hormone production and potentially manage hyperthyroidism in cats. After more than a decade of research and development, a limited-iodine therapeutic food (Hill's® Prescription Diet® y/d™ Feline) containing < 0.3 ppm (mg/kg) iodine on a dry matter basis (DMB), is now available as an option for managing cats with hyperthyroidism.

Iodine content of commercial cat foods

Iodine occurs naturally in many ingredients typically used in the manufacture of commercial pet foods (particularly fish, shellfish and fresh meats) and unless steps are taken to strictly control the iodine content of ingredients, the final iodine concentration in pet foods varies widely.²²⁻²⁵ Commercial cat foods in New Zealand had iodine amounts ranging from 0.19 to 21.2 ppm in one study whereas in Germany a range of 0.22 to 6.4 ppm was reported.^{22,26} Evaluation of 28 canned cat foods in the US revealed an iodine content ranging from 1.09 to 52.3 ppm (mean = 7.83) and 14 dry cat foods contained iodine amounts ranging from 1.34 to 5.94 ppm (mean = 2.77).²⁵ Based on these studies, the amount of iodine is much higher in many canned foods compared with dry foods and variability of iodine content is much greater in canned food.^{22,25-26}

Multiple feeding trials have been conducted in a research colony using over 100 cats with naturally occurring hyperthyroidism to determine the safety and effectiveness of limited dietary iodine in the management of the disease. The results of all studies support that a therapeutic food with dietary iodine ≤ 0.3 ppm iodine (dry matter basis) provides a safe and effective management option for cats with naturally occurring hyperthyroidism. Serum total thyroxine concentrations return to the normal range within 4 to 12 weeks of initiating nutritional management and 90% hyperthyroid cats maintained on the limited-iodine food as the sole source of nutrition become euthyroid.

Three studies were designed to determine the magnitude of iodine control necessary to return newly diagnosed cats to a euthyroid state;²⁷ the maximum level of dietary iodine that maintains cats in a euthyroid state;²⁸ and the effectiveness of a therapeutic food formulated based on the previous studies to control naturally occurring hyperthyroidism in cats.²⁹ In summary, results of these studies demonstrated that a food with 0.17 or 0.32 ppm iodine (DMB) maintained normal thyroid hormone concentrations in hyperthyroid cats, helping to further define the range of iodine effective for managing hyperthyroidism.

We have treated 22 cats to date with feline y/d with follow-up data for at least 6 months. All of the cats found at least one form of the diet (dry or canned) to be palatable. Nineteen of 22 (86%) cats experienced clinical improvement with normalization of their TT4 concentrations. Of the three cats that failed to achieve remission, 2 cats were discovered to be eating foods other than y/d and when the owners switched them to y/d exclusively remission of hyperthyroidism was achieved. One cat (5%) failed to respond to dietary therapy and was subsequently treated with 131-I.

We are currently conducting a prospective study evaluating the efficacy of feline y/d in managing feline hyperthyroidism to include monitoring of thyroid function (TT4, fT4ED, TSH), clinical signs, body weight, renal function and blood pressure pre and post-treatment. The study should be completed in 2015.

Newly diagnosed patients

After confirming the diagnosis and performing a thorough patient evaluation, nutritional management should be discussed along with other options for managing hyperthyroidism. If selected as the management option, gradual transition to the limited-iodine food (Hill's® Prescription Diet® y/d™ Feline) over at least 7 days is recommended. It is very important to counsel owners so they understand that success of nutritional management depends on the limited-iodine food being the sole source of nutrition for their cat.

The first recheck evaluation should be done 4 weeks after completing the transition to y/d Feline (i.e., once the cat has eaten y/d exclusively for 4 weeks) and as a minimum should include physical examination and measurement of T₄, BUN, serum creatinine, and urine specific gravity. All cats should have decreased T₄ concentrations compared with baseline and many will have returned to normal by the 4-week evaluation. Clinical improvement including weight gain, improved hair coat and decreased tachycardia/cardiac murmur also may be noted by the first evaluation. Clinical signs should continue improving by the next re-evaluation at 8 weeks and most cats will be euthyroid. Some cats require slightly longer to become euthyroid; however, it's expected that 90% will have normal T₄ concentrations if the limited-iodine food is their sole source of nutrition.

If euthyroidism is not achieved within 4 to 12 weeks, a thorough history is indicated to confirm that only the limited-iodine food is being fed.

Managing hyperthyroid cats with concurrent kidney disease

Chronic kidney disease (CKD) and hyperthyroidism are more likely to be diagnosed in older cats so it's not surprising that many hyperthyroid cats have CKD. Untreated hyperthyroidism complicates the diagnosis of CKD because it's associated with increased glomerular filtration rate (GFR) and therefore often masks biochemical markers of CKD. Regardless of the therapeutic modality (methimazole, surgical thyroidectomy, or radioiodine), decreased GFR, increased serum urea and creatinine concentrations and development of overt clinical signs of kidney disease have been reported after successful treatment of hyperthyroidism.^{4,33-36} The presence of underlying CKD may affect the prognosis - one study documented a shorter survival time in hyperthyroid cats with azotemia.⁷ However, two recent studies comparing survival of cats that developed azotemia with those that did not after treatment of hyperthyroidism found no significant difference between the two groups if cats did not become hypothyroid post-treatment.^{38,39}

The reported occurrence of azotemia after treatment of hyperthyroidism ranges from 15 to 49%.^{31,35-37,40} Iatrogenic hypothyroidism has been reported to decrease GFR in human patients.⁴¹ Post-treatment iatrogenic hypothyroidism has been reported in cats after radioiodine therapy and bilateral thyroidectomy, which constituted the predominant therapeutic modalities in previous studies.⁴⁰ In one recent study, cats with iatrogenic biochemical hypothyroidism were almost twice as likely to develop azotemia post-treatment as euthyroid cats.³⁸ The hypothyroid cats with azotemia had shorter survival times than cats without azotemia, whereas, consistent with previous reports, there was no difference in survival times of euthyroid cats with or without azotemia.

It's not possible to consistently predict which cats will develop overt CKD after treatment of hyperthyroidism or have progression of their kidney disease. This should be considered when deciding on treatment options, particularly those that are irreversible (thyroidectomy, radioactive iodine). Regardless of the option selected for managing hyperthyroidism, it's important to remember that the only intervention shown to improve quality of life and prolong survival time in cats with naturally occurring CKD is feeding a therapeutic renal food.^{42,43} Until recent availability of limited-iodine food, nutritional recommendations have not generally been considered for hyperthyroid cats without azotemia. In cats with compromised renal function, but without azotemia (IRIS Stage 1), the decrease in GFR associated with normalizing serum T₄ levels may be sufficient to prevent effective clearing of protein metabolic by-products (BUN and creatinine) when dietary intake of protein and phosphorus is high. This could contribute to the occurrence of post-therapy azotemia in hyperthyroid cats.

In our work with 22 cats with hyperthyroidism treated with feline y/d, 4/22 cats (18%) were azotemic (IRIS Stage 1 and 2 CKD) prior to starting the diet. All 4 cats experienced normalization of their BUN and creatinine within 30-150 days along with normalization of their TT4's. One potential explanation is that the expected decrease in GFR associated with normalizing serum T₄ may be offset by the nutrient profile of the limited-iodine food which is similar foods for mature adult cats or cats with early CKD. Additional study is needed to better understand the effects of using limited-iodine food on hyperthyroid cats with concurrent kidney disease.

Conclusions/summary

Hyperthyroidism is the most common endocrine disease of older cats worldwide. While the pathogenesis is unclear, several effective management options are available. All should be discussed with pet owners, including pros/cons, so that the best option can be selected for individual patients and their owners. Feeding a limited-iodine food is now available as an option for effective management of hyperthyroid patients. When fed as the sole source of nutrition, approximately 90% of hyperthyroid cats become euthyroid within 4 to 12 weeks. To date, over 150 cats with naturally occurring hyperthyroidism have been managed successfully by feeding a limited-iodine food, most for 2-3 years and some cats for as long as 6 years.

Getting to the Bottom of Polyuria and Polydipsia

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Introduction

- A. Polyuria and polydipsia (PU / PD) refer to excessive water consumption and urine production respectively. These are common clinical signs in both dogs and cats.
- B. Water consumption exceeding 100 ml/kg or urine production exceeding 50 ml/kg body weight per day is considered abnormal and should be pursued. These numbers have been established in laboratory reared dogs and may not reflect "normal" water consumption in pets. They are to be used only as guidelines.
- C. Water consumption can vary greatly from day to day so it is important to have owners subjectively assess water consumption in the home environment for several consecutive days in order to obtain an accurate picture before beginning unnecessary and expensive diagnostic tests. Actual quantification of water consumption can be very difficult and may not be practical for the majority of pet owners.

Normal water homeostasis

- A. Extracellular fluid volume is maintained by regulation of fluid intake and urine production.
- B. The thirst center is stimulated by an increase in plasma osmolality (sodium concentration) and/or a decrease in blood volume (hypovolemia) resulting in an increase in water consumption.
- C. Increasing plasma osmolality and hypovolemia also stimulate osmoreceptors in the anterior hypothalamus and baroreceptors in the aortic arch resulting in the release of antidiuretic hormone (ADH) from the anterior pituitary.
- D. ADH circulates and binds to receptors on the renal tubular cells of the distal tubules and collecting ducts resulting in the production of cAMP. This causes the opening of pores in the luminal membrane of the tubular cells and allows for reabsorption of water from the glomerular filtrate resulting in a concentrated urine. In order for water to be pulled out of the tubule it must move along a concentration gradient maintained by the hypertonic renal medullary interstitium. Loss of this gradient (medullary washout), will result in an inability to concentrate urine even in the face of normal ADH activity. Urea and sodium are largely responsible for maintaining the hypertonicity of the interstitium.
- E. The sensation of thirst and secretion of ADH are suppressed when plasma osmolality and blood volume are returned to normal.

Differential diagnosis: Mechanisms of PU/PD

- A. Renal disease:
 - a. Chronic renal failure: A decrease in the number of functional nephrons causes an increase in tubular flow in the remaining nephrons and leads to a solute diuresis. A decrease in urine concentrating ability may be the only laboratory abnormality indicating renal disease (especially in feline patients) presented for PU/PD.
 - b. Pyelonephritis: Bacterial induced tubular destruction and an increase in renal blood flow cause a decrease in medullary hypertonicity.
 - c. Primary renal glycosuria (Fanconi's Syndrome): A proximal tubular defect results in renal glycosuria leading to an osmotic diuresis. The blood glucose is normal.
 - d. Post-Obstructive diuresis: May be seen in previously blocked cats. Due to osmotic diuresis from loss of large amounts of sodium and urea into the urine following relief of urethral obstruction.
- B. Diabetes mellitus:
 - a. Hyperglycemia results in glycosuria and an osmotic diuresis. Threshold for renal glycosuria is a blood glucose of 180 – 220 mg/dl (dog) and 240 – 300 mg/dl (cat).
- C. Liver disease:
 - a. PU/PD may occur as the result of: (1) decreased production of urea which is a major component of the hypertonic medullary interstitium, (2) increased renin and cortisol levels due to a lack of hepatic degradation, (3) increased aldosterone concentration leading to increased sodium concentration, and (4) hypokalemia (see hypokalemic nephropathy).
- D. Hyperthyroidism:
 - a. Increased total renal blood flow reducing the tonicity of the medullary interstitium.
 - b. Psychogenic polydipsia or primary polydipsia is reported in humans with hyperthyroidism.
- E. Hypercalcemia:
 - a. Interference with cAMP activation by ADH, damage to ADH receptors, and mineralization of renal tubular

- cells.
- F. Hyperadrenocorticism:
 - a. Glucocorticoids interfere with the action of ADH at the renal tubule and decrease
 - b. ADH secretion by reducing osmoreceptor sensitivity to rising plasma osmolality.
- G. Hypoadrenocorticism:
 - a. Renal sodium wasting leads to decreased medullary hypertonicity.
- H. Pyometra:
 - a. coli endotoxins interfere with sodium reabsorption and damage ADH receptors and may result in an immune-complex glomerulonephritis.
- I. Hypokalemia:
 - a. Degeneration of renal tubular cells, (2) decreased medullary hypertonicity, stimulation of thirst, and (4) stimulation of renin release.
- J. Polycythemia:
 - a. Mechanism unknown; may be related to sluggish blood flow in kidney or hypothalamus.
- K. Medications:
 - a. Exogenous steroids, diuretics, salt supplementation, primidone, phenobarbital, KBr and vitamin D.
- L. Pituitary or central diabetes insipidus (CDI):
 - a. Due to inadequate production, storage or release of ADH. May occur as a congenital defect or secondary to trauma, mass lesions, infection or infarction of the pituitary or hypothalamus.
- M. Nephrogenic diabetes insipidus (NDI):
 - a. Congenital structural or functional defects in ADH receptor. Rare in dogs and cats.
- N. Primary polydipsia or psychogenic polydipsia:
 - a. Underlying cause unknown (possible CNS lesion); results in increased renal blood flow and a decrease in medullary hypertonicity. Extremely uncommon in dogs and cats and is largely a diagnosis of exclusion.

Diagnostic approach to PU / PD

- A. Document PU/PD actually exists. Recommend assessment of water consumption in the home environment. Hospitalized animals frequently do not drink as much as they would in their natural surroundings.
- B. Quick evaluation of urine specific gravity and glucose is cheap, easy, and very helpful in evaluating animals for possible pathologic PU/PD. If the urine specific gravity of a non- glycosuric sample, obtained from a dog or cat without signs of dehydration, is greater than 1.030 (dog) or 1.035 (cat), the likelihood of pathologic PU/PD is small and further work-up may not be required.
- C. Most causes of PU/PD will be identified following a good history, physical examination, and an initial data base consisting of a CBC, chemistry profile, and urinalysis with bacteriologic culture.
- D. If a cause has not been discovered after step C, the most likely diagnoses are hyperadrenocorticism (dog only, cats with Cushing's are usually overtly diabetic), central and nephrogenic diabetes insipidus, and primary polydipsia. As hyperadrenocorticism is far more common than either of the other causes, an ACTH stimulation test, urine cortisol/creatinine ratio or low-dose dexamethasone suppression test should be performed before proceeding to the modified water deprivation test (See Canine Hyperadrenocorticism).

Modified water deprivation test (MWDT)

- A. This test is designed to help differentiate CDI, NDI, and primary polydipsia. It is not very helpful unless other causes of PU/PD have been ruled out.
- B. The test is designed to determine whether ADH is released in response to dehydration and whether the kidneys can respond to the circulating ADH.
- C. **VERY IMPORTANT !! THE TEST SHOULD NEVER BE PERFORMED ON AN ANIMAL WITH PRE-EXISTING AZOTEMIA OR OBVIOUS DEHYDRATION. DOING SO IN ANIMALS WITH RENAL INSUFFICIENCY MAY RESULT IN DECOMPENSATION AND THE DEVELOPMENT OF OLIGURIC RENAL FAILURE OR ANURIC RENAL FAILURE.**
- D. Severe dehydration can occur very rapidly (4-6 hours) especially in animals with diabetes insipidus. Leaving them unattended without water for several hours or overnight may result in severe hyperosmolality, coma, and death.
- E. Gradual water restriction should be instituted at home for 2-3 days prior to performing the MWDT in order to help minimize medullary washout from long-standing PU/PD.

Phase one

1. Animal is weighed, bladder emptied and urine saved for specific gravity and osmolality (if available).

2. Blood is obtained for BUN and osmolality.
3. Water is withheld. BUN, plasma osmolality and body weight are obtained hourly. The bladder is emptied every hour and a sample is saved for specific gravity and osmolality.
4. Test concluded with either a 5% loss in body weight, azotemia (BUN > 30), or urine specific gravity > 1.030 (1.035 cats). The bladder is emptied and urine is saved for specific gravity and osmolality, and plasma is obtained for osmolality.

Phase two

1. Aqueous vasopressin (Pitressin) 2 - 3 units (dog) or 0.25 U/# (cat) is given SQ. Alternatively DDAVP may administered into the conjunctival sac (1 – 2 drops for dogs and 1 drop for cats).
2. Urine and plasma osmolality and urine specific gravity are obtained every 30 min for 90 minutes.
3. Bladder must be emptied at every 30 minute sampling period.
4. Water is withheld throughout the test.

Interpretation of the MWDT

- A. Normal Animals: Following water deprivation will concentrate urine to > 1.030 (dog) or 1.035 (cat). Urine osmolality in excess of 1,200 mOsm/kg.
- B. CDI: Unable to concentrate urine in excess of 1.008 (< 300 mOsm/kg). After ADH administration, urine specific gravity should increase to greater than 1.012 with a 50 - 500 % increase in urine osmolality.
- C. NDI: Similar to CDI following water deprivation. No further response following ADH injection.
- D. Partial CDI: Results depend on how much ADH is available. Following water deprivation urine specific gravity between 1.008-1.019 and urine osmolality between 300 to 1,000 mOsm/kg. Urine specific gravity and osmolality increase after ADH administration. Similar response seen with hyperadrenocorticism and a number of the other causes of PU/PD. This is why it is important to rule-out these processes prior to a MWDT.
- E. Primary polydipsia: Depends on degree of medullary washout. With minimal washout results are similar to normal animals. More severe washout gives results similar to partial diabetes insipidus.

Treatment of polyuria and polydipsia

- A. Treat the underlying disorder !
- B. Treatment of CDI
 - a. DDAVP (Desmopressin acetate) 1-2 drops into the conjunctival sac or 0.01 to 0.05 mls subcutaneously SID or BID. May also dose orally with 0.1 to 0.2 mg once or twice a day.
 - i. 1 drop = 1.5 to 4.0 ug. Can use TB syringe to dose.
 - ii. Duration 8 - 24 hours.
 - iii. Redosed when polyuria returns.
 - iv. Most commonly used treatment today.
 - v. Use the intranasal preparation.
 - b. Chlorpropamide (Diabinese)
 - i. Oral hypoglycemic. Stimulates ADH release and potentiates ADH action. Hypoglycemia is the limiting factor.
 - ii. 25 - 40 mg once or twice a day (cat). Limited experience.
- C. Treatment of NDI
 - a. Salt restriction
 - b. Thiazide diuretics:
 - i. Natriuresis results in a decrease in blood volume and increased sodium reabsorption in the proximal tubule.
 - ii. Hydrochlorothiazide 12.5 - 25 mg once or twice a day (cat).
 - iii. Chlorthiazide 20 - 40 mg/kg BID (dogs).
 - iv. May also help with partial CDI.
- D. Treatment of Primary Polydipsia
 - a. Treatment to restore hypertonic renal medullary interstitium.
 - b. Gradual water restriction over several days.
 - c. Behavioral modification or referral to a behaviorist may be needed.

Diabetes in Dogs- Acute Care and Long-Term Management

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Diabetes mellitus is a common endocrine disorder in dogs and cats. Recent data has shed light on the pathogenesis of the disorder in dogs and cats and has highlighted the role of diet, insulin and novel hypoglycemic therapies. In the majority of cases, the most appropriate therapy in both dog and cats includes the administration of insulin.

The key to successful management of the diabetic patient lies in close communication with the pet owner and prompt recognition and treatment of concurrent disorders.

Key facts

1. Insulin is still the mainstay of therapy in the majority of dogs and cats with diabetes mellitus.
2. Diet is an important part of diabetic management especially in obese patients and cats.
3. Auto-immune disease, pancreatitis and amyloidosis are the most common causes of diabetes in dogs and cats.

Successful management of the diabetic patient involves many factors. An understanding of dietary therapy, insulin preparations, oral and novel hypoglycemic agents and management of concurrent illness, are all required to optimize glycemic control. The goals of therapy are to control clinical signs, prevent or slow the progression of cataracts, avoid hypoglycemia and maintain ideal body weight. An additional goal in cats is to obtain remission. The challenge is to address these concerns while attempting to help the owners deal with what they may consider a time consuming, expensive and chronic medical condition.

Diabetes Mellitus in dogs and cats results from a decrease in insulin secretion from the beta cells of the pancreas and/or a decrease in insulin action. There are three classifications of diabetes:

Type I diabetes is comparable to insulin dependent diabetes mellitus (IDDM) in humans. It results in low basal insulin concentrations with impaired insulin secretion following a glucose load. Treatment requires insulin injections. It is the most common form of diabetes in dogs.

Type II diabetes is similar to non-insulin dependent diabetes (NIDDM) in humans and is managed with dietary therapy and oral hypoglycemics. It causes normal to increased basal insulin concentrations with decreased secretion following a glucose load. Insulin may or may not be required for animals with Type II diabetes.

Type III diabetes is seen most commonly in hormonally-induced diabetes in dogs and cats and is similar to impaired glucose tolerance (IGT) in humans. Diabetogenic hormones (epinephrine, cortisol, glucagon and growth hormone) or medications interfere with insulin action and cause glucose intolerance, which can lead to diabetes.

Etiology and signalment

Canine

There are some distinct differences in the etiology of canine and feline diabetes. In dogs, it is generally thought to be an immune mediated disease with gradual destruction of beta cells. The progression from normal, to glucose intolerant, to diabetes, is generally slow so that most islets (over 90%) are lost before diabetes occurs. Other causes of diabetes in dogs include genetic predisposition, chronic pancreatitis and medication-induced diabetes (*glucocorticoids* and *megestrol acetate*).

Genetic predisposition to diabetes is most common in the following breeds: German Shepherd dogs, Schnauzers, Beagles, and Poodles. Golden Retrievers and Keeshonds are more prone to juvenile diabetes.

Gender is a factor in dogs with females being three times more likely to develop diabetes than males. Generally, diabetes occurs in dogs in middle age (6-9 years) but can also present earlier for specific breeds, particularly the Golden Retriever and Keeshond.

Feline

The most common causes of diabetes in cats are obesity, pancreatitis and most commonly, amyloidosis of the pancreatic beta cells. There appears to be very little gender predisposition to this disease in cats, although it is slightly more common in males than females. As with dogs, the onset of diabetes in cats occurs most often in middle age.

Clinical signs

The clinical signs of diabetes include PU/PD (polyuria and polydipsia) from hyperglycemia, resulting in glycosuria and a resultant osmotic diuresis. Polyphagia and weight loss is common although many animals will still be obese upon presentation. In addition to the polyphagia, there may be variable degrees of dehydration especially in the cat. Cataract formation is very common in dogs with diabetes, but rare in cats. Cats often present with icterus as a result of concurrent hepatic lipidosis and/or pancreatitis. Icterus is not common in dogs unless they have pancreatitis. Cats may also exhibit a plantigrade stance (peripheral neuropathy) that is directly related to the severity and duration of hyperglycemia. Clinical neuropathies do occur in dogs, but are extremely rare.

Differential diagnoses include: hyperthyroidism (in cats), gastrointestinal lymphoma, hepatic disease, renal disease, pancreatitis, hyperadrenocorticism, and acromegaly.

Diagnosis

Diagnosis involves testing for persistent fasting hyperglycemia, with fasting blood glucoses greater than 200mg/dl. Clinicians also will need to rule out transient hyperglycemia that may be due to: post-prandial hyperglycemia; diabetogenic hormones (endogenous or exogenous); and stress hyperglycemia. Stress hyperglycemia can be a problem in cats due to the release of epinephrine when stressed or handled.

Laboratory abnormalities include:

- Hemogram
 - non-specific
 - signs of dehydration
- Biochemistry profile
 - hyperglycemia
 - increases in SAP and ALT
 - increases in bilirubin (usually in cats)
 - hepatic lipidosis
 - pancreatitis
- Urinalysis
 - glycosuria
 - renal threshold for glucose
 - canine 180-220mg/dl
 - feline 240-300 mg/dl
 - ketonuria
 - up to 40% of patients will have positive urine cultures in the absence of an active urine sediment.

Treatment

The number one cause of death in diabetic dogs and cats is not the disease itself, rather, it is the owner's frustration with the disease. This is an extremely important point to remember when treating diabetic animals. Good communication with the pet owner is perhaps the most important component of managing the disease.

It is recommended that clinicians schedule a 30-minute appointment with the client at the time of discharge before sending the diabetic patient home for the first time. During this appointment, clinicians should thoroughly discuss the care required for the patient. Include the following instructions in that discussion: how to give the animal injections; how to store insulin, what types of food to feed and how often; how to recognize the signs of hypoglycemia and how to react to this condition. Also include information on what clinical signs to look for in terms of monitoring water intake and urine production. The client should be given written instructions for use as a reference once they are caring for the patient at home. It is essential that the clinician and veterinary staff strive to educate the caregiver and motivate them to get involved in the care of their diabetic pet.

The goals of treatment include elimination of the clinical signs of diabetes, prevention or slowing of cataract formation and resulting blindness, prevention of potentially dangerous hypoglycemia, and prevention and/or treatment of concurrent illness.

Therapy for diabetes centers on three main areas: Treatment of concurrent illness (i.e., urinary tract infections, pyoderma, etc.), insulin therapy, and dietary management.

Concurrent illness

Monitoring for concurrent illness is very important in effectively managing diabetic dogs and cats. Clinicians must effectively recognize and treat the other disorders because the concurrent illness will impact the diabetic regulation and many common diseases have similar clinical signs to diabetes mellitus. Even simple problems such as UTI's and pyoderma can result in activation of stress hormones and result in insulin resistance.

Insulin therapy

There has been a considerable amount of confusion over the various insulin preparations that are available. In general, animal origin insulins are being discontinued as the desire and ability to treat people with human derived insulin preparations has progressed.

There is concern that animals receiving human insulin will develop antibodies resulting in decreased insulin activity and/or effectiveness. Dogs receiving any insulin product that is not derived from pork may make antibodies. However, studies have shown that those antibodies do not interfere with the glucose control. In fact, dogs that made antibodies against insulin had a longer duration of insulin action, which actually enhanced the effect of the insulin rather than decreased its efficacy. A recent study in cats showed that 13% developed anti-insulin antibodies. None of the cats showed signs of insulin resistance.

The options with human insulin include ultra short acting, short acting, intermediate acting, and long-acting insulins. The short acting insulins are primarily used for ketoacidosis, and therefore, are not covered in this article. The intermediate acting insulins are classified as either NPH or Lente. It is important to note however, that even though they are classified as intermediate, they do not behave the same way in the dog or cat. Lente is actually a mixture of two different insulin preparations, which results in a bimodal onset of actions. This is helpful in some patients because it helps block post-prandial hyperglycemia. Conversely, a lente insulin is not recommended for use in an animal that does not develop post prandial hyperglycemia. It is recommended that NPH be used in the majority of dogs and cats with diabetes and it is also understood that most patients will require two injections a day to achieve glycemic control.

Canine patients

Newly diagnosed patients

1. Vetsulin (porcine origin lente): A zinc, porcine, intermediate acting insulin. Canine and porcine insulin have an identical amino acid sequence thereby eliminating the theoretical complication of anti-insulin antibodies and their effect on glycemic control. The suggested, initial starting dose is 0.5 units/kg BID. This insulin is only available at a concentration of 40 IU/ml (U-40) so please make sure that proper insulin syringes are provided to the owner. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy. This insulin must be thoroughly shaken before administration. For additional information see: www.vetsulin.com.
2. Humulin N or Novolin N; These are both intermediate acting, human origin insulins. Suggested starting doses are 0.5 units/kg BID. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy. I would avoid NPH insulins from Wal Mart due to product inconsistencies.
3. Glargine:
4. Detemir:
5. PZI:

Transitioning canine patients

If you have canine patients currently taking Humulin L lente insulin, I would switch them to either Vetsulin or Humulin N. The initial dose of Vetsulin or Humulin N will remain the same with re-assessment of clinical signs and a serial blood glucose curve performed 1 week after changing insulin preparations.

With the recent introduction of the AlphaTrak Blood Glucose Monitoring System (Abbott) we have the ability to very accurately measure blood glucose concentrations in both dogs and cats using very small quantities of blood. This will allow both veterinarians and pet owners to obtain very reliable results in both the hospital and home setting. This information can then be used to make informed decisions regarding the management of diabetic patients. These decisions impact the type and dose of insulin selected, the frequency of insulin administration, aid in the assessment of glycemic control, help in preventing hypoglycemic episodes and monitor for remission of diabetes especially in feline patients.

Glycemic control can be evaluated in a number of ways. Owner assessment of clinical signs (polyuria, polydipsia, weight gain or loss), progression of diabetic cataracts (dogs), presence of peripheral neuropathy (cats), and episodes of hypoglycemia are often the best indicators of glycemic control. Changes in insulin dosage or documenting remission of diabetes, is best determined by blood glucose measurement. Recognizing that the measurement of blood glucose concentrations can be problematic in the hospital setting (especially in cats as a result of stress induced hyperglycemia) recent work has evaluated the practicality and value of at home blood glucose monitoring in dogs and cats. At home blood glucose monitoring is essential in the management of human patients with diabetes given that a number of the complications associated with long term diabetes are directly related to persistent hyperglycemia. While diabetic retinopathy, nephropathy, painful neuropathies and cardiovascular disease are rare in our veterinary patients, adequate glycemic control is required to eliminate clinical signs and decrease morbidity and mortality in dogs and cats. Control of clinical signs does not require the restoration of euglycemia but rather involves keeping the blood glucose levels below renal threshold for the majority of the day. Renal threshold for glucose is 180 mg/dl in the dog and approximately 280 mg/dl in the cat. It is very important that we remember the owners of diabetic dogs and cats are being asked to do a great deal to help in the management of their pet's chronic illness and we need to do whatever we can to make the clients job easier while at the same time taking steps to assure maximal diabetic control.

Using the information derived using at home or in hospital glucose monitoring

Dogs

- Dogs on NPH or Lente Insulins
 - If the preinsulin blood glucose concentration is > 360 mg/dl and/or the nadir blood glucose concentration is > 180 mg/dl the dose of insulin is increased by 25%..
 - If the preinsulin blood glucose concentration is 270 to 360 mg/dl and/or the nadir blood glucose concentration is 90 - 180 mg/dl the dose of insulin is maintained.

- If the preinsulin blood glucose concentration is 190 - 270 mg/dl and/or the nadir blood glucose concentration is 54 - 90 mg/dl use the nadir, clinical signs and the next preinsulin glucose concentration to determine if the dose is decreased (50%) or maintained.
- If the preinsulin blood glucose concentration is < 180 mg/dl and/or the nadir blood glucose concentration is < 54 mg/dl the dose of insulin is decreased by 50%.

The use of the AlphaTrak Blood Glucose Monitoring System both in the clinic and at home will greatly improve our ability to assess glyemic control and improve insulin therapy. In conjunction with close observation of clinical signs, at home glucose monitoring should go a long way towards improving the quality of life of diabetic pets and their owners.

Diet

There is a considerable amount of reliable research data showing that diets high in carbohydrates, low in fat and high in fiber are helpful in regulating diabetic dogs. These types of diets lower the average insulin dose, the average blood sugar, the amount of urine being produced and glycosolated hemoglobins and fructosamine levels.

The carbohydrates in these diets are complex carbohydrates. It is important to avoid diets high in simple sugars, which includes any commercial semi-moist food, primarily those packaged in foil packets. Diets high in simple sugars are absorbed very rapidly before the insulin has time to work. The goal with diet is to balance the absorption of sugar with the onset of action of the insulin. A high carbohydrate/low fat diets also decreases plasma free fatty acid and cholesterol concentrations, and increases the number and activity of insulin receptors.

High fiber diets reduce insulin resistance. The fiber acts to decrease post prandial hyperglycemia, primarily because it delays gastric emptying. A high fiber diet also decreases absorption of glucose and increases insulin action at the receptor.

It has recently been suggested that diabetic cats be fed a high protein/low carbohydrate diet. This can be accomplished with several commercially available canned diets (Hill's M/D, IVD Development, Purina DM, many other canned kitten diets). These diets may result in remission of the diabetes and elimination of the need for exogenous insulin and/or oral hypoglycemic agents. High protein/low carbohydrate diets more closely resemble the diet of felines in the wild and may help reduce glucose intolerance, insulin resistance and obesity.

Feeding

Ideally, the feeding schedule should be coordinated with the onset of action of the insulin. With dogs, this is fairly easy to regulate, but with cats, it is nearly impossible due to their "grazing" style of eating. For cat owners who may not be able to follow a strict feeding schedule or those with multiple pet households, insulin therapy will have to be adjusted to meet the owner's needs. The most important component of the dietary plan is to stress consistency in the diet. The following feeding schedule can be used for dogs and some cats. With insulin given once a day, feed three meals a day (of equal calories) at six-hour intervals. Give the first meal at the time of the insulin injection. For animals receiving insulin twice a day, feed four meals a day. Schedule them to coincide with the insulin injections and feed mid-afternoon and late evening.

If the owner is unable to follow this schedule, advise them to feed twice a day, at the time of injection and 8-10 hours later (for once a day insulin patients); or at the times of insulin injections (for twice a day insulin patients).

Home management

1. Instruct owner on proper injection techniques, injection locations, storage and handling of insulin.
2. Instruct owner on how to monitor clinical signs.
3. Continue feeding schedule and dietary therapy.
4. Instruct owners to initially monitor urine glucose/ketone levels daily, usually in the morning or evening prior to feeding. If persistent glycosuria or ketonuria is observed, ask owner to contact the veterinary hospital.
5. Advise owners of the signs of and treatment for hypoglycemia. Have owners keep a bottle of Karo syrup on hand if signs occur (i.e., weakness, ataxia, seizures) so they can rub syrup on the gums immediately. Instruct them to call the veterinary hospital.
6. Home monitoring of a diabetic cat is frequently based on observance of clinical signs only.
7. Serial sugars after the first week of home management.

Re-check evaluations

1. Obtain owner assessment of clinical signs.
2. Serial blood sugars are helpful due to:
 - a. Variability of insulin action in a given patient.
 - b. Inaccuracy of random blood or urine sugars in monitoring the degree of glyemic control.
 - c. Not particularly helpful as a routine procedure in animals that are well controlled clinically.
3. Body weight
4. Physical examination/ophthalmic exam

5. Discuss urine log book with owner
6. Laboratory work as clinically indicated
 - a. Role of glycosylated hemoglobin and fructosamine:
 - b. Fructosamine may be helpful in distinguishing stress-induced hyperglycemia from diabetes in cats. These tests can be used every 3 – 4 months as an indicator of long term (2-3 weeks fructosamine; 4-6 weeks glycosylated hemoglobin) glucose control. Rising values indicate the need for further evaluation.

Problems with insulin therapy

- Insulin induced hyperglycemia (Somogyi phenomenon)
 - Hypoglycemia (<65mg/dl) followed by hyperglycemia (>300mg/dl) within 24 hours of insulin injection.
 - Suspect when insulin requirements exceed 2 U/kg and clinical signs persist.
 - Suspect when animal has signs of hypoglycemia in afternoon.
 - Diagnosis with serial sugars.
 - Treat by decreasing insulin dose 25-50% and review insulin administration with the owner to rule out management problems.
 - Re-check serial sugars in one week.
- Rapid insulin metabolism
 - Duration of insulin less than 18 hours.
 - Signs return in the evening.
 - Diagnosis is with serial sugars. Hyperglycemia (>250) within 18 hours of insulin injection without previous hypoglycemia.
 - Treatment:
 - Review management with owner
 - Switch to twice daily insulin administration. Most dogs and cats require insulin twice a day to achieve adequate glycemic control. Consider switching to PZI in cats.
- Insulin Resistance
 - Hyperglycemia (>300) throughout the day, despite insulin dosages > 2 U/kg.
 - Diagnosis based on serial sugars.
 - Potential causes of insulin resistance:
 - Management problems
 - Hyperadrenocorticism
 - Steroid or Ovaban administration
 - Diestrus or pregnancy
 - Acromegaly
 - Concurrent illness, infection
 - Anti-insulin antibodies
 - Hypothyroidism (dogs), hyperthyroidism (cats)
 - If insulin dose exceeds 2U/kg, the animal should be evaluated for one of these causes of resistance.
- Hypoglycemia
 - Insulin overdosage
 - Suspect if animal shows weakness, shaking, ataxia, seizures at time of insulin's peak effect.
 - Therapy (instructions for owners)
 - Mild signs - give food and call veterinarian
 - Moderate signs - apply Karo syrup to the mouth, offer food when alert and then notify veterinarian.
 - Comatose - apply Karo syrup to mouth and take animal to hospital.
 - When hypoglycemia occurs, serial sugars should be performed to re-assess insulin dose

Epidemiology for the Practicing Veterinarian

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In the era of evidence-based medicine – or the “...*conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients*” [1] – it is critical that practitioners have a strong epidemiological foundation upon which clinical experience and best available external evidence can be integrated. Implied in this is that the best evidence is clinically relevant to the case at hand. By using epidemiology, practitioners can evaluate the quality of the available evidence and apply it appropriately to manage individual patients and patient populations.

Disease does not occur randomly in populations – So why are some more likely to develop disease than others? In the occurrence of health and disease one must consider the interaction among the agent, the host, and the environment (i.e., the epidemiological triad) and how differential exposure to disease “causes” may account for variability in disease occurrence. By looking at patterns of disease in populations, making comparisons between groups, and describing changes over time, we can begin to understand factors contributing to the “cause” of disease. This is critically important as we can only prevent disease by removing exposure to causal factors.

Causal relationships are not always simple – many can be quite complex with multiple contributing factors (i.e., causal factors). To gain an understanding of such complex causal relationships we often turn to models such as the necessary-sufficient-component causes model, path models, Venn diagrams, and statistical models. Each contributes to our understanding in different ways. The necessary-sufficient-component causes model suggests that there are factors or component causes, that together provide the complement of factors contributing to the occurrence of disease [2]. Among those are causes that are necessary for the occurrence of disease (these are always present when disease occurs) and a constellation of factors which interact to produce a sufficient cause (a group of factors that when present results in disease). Alternatively, while path models provide some insight into the sequence of occurrence for the causal factors contributing to disease development, Venn diagrams show the magnitude and interaction of these factors in diagrammatic form. Finally, statistical models can help us understand which factors may be associated with the occurrence of disease and provide some insight into its magnitude of effect.

While we spend a significant amount of time on the “cause” of disease, causation can never definitively be proven. Rather we can establish the presence of causal relationships through the use of Koch’s Postulates, Hill’s Criteria, statistics, and scientific judgment. Koch’s Postulates are based on the premise that one agent leads to one disease and are stipulated as follows: 1) the agent is found in all cases of disease; 2) the agent is not found in other individuals as a non-pathogen; 3) it must be possible to produce a pure, sustainable culture of the agent; and 4) it must be possible to produce the same disease in a susceptible host [3]. While these postulates may prove useful for diseases such as rabies, they are too limited for more complex causal relationships which may have many different sufficient causes such as bovine respiratory disease. Hill’s Criteria were put forward by Sir Austin Bradford Hill as a means for identifying causal relationships [4]. The criteria include the following: 1) time sequence (i.e., the exposure must precede disease); 2) strength of association (exposure is more common in disease and there is a large difference in disease risk); 3) consistency of findings (relationships demonstrated in different populations using different study designs are more likely to be causal); 4) biological gradient or dose effect (changes in exposure lead to changes in disease risk); 5) specificity of association (one exposure – one disease); 6) coherence with established facts; and 7) biological plausibility. We reach for statistics when defining the role of chance, i.e., to be objective in our confidence in the data; trying to answer the question of was the outcome of the study a coincidence or did a causal mechanism exist? Statistics uses both the magnitude of the difference and precision in the estimates to draw conclusions about the existence of a causal relationship.

Applying best-practices to the practice of veterinary medicine not only requires practitioners to be aware of current evidence, but requires them to be able to assess the quality of that evidence and determine if it is applicable to the patient standing before them. This demands a basic understanding of study design, measures of disease occurrence (e.g., incidence and prevalence), and measures of association (e.g., relative risks and odds ratios). Through using the tools in their epidemiological toolbox and critically evaluating the literature, practitioners can provide high-quality care to patients and populations alike.

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Infection Control 101

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Veterinarians must take appropriate precautions to mitigate the risk of infectious disease in patients and hospital personnel. Veterinary hospitals are continually faced with the potential introduction of infectious diseases into the hospital environment. In a survey of infection control programs at Veterinary Teaching Hospitals (VTHs), 82% reported outbreaks of healthcare-associated infections (HCAIs) in the previous 5 years with 58% restricting patient admissions and 32% closing part of the facility to aid in mitigation efforts [1]. Further, 50% also recognized zoonotic infections in personnel. In order to provide excellent patient care, veterinary practices must implement an infection control program to protect the personnel, the patients, and the hospital. Not only is there an ethical responsibility to consider infection control in daily practice, but there is a recognizable standard of care with respect to infection control [2]. The veterinarian not only has a clear duty to recommend preventive measures to reduce the risk of zoonotic disease and to counsel clients to seek medical attention in the event of zoonotic disease exposure, but veterinarians are key partners in the promotion of public health – having both the knowledge base and practical experience to identify potential risks and employ both epidemiologically and scientifically sound prevention strategies [3].

The Study on the Efficacy of Nosocomial Infection Control (SENIC), conducted in U.S. human healthcare facilities from 1970-1976, found that an effective infection control program can have a significant impact on HCAI rates – estimating a 32% reduction in overall rates [4]. This study specifically identified employing trained infection control personnel, conducting surveillance activity, and having a system for reporting back to stakeholders as key components in a comprehensive program. Currently, equivalent data is lacking in veterinary medicine, however, it is not unreasonable to assume a similar reduction in veterinary hospitals implementing similar infection control programs.

Every veterinary facility is unique with its own physical and operational limits – each having specific infection control program components tailored to the needs of each facility. While each program will be unique with respect to its finer details, they will be based on foundational infection control principles. There are general systematic approaches, such as the Hazard Analysis and Critical Control Point (HACCP) system, which can aid in policy and program development [5]. The first step in any control effort should be the identification of risks and hazards specific to the facility. Consider pathogens which are zoonotic, foreign to the region, agents with a high nosocomial transmission risk, and those likely to have a major impact on patient management and welfare. Second, identify critical control points (CCP) or points at which a hazard can be prevented or minimized by applying a control measure. Consider physical areas or processes where the transmission of pathogens is likely to occur. Critical control point monitoring is essential to determine when a critical limit has been exceeded triggering a corrective or preventive action. The level and type of monitoring will be specific to each facility and depend upon stakeholder level of risk aversion and the available resources, both financial and personnel. It is important to note that conducting active surveillance for an organism which survives relatively well in the environment not only can help identify important pathogen reservoirs, but can also indicate overall protocol compliance and effectiveness. Establishing a corrective action plan in response to recognized problems is central to an effective biosecurity program; allowing for an efficient and effective response.

There are many simple practices that can aid in the prevention of disease transmission such as decreasing contact by implementing barrier nursing precautions, creating separation and isolation, or even employing hospital closure during times of epidemic disease. This decision in part will be based on the infectious agent of concern, the hospital population, and the intended purpose for the precaution or action. Barrier nursing is intended to create a barrier between “clean” and “contaminated.” Separation creates hospital areas with differing levels of biosecurity. These areas may be related to species (e.g., small animal vs. large animal or equine vs. bovine), to the type of animal (e.g., adult vs. foal), to the disease severity (e.g., colic, systemic disease, or elective surgery), or to the type of patient (e.g., inpatient vs. outpatient). Isolation is typically reserved for confirmed cases of infectious disease or those considered at highest risk and hospital closure is generally thought of as a means of outbreak containment within an affected facility – but can also be a measure to prevent disease introduction at times of widespread outbreaks in a given geographic location.

Reducing the environmental load of potential pathogens is critical in an environment where animals from many different herds in varying states of immune compromise are comingled. A recent report of epidemic salmonellosis in a VTH sighted ineffective cleaning and disinfection as an important factor in the outbreak which resulted in patient fatalities, hospital closure, and an estimated financial cost of US\$4.1 million [6]. Proper use of cleaning and disinfection is key in eliminating sources of infectious agents and breaking the cycle of transmission. While rigorous cleaning alone can reduce the bacterial load on a concrete surface by 90%, applying a disinfectant after cleaning can reduce this by an additional 6% [7].

Cleaning and disinfection efficacy should be routinely monitored to ensure the ICP is effective in an ever changing landscape. There are many methods for accomplishing this including surveillance for syndromes commonly associated with HCAIs or routine environmental monitoring using electrostatic wipes or sterile sponges to culture specific organisms of concern, or contact plates (i.e.,

Rodac plates) to enumerate non-specific bacterial growth [8-12]. Incorporating environmental surveillance into an ICP requires consideration of sample type, sample collection and detection method, selection of a diagnostic laboratory, and available resources (both financial and personnel); as well methods should be appropriately validated and optimized for their intended use. To gain meaningful information, environmental testing should be performed regularly to establish a baseline level of contamination to which future findings can be compared. In this way potential environmental reservoirs of microorganisms can be detected and cleaning effectiveness can be continually monitored.

Routine cleaning and disinfection helps to minimize the burden of bacteria in the environment that may serve as a source for HCAs. While all housing areas should be cleaned and disinfected between patients, special attention should be paid to areas known to have housed patients with suspected infectious diseases and tended to immediately after use to minimize inadvertent trafficking of pathogens from contaminated to clean areas. Equipment in contact with animals suspected or confirmed of having an infectious disease should be cleaned and disinfected before reuse and handled in a manner to prevent contamination of hospital surfaces. Keep in mind that for equipment contacting mucous membranes (e.g., endotracheal tube, nasogastric tube) disinfection should be attained via dry/moist heat sterilization or application of an antiseptic (a product approved for use on living tissue). It is critical that cleanable surfaces be maintained throughout veterinary hospitals. Dirt floors or porous surfaces (e.g., untreated wood) cannot be effectively disinfected and therefore should be avoided. If porous surfaces are present, they can be rendered less so by painting or sealing the surface – which may need to be done routinely throughout the lifetime of the facility.

Animals in the general population are typically considered to be healthy. As such, the focus of an infection control program for a premise may be weighted more heavily toward preventing the entry of an infectious agent onto the premises through traveling horses, non-resident horses, or visiting personnel (i.e. veterinarian, farrier). In general, premise biosecurity program development should consider five key areas: animals, people, environment, access, and movement. As previously stated, designing a program can be facilitated by using a systematic approach, such as HACCP, to evaluate risks, implement control points, and program monitoring [5]. The adoption of biosecurity practices on an animal operation is a balance of perceived benefit versus the impact of implementation. The benefits of a biosecurity program can be hard to realize as it is difficult to measure the cost of an outbreak averted.

Practice managers must keep in mind that an infection control program is dynamic in nature and should be pliable enough to accommodate many different situations – evolving with the facility, its patient population, its staffing situation, and the changing risk of infectious disease. Infection control procedures should be rigorous, but not to the detriment of patient care. As veterinarians, it is our obligation and responsibility to become educated and aware of the risks posed to personnel, patients, and the hospital in the daily practice of veterinary medicine.

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Protecting the Patients of Tomorrow: Hospital-Based Infection Control

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Veterinary hospitals, by their very nature, create a high risk environment for the transmission of infectious agents – bringing together animals from many different farms with varying levels of compromise. Outbreaks of healthcare-associated infections commonly occur in veterinary hospitals with 82% of American Veterinary Medical Association (AVMA) accredited veterinary teaching hospitals (VTHs) reporting such events within the previous 5 years [1]. In addition, 50% reported the occurrence of zoonotic infections during the previous 2 years [1]. In order to practice high-quality patient care, infection control should be integrated into the patient management plan to protect the people, the patients, and the hospital.

While veterinarians are in a profession recognized to increase the lifetime risk for contracting a zoonotic infection, there is a general disregard for utilizing those practices known to be effective prevention measures. Among AVMA member veterinarians, only 55.2% of small animal practitioners and 28.1% of large animal and equine practitioners reported always washing their hands prior to eating, drinking, or smoking at work; and only 48.4% of small animal practitioners and 18.2% of large animal and equine practitioners reported always washing their hands between patient contacts [2]. Despite veterinarians expressing concern about risks associated with gastrointestinal parasites and gastrointestinal bacteria, 71.2% and 70.9%, respectively, of small animal practitioners, and 35.7% and 39.8%, respectively, of large animal practitioners, reported not using appropriate personal protective equipment (PPE) when evaluating an animal with gastrointestinal signs [2].

Clearly, the biggest challenge in veterinary infection control is simply to do it. Why don't practitioners use best practices with respect to infection control in the practice of veterinary medicine? While there is a paucity of information in the literature specific to veterinarians, we can glean something from evaluations of this issue in human medicine. Consider the barriers which may affect effective implementation of practice guidelines – such as knowledge, attitudes, and behavior. In a systematic literature review, there were multiple factors contributing to each of these barriers including intrinsic factors such as a general lack of familiarity or of awareness with published practice guidelines, a lack of agreement with specific guidelines or with guidelines in general, a belief in a lack of expected outcome, a lack of self-efficacy, and the habit or routine of previous practices; and extrinsic factors such as guideline characteristics, patient influences, and environmental factors (e.g., time and available resources) [3].

While some of these barriers may be relatively simple to overcome (i.e., time and available resources), what it really comes down to is social cognitive behavior – specifically knowledge, motivation, intention, perception of a threat, outcome expectancy, perceived behavioral control, and social pressure – and understanding what motivates a particular behavior [4]. Case in point – Ignaz Semmelweis, (1818-1865), the father of hand hygiene, deduced in 1846 that patients were dying due to “pathogenic causes” associated with deficient hand hygiene practices by physicians [5]. While the prevention strategy he implemented was epidemiologically sound, it was not well received by colleagues and in fact he was relieved of his hospital duties [4]. So why the failure? Not only did this event occur before the germ theory even existed, but his observations were also not reported in a timely fashion, thus there was a general lack of knowledge leading to disbelief by his colleagues. Rather than educating his colleagues on the threat and expected outcome, he chose a more autocratic approach to intervention implementation. Had he approached this in a different manner – taking into account social behavior theory – results may have differed.

An infection control culture is part-in-parcel with creating a workplace safety culture through the integration of behavior based safety programs and the organization's safety culture [6]. Behavior-based safety programs use a bottom-up approach that rely on continuous processes which are data-driven and setting-specific. These programs define critical behaviors, set performance goals, monitor performance, provide feedback, and strive to reinforce the desired behavior. Organization safety culture uses a top-down approach that is a more subjective, self-sustaining process that typically uses surveys to identify and assess personnel assumptions and beliefs. Findings are then used to stimulate organizational change through participation of personnel including leadership. A strong safety culture should have 3 components; 1) norms and rules which explicitly define risks and provide guidelines; 2) individual and group attitudes that place safety as highly important and that motivates personnel to act in this regard; and 3) use reflexivity to continuously understand risk and its mitigation [7].

In practice, fostering an infection control culture can be very difficult – everything we ask personnel to do is inconvenient. It takes time to wash your hands before and after every patient contact, it takes time to don and doff PPE. So how do veterinary practices develop a strong safety culture of infection control and worker safety when it comes down to influencing behaviors and attitudes? The Ecological Model of Behavioral Change suggests that behavior is both affected by and affects several levels of influence including intra-personal factors (e.g., knowledge, attitudes, beliefs), inter-personal factors (e.g., social identity, support network, peer group pressure), community factors (e.g., social networks and norms), and institutional factors (e.g., administrative support) [4]. When applying this to organizational culture – consider that this is a multidimensional concept with core assumptions being at its deepest

level, followed by beliefs and values, and finally norms at its most superficial level [7]. As such, it will take a multifaceted approach to implement change. For example, if a facility wants to embark on a hand hygiene campaign it must first gain personnel involvement and ownership of the issue with a commitment to a solution. Individuals within the organization may champion the cause, providing verbal instruction and training on proper procedures based on the best evidence currently available, in addition to demonstrating best-practices in their daily practice. Management must be committed to the cause, providing resources such as hand hygiene stations and financial support for the effort. In addition, the facility may choose to endorse the program through the development of slogans and posters to promote effective hand hygiene practices. In this way the “culture” of the facility can gradually change to one where the expected norm is one of excellent hand hygiene practices where personnel ensure effective implementation through social influences, alteration of individual beliefs and intentions, and ultimately, permanent changes in behavior.

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Environmental Contamination of *Salmonella Enterica*: Where Should We Focus Our Efforts?

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Epidemics of healthcare-associated infections in veterinary teaching hospitals are commonly attributed to *Salmonella enterica* [1]. Although veterinary hospitals employ rigorous personal and environmental hygiene practices into infection control programs, large outbreaks still occur with high case fatality rates and at considerable financial cost [2]. During times of epidemic disease, there is typically widespread environmental contamination and it is not uncommon for patient and environmental isolates to be phenotypically similar (i.e., serotype and antimicrobial susceptibility pattern); a phenomenon that has also been identified during times of endemic disease, suggesting animals to be a likely source for contamination [2-5]

Managing *S. enterica* in equine populations should take into consideration both factors related to the occurrence of epidemic and endemic disease. During times of epidemic disease, environmental hygiene is commonly identified as a contributing factor including ineffective infection control policies and the presence of floor surfaces which allow contamination to accumulate [2; 6; 7]. Contamination of common use equipment (e.g., buckets, nasogastric tubes, and rectal thermometers) is also a common characteristic [6-8]. During the course of an outbreak, horses with severe disease are frequently identified as shedding *Salmonella* and likely contribute to ongoing environmental contamination and transmission among hospitalized patients [6; 8-10].

Historically, *Salmonella* shedding among horses has been associated with a triad of clinical signs – diarrhea, fever and leukopenia – an observation supported in a recent case-control study [11]. However, this triad of clinical signs can occur rather infrequently, accounting for only 2.7% of shedding among a hospital population (the population attributable fraction) [12]. In addition, findings from experimental studies suggest that by the time fever and/or diarrhea are apparent, animals are frequently shedding *Salmonella* in their feces; emphasizing the importance of identifying commonly occurring, easily recognizable factors or groups of factors that would allow for the rapid implementation of prevention strategies [13].

It is generally believed that horses with more severe disease (e.g., gastrointestinal disease, abdominal surgery) and those receiving antimicrobial therapy are more likely to shed detectable quantities of *Salmonella* in their feces. While this seems to make biological sense – it is important to note that over the years this has not been a consistent finding [8; 11; 14-17]. Many of these studies targeted high risk groups and extrapolating findings from studies observing limited patient populations should be done with caution.

Studies focusing on the general patient population found that both patient and hospital factors may be important [12; 17-20]. Patients with systemic illness – regardless of body system affected – and those having any one of the classic triad of clinical signs are more likely to shed *Salmonella*, but shedding is not limited to these particular patients [12]. These clinical signs are specific indicators for identifying shedding, but they are not perfectly sensitive. Additional factors that may affect the likelihood of shedding include patient management factors such as transportation distance, antimicrobial therapy, and duration of hospitalization, as well as species or rearing circumstances (intensively managed cattle being much more likely to shed than horses – an element that should not be overlooked when managing horses in a multi-species hospital) [12; 20]. In addition, reports consistently show a seasonal occurrence to shedding – highest in late summer and early fall, and lowest in the spring [12; 14; 21-23].

The intermittent nature of *Salmonella* shedding, often in the absence of clinical signs, makes it challenging to effectively manage this risk. Patient shedding prevalence can vary from 0.5% up to 7% with horses admitted for elective procedures and those in the general equine population having a lower prevalence; as well those tested on admission typically have a lower prevalence than horses tested throughout hospitalization [18; 19; 21; 23]. A higher shedding prevalence has been reported in horses with gastrointestinal disease or colic ranging from 4.3% up to 13% [14; 16; 19]. Differential management may be warranted for patient subgroups depending upon the likelihood of *Salmonella* shedding on admission or throughout the duration of hospitalization.

Routine surveillance by testing fecal samples may be an effective method to detect *Salmonella* shedding among patients. Consideration should be given to how this may be implemented – test all patients or target a high risk group such as horses with gastrointestinal disease. While research does show that targeted surveillance of horses presenting for acute colic or diarrhea can be an effective method for identifying fecal shedding it also shows that many horses can be shedding *Salmonella* in the absence of clinical signs [3; 11; 24]. An alternative may be to use syndromic surveillance – a method that has been shown to be effective at detecting adverse events in hospitalized horses [25]. Some facilities may choose to conduct surveillance of the hospital environment rather than of patients as environmental contamination is commonly detected near where positive patients are managed [4; 17]. This could be conducted as either routine or periodic surveillance of high-traffic areas. Yet others may choose to conduct both active surveillance of patients and the environment. As complementary techniques, this may allow for earlier detection of endemic shedding among patients and to identify outbreaks early in their time course [3].

Environmental contamination cannot be completely eliminated, therefore the goal is to reduce contamination of the environment to a level that becomes biologically irrelevant. Veterinary hospitals can be frequently contaminated near where positive patients are

managed with floors, floor drains, cracks and crevices being common sights for contamination [4; 24; 26; 27]. To gain meaningful information, environmental testing should be performed regularly to establish a baseline level of environmental contamination to which future findings can be compared. In this way potential environmental reservoirs of Salmonella can be detected and cleaning effectiveness can be continually monitored.

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Rapid Diagnostic Testing for *Salmonella* in Clinical Practice

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Salmonella enterica is commonly associated with epidemic disease in veterinary hospitals and on-farm environmental contamination [1; 2]. As such it garners much of our attention. Unfortunately, testing techniques for the detection of *Salmonella* in fecal and environmental samples is variable among laboratories and current testing methodology generally lacks in sensitivity. Consequently, testing strategies generally test multiple samples, use lengthy enrichment steps, and may take 3-5 days to obtain results. In that time, significant environmental contamination and disease transmission can occur, thus risk recognition and rapid identification are critical to effectively managing this agent in populations and their environments.

There are many methods available for the detection of *S. enterica* in samples relevant to veterinary medicine – including enriched culture, polymerase chain reaction (PCR), and lateral flow immunoassays (LFIs) – all requiring varying levels of expertise and can impact time to detection, test results and interpretations, and ultimately disease control efforts [3-7]. The reliability of bacterial culture for *S. enterica* detection can be affected by the type of sample (feces, swab, or rectal biopsy), heterogeneity of target organism in the sample, sample weight, intermittent shedding, bacterial culture method, and laboratory proficiency.

While experimentally, the analytic sensitivity of equine fecal culture has been found to be as few as 4 cfu/gram of feces when enriched in tetrathionate broth [8] and 100 cfu/gram of feces when enriched in selenite broth [9]; in practice, fecal culture is a relatively insensitive method. This is likely due to intermittent shedding of relatively few organisms per gram of feces [10; 11], as well as the heterogeneous distribution of organisms within fecal samples [12]. Because of the need to use one or more enrichment steps, it can take up to 3 days to realize test results for a single fecal sample and the limited test sensitivity means that we typically need 3-5 cultures per animal, interpreting tests in parallel, to achieve reasonable sensitivity for the overall diagnostic process.

Polymerase chain reaction (PCR) is generally considered to be a highly sensitive and specific method of *Salmonella* detection as most assays target highly conserved genes allowing for the detection of many different serotypes while minimizing cross-reaction with other common bacteria [13; 14]. The analytic sensitivity of PCR varies from 100 cfu/gram of equine feces with overnight enrichment to 1000 cfu/gram without enrichment; and PCR is generally more rapid than enriched culture, providing results within 1-2 days (versus 2-5 days) [9; 14-16]. Keep in mind that PCR does not replace the need for culture as generally we need more than a dichotomous (positive/negative) result to facilitate epidemiological investigations and on-going surveillance.

Commercially-available lateral flow immunoassays (LIAs), developed for use in food safety microbiology, are a promising practical alternative to more traditional detection methods [8; 17]. In experimentally-inoculated equine fecal samples they have been shown to have an analytic sensitivity of 4 cfu/gram of feces after 18-hrs in selective broth culture [8]. The use of these tests does not require any specialized training or equipment – just need an incubator and pre-made media. There is some variability in the ability of LFIs to detect different strains (serotypes) of *Salmonella*, however their low cost, ease of use, and reliability make them an appealing option for point-of-care testing in equine practice [18]. Follow-up culture of samples that are LFI-positive should be performed to characterize isolates and inform epidemiological investigations.

Detecting *Salmonella* in equine practice can be challenging – horses typically shed low numbers of organisms and tend to do so intermittently [10; 11]. Regardless of the analytical sensitivity of test methods, this causes the overall detection system (i.e., sample type combined with sample processing and detection method) to have poorer epidemiological sensitivity (i.e., lower probability of detecting truly infected/shedding horses). While testing larger sample volumes will improve upon test sensitivity up to a point [19], testing of multiple samples may also be utilized. Interpreting multiple test results in parallel can improve the overall sensitivity of the testing strategy. Case in point, a truly positive patient is more likely to culture-positive with increased number of samples tested [20]. In application this is generally accepted to be a minimum of 3-5 cultures obtained in a relatively short time frame – if all are negative then we can be reasonably sure that there is a low risk of *Salmonella* shedding [10]. Assuming independence of test results, this equates to an estimated sensitivity of 44% for a single culture, 66% for two cultures, 82% for three cultures, and 97% for 5 cultures [21].

There are many different *Salmonella* serotypes and their distribution can change over time [22]. Therefore, it is important to ensure that the test can detect the most commonly detected serotypes in a given geographic or practice location [6]. Finally, it is important to use tests that have been appropriately validated for use on veterinary relevant samples.

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Diagnostic Testing: What do those Results Really Mean?

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Diagnostic testing is an integral part of the practice of veterinary medicine – but are all test results equal? Let's consider what constitutes a clinical test. A clinical test can be anything that predicts health status better than chance. When applied to apparently healthy individuals for the purpose of early disease detection it is considered a screening test. When applied to individuals for the purpose of confirming or ruling-out a specific diagnosis it is considered a diagnostic test.

No test is perfect – so what we can do is characterize the “correctness” of a test through reference based evaluation (i.e., compare to a gold standard) or through non-reference based evaluation (i.e., latent class Bayesian analysis). Traditional reference based evaluations typically compare test results from two tests on two groups, one that is clearly diseased and one that is clearly non-diseased. While this does provide some insight into test performance, as from this test sensitivity and specificity can be estimated, these are not typically the patients to which tests are applied. Rather we use tests to help us determine the most likely differential for patients that fall somewhere in the middle – neither clearly diseased nor clearly non-diseased. Alternatively, tests can be characterized using non-reference based latent class analysis (i.e., no gold standard) to determine a more accurate (i.e., unbiased) estimate of test sensitivity and specificity.

Test sensitivity and specificity are generally considered to be constant and are evaluated before the test is applied. However, in practice what we really want to know is how to interpret test results after it is applied. This is the predictive value of a test – given a test result the probability of true disease status. The key here is that predictive values change – they are closely related to prevalence and cannot be applied beyond the population in which they were established. Thus it is important for practitioners to be aware of common diseases in their given practice region.

What if there is no single “best” diagnostic test? In this instance we can employ a multiple tests (i.e., 2 or more tests) and interpret them in series or in parallel. When testing in series, a patient must prove that it is truly diseased as any negative test is interpreted as the patient being negative. This will improve the overall specificity of the testing strategy and the positive predictive value. When testing in parallel the patient must prove that it is truly healthy as any positive test is interpreted as the patient being positive. This, then, will improve the overall sensitivity of the testing strategy and the negative predictive value. Choosing a test to apply depends upon the reason(s) for testing the patient and its perceived value. In general, using a highly sensitive test will identify all infected or diseased individuals, will help rule-out a particular condition, and will increase confidence in a negative result (e.g., early in the diagnostic process). Alternatively, using a highly specific test will help rule-in a particular condition and will increase confidence in a positive result (e.g., when you want to confirm a disease).

While diagnostic testing is a key component in patient management – not all tests are equal. Practitioners must be aware of test sensitivity and specificity, the expected prevalence of a condition in a given practice region, understand how prevalence can impact predictive values, and recognize that the value of diagnostic tests is highly variable among different diseases.

The Dos and Don'ts of Outbreak Management

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Disease epidemics can progress slowly, affecting only a few animals, or they can progress very rapidly affecting many animals in a wide geographic region, as was seen in the equine herpesvirus-1 (EHV-1) outbreak in 2011 in the western U.S. and Canada. As the first line of defense, veterinary practitioners must be prepared to recognize epidemics of disease and have a plan in place to logically and systematically collect data and effectively manage the outbreak.

There are five basic components of managing and investigating an outbreak: define the problem, treat those affected, prevent disease transmission, determine a cause, and try to prevent its reoccurrence [1]. The first step in defining the problem is to determine if in fact there is an epidemic of disease, i.e. an outbreak. By definition, an epidemic occurs when the proportion of those at risk of developing disease is greater than what is expected normally. An owner may call for veterinary assistance, once an epidemic has already been identified, to determine its source. As the investigator, the tentative diagnoses should be confirmed and a case definition must be developed. A case definition is crucial to any investigation, allowing for a more focused effort and the collection of appropriate data. The case definition must include those animals with the primary disease being investigated, but exclude all other healthy animals as well as those affected by other conditions. In defining a case and investigating an outbreak, consider the 5 W's: who, what, where, when and why. By collecting this data the investigator can not only determine the scope of the problem, but can begin to describe the temporal and spatial pattern of disease. During the investigation, it is prudent to calculate an attack rate, comparing it to the attack rate in a similar population, to determine if an outbreak is actually occurring. Once all data is collected and collated, the investigator can begin to analyze the data simply by looking at attack rates between exposed and non-exposed animals, hopefully identifying the likely source of the outbreak. A final written report of the investigation findings should be provided, including measures to prevent a future occurrence.

Managing a disease outbreak can be a very strenuous, stressful experience. It is important for practitioners to be prepared should they be called upon to assist with such an event. Treatment of affected animals should be initiated as soon as possible, symptomatically until a working diagnosis can be established. Generic control measures should be put in place, such as movement restriction and personal protective equipment, in an effort at containment. Practitioners should have a biosecurity toolkit containing personal protective equipment in their practice vehicle for an emergent situation. It is imperative to break the cycle of transmission. Keep in mind that infectious disease transmission can occur via multiple avenues including direct contact, indirect contact, and vectors. An effort should be made to identify the agent, allowing for agent specific treatment and control measures to be implemented. Communication is an important component of outbreak management, not only to the client but to veterinary authorities if warranted.

As the first line of defense, practitioners must be prepared for the event of an outbreak, developing his/her infection control toolbox prior to calling it into use. Have a plan in place to systematically compile background information (the 5 W's) and determine if an epidemic is actually occurring. Take care of not only individual patients, but also of the population (movement control, contact control, hygiene). Seek expert advice from colleagues and veterinary authorities, and provide excellent communication throughout the duration of the outbreak.

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Creating an Infection Control Culture in Veterinary Practice

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Veterinary hospitals, by their very nature, create a high risk environment for the transmission of infectious agents – bringing together animals from many different farms with varying levels of compromise. Outbreaks of healthcare-associated infections commonly occur in veterinary hospitals with 82% of American Veterinary Medical Association (AVMA) accredited veterinary teaching hospitals (VTHs) reporting such events within the previous 5 years [1]. In addition, 50% reported the occurrence of zoonotic infections during the previous 2 years [1]. In order to practice high-quality patient care, infection control should be integrated into the patient management plan to protect the people, the patients, and the hospital.

While veterinarians are in a profession recognized to increase the lifetime risk for contracting a zoonotic infection, there is a general disregard for utilizing those practices known to be effective prevention measures. Among AVMA member veterinarians, only 55.2% of small animal practitioners and 28.1% of large animal and equine practitioners reported always washing their hands prior to eating, drinking, or smoking at work; and only 48.4% of small animal practitioners and 18.2% of large animal and equine practitioners reported always washing their hands between patient contacts [2]. Despite veterinarians expressing concern about risks associated with gastrointestinal parasites and gastrointestinal bacteria, 71.2% and 70.9%, respectively, of small animal practitioners, and 35.7% and 39.8%, respectively, of large animal practitioners, reported not using appropriate personal protective equipment (PPE) when evaluating an animal with gastrointestinal signs [2].

Clearly, the biggest challenge in veterinary infection control is simply to do it. Why don't practitioners use best practices with respect to infection control in the practice of veterinary medicine? While there is a paucity of information in the literature specific to veterinarians, we can glean something from evaluations of this issue in human medicine. Consider the barriers which may affect effective implementation of practice guidelines – such as knowledge, attitudes, and behavior. In a systematic literature review, there were multiple factors contributing to each of these barriers including intrinsic factors such as a general lack of familiarity or of awareness with published practice guidelines, a lack of agreement with specific guidelines or with guidelines in general, a belief in a lack of expected outcome, a lack of self-efficacy, and the habit or routine of previous practices; and extrinsic factors such as guideline characteristics, patient influences, and environmental factors (e.g., time and available resources) [3].

While some of these barriers may be relatively simple to overcome (i.e., time and available resources), what it really comes down to is social cognitive behavior – specifically knowledge, motivation, intention, perception of a threat, outcome expectancy, perceived behavioral control, and social pressure – and understanding what motivates a particular behavior [4]. Case in point – Ignaz Semmelweis, (1818-1865), the father of hand hygiene, deduced in 1846 that patients were dying due to “pathogenic causes” associated with deficient hand hygiene practices by physicians [5]. While the prevention strategy he implemented was epidemiologically sound, it was not well received by colleagues and in fact he was relieved of his hospital duties [4]. So why the failure? Not only did this event occur before the germ theory even existed, but his observations were also not reported in a timely fashion, thus there was a general lack of knowledge leading to disbelief by his colleagues. Rather than educating his colleagues on the threat and expected outcome, he chose a more autocratic approach to intervention implementation. Had he approached this in a different manner – taking into account social behavior theory – results may have differed.

An infection control culture is part-in-parcel with creating a workplace safety culture through the integration of behavior based safety programs and the organization's safety culture [6]. Behavior-based safety programs use a bottom-up approach that rely on continuous processes which are data-driven and setting-specific. These programs define critical behaviors, set performance goals, monitor performance, provide feedback, and strive to reinforce the desired behavior. Organization safety culture uses a top-down approach that is a more subjective, self-sustaining process that typically uses surveys to identify and assess personnel assumptions and beliefs. Findings are then used to stimulate organizational change through participation of personnel including leadership. A strong safety culture should have 3 components; 1) norms and rules which explicitly define risks and provide guidelines; 2) individual and group attitudes that place safety as highly important and that motivates personnel to act in this regard; and 3) use reflexivity to continuously understand risk and its mitigation [7].

In practice, fostering an infection control culture can be very difficult – everything we ask personnel to do is inconvenient. It takes time to wash your hands before and after every patient contact, it takes time to don and doff PPE. So how do veterinary practices develop a strong safety culture of infection control and worker safety when it comes down to influencing behaviors and attitudes? The Ecological Model of Behavioral Change suggests that behavior is both affected by and affects several levels of influence including intra-personal factors (e.g., knowledge, attitudes, beliefs), inter-personal factors (e.g., social identity, support network, peer group pressure), community factors (e.g., social networks and norms), and institutional factors (e.g., administrative support) [4]. When applying this to organizational culture – consider that this is a multidimensional concept with core assumptions being at its deepest level, followed by beliefs and values, and finally norms at its most superficial level [7]. As such, it will take a multifaceted approach

to implement change. For example, if a facility wants to embark on a hand hygiene campaign it must first gain personnel involvement and ownership of the issue with a commitment to a solution. Individuals within the organization may champion the cause, providing verbal instruction and training on proper procedures based on the best evidence currently available, in addition to demonstrating best-practices in their daily practice. Management must be committed to the cause, providing resources such as hand hygiene stations and financial support for the effort. In addition, the facility may choose to endorse the program through the development of slogans and posters to promote effective hand hygiene practices. In this way the “culture” of the facility can gradually change to one where the expected norm is one of excellent hand hygiene practices where personnel ensure effective implementation through social influences, alteration of individual beliefs and intentions, and ultimately, permanent changes in behavior.

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The Most Sensitive Method of Detecting and Evaluating Forelimb Lameness in Horses

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Lameness in horses is most effectively understood by studying vertical motion of the torso. Vertical motion of the torso follows and therefore mimics the reduced ground reaction forces that occur (and are understood on physical first principles) with lameness. Forelimb movement, especially during the swing phase of the stride, is highly dependent on “other” factors besides lameness, most notably anatomical conformation. Timing of lameness, in other words whether maximum pain occurs during impact (first ½ of stance) or pushoff (second ½ of stance), may also affect limb movement. As an example consider amplitude of forelimb protraction. Decreased forelimb protraction is frequently proposed as a sensitive general indicator of forelimb lameness. Horses with navicular disease frequently display this restricted motion to avoid normal heel-first landing. Yet, horses with laminitis, or pain primarily in the dorsal region of the foot, display the opposite, or increased protraction. The dependence of forelimb movement pattern on timing of lameness indicates that this parameter is not present in all forelimb lameness, so there is a potential for “false negatives” and “false positives” when using forelimb movement to detect and evaluate forelimb lameness in horses. Also, determination of an absolute decreased or increased amplitude of movement, whether it be in the limbs or torso, requires high spatial resolution, which degrades with distance from source. Very small decreases in “normal” movement cannot be reliably detected by the naked human eye. Research has shown that the most reliable indicator of lameness is to detect asymmetric pattern of movement. Asymmetric movement of the torso is the reliable indicator of lameness in quadrupeds.

The concept of using vertical motion of the torso as the primary indicator of lameness in quadrupeds is relatively straight forward to understand. To reduce force on a painful forelimb during weight bearing (since force = mass x acceleration), the animal causes the torso to fall less than normal. The mechanism most available to the horse is to use the head. It is a large counterweight on a first class lever arm. Another way to conceptualize the relationship of head to “rest of body” movement is a 2-component free body system (see below). The head will always be moved upward (by the neck muscles) to reduce peak vertical ground reaction force (against the mass of the body) applied through the affected forelimb.

Figure 1: Two-component model of vertical head and “rest of body” movement in the trotting horse

The classic “head nod” depicts that in a lame horse the whole front of the torso (including the head) moves down when the good (not lame) limb is on the ground, and then up when the lame limb is weight bearing. This is an extreme simplification that is really only true in horses with severe lameness. But, in horses that are trotting, the head must follow the center of mass of the body, which moves down when the horse is landing on a limb and then up when the horse pushes off that limb. This downward and then upward movement repeats itself when the opposite limb lands and then pushes off. So, a horse moves its head down and then up twice in one complete stride, whether it is lame or not. The head does not just move up during the stance phase of the lame limb and down during the stance phase of the sound limb. So where does this maxim “down on sound” come from?

Examining the different shapes of the trajectories of vertical head movement as forelimb lameness increased reveals the origin and context of this maxim. With very mild lameness the asymmetry of the normal down and then up movement (twice per stride) is small, so maybe there is just a little less downward motion of head (upper left figure 1) during lame limb stance. As the lameness is increased, this asymmetry is increased, the overall shape of the vertical head movement trajectory (upper right and lower left figure 1), which is down and then up, is retained. Eventually, as the amplitude of lameness is increased, this asymmetry in downward and then upward movement of the head increases to a point where movement of the head due to lameness overtakes, or swamps, this normal overall pattern following the downward and then upward movement of the center of mass of the body. This is a simple wave summation phenomenon. At this last stage (lower right figure 1) the horse is very lame and it is only now that the predominant pattern of head movement truly is upward only during the stance phase of the lame limb and downward only during the stance phase of the sound limb. Thus, this maxim, “down on sound”, is only true for detecting lameness in horses with severe lameness. So, in the practical sense, it is not useful.

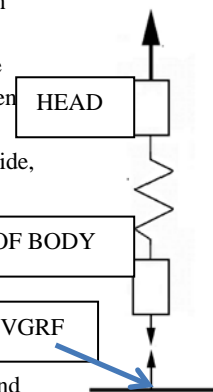
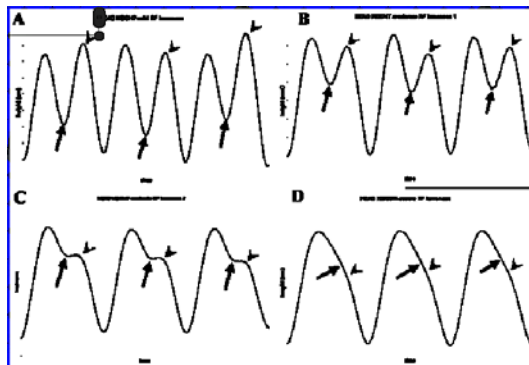


Figure 2: Vertical head trajectory with gradually increasing (A-D) forelimb lameness

But, what then should one look at to detect forelimb lameness? Should then one look at total excursion of the head, or its total distance of movement from a high to a low position, or should one look at the end position relative to the ground after this movement? The maxim, “down on sound”, would also suggest that you should look at excursion, but this is incorrect. However, experimental evidence and physical first principles suggests the later will always be true. One should look at position. The maxim should more

specifically state “low on sound”, not down on sound. In most forelimb lameness the head reaches its lowest position when the sound limb is on the ground.

Examining this a little more closely, and hinted at earlier, shows quite simply that there are two, you could say competing, reasons that a horse moves its head down and then up during a trotting stride. The first is simply the head following the center of mass of the body as it moves down and then up during a stride at the trot. The second, which is only present with lameness, and which occurs at half the frequency (if the lameness be unilateral), is the head moving away, that is upward, from the affected limb with maximum amplitude or intensity at the time of peak pain during the stride (impact, midstance, pushoff). The head also moves backward for the same reason but this is not important to understand the phenomenon. Movement of the head upward will always reduce force on the forelimbs.



Experimental evidence has shown that the pattern seen most commonly in horses trotting at relatively slow speed, without a rider and moving in a straight line, displays an asymmetry in both high and low positions of the head. Let us first consider a lameness in the first part of stance, which is the decelerating phase of stance (the torso is moving down and decelerating). The horse moves its head up more than normal during pushoff of the good limb so that its head is at a maximum height at the beginning of lame limb stance. In more severe lameness the head may actually be still accelerating upward (though the torso is decelerating downward) as the lame limb hits the ground. This effectively reduced load on the limb during the first part of stance. The head then falls during the lame limb stance but less than it normally would have fallen if the limb was not painful. The total distance of this fall, because the fall started from such a high position, may actually be larger than that that occurs during the stance phase of the non-lame limb. But the fall is aborted (damped may be a better word) so that its lowest position (which occurs about midstance) is higher than the low position at midstance of the non-lame limb. So, “low on sound” picks the correct limb, but “down on sound” does not. As the lameness (or time index of the amplitude of peak pain) shifts from early stance, through midstance, into late in stance (end of stance), the head continues to fall less than it normally would have fallen, but the pattern of upward movement of the head begins to change. With lameness in the second half of stance (the impulsion or acceleration phase) the head begins to move up more than it normally would have. Thus, in addition to “low on sound” the horse displays an “up on bad”, or “high on bad” vertical head movement pattern. Notice, that this is just the opposite for a lameness that occurs during the first half of stance, during which the horse will move its head up more pushing off the good limb.

Based on all these studies, this is what I now teach students about how to detect and evaluate forelimb lameness. First, avoid getting sidetracked by concentrating on the limbs, second, start always with “low on sound” not “down on sound”. If you cannot tell for certain using this method then either revert to “up on bad” or “high on bad”, and not the other way around. Do not start with “up on bad” first, or you may miss horses with strong impact type lameness.

Core information in support of these proceedings can be found in the following manuscripts and text chapters

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The Most Sensitive Method of Detecting and Evaluating Hind Limb Lameness in Horses

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Lameness is a clinical sign. Detecting lameness and evaluating its amplitude is important to equine veterinary practice. Because it is important we should understand it well. Detecting and evaluating hind limb lameness, compared to forelimb lameness, seems to be especially difficult. To explain the mechanics of hind limb lameness detection and evaluation with nebulous, unmeasurable, and clearly subjective terms like “behind the bit”, “hind limb engagement”, or “hind limb impulsion” demeans the scientific reputation of our profession. We must, instead, use objective evidence to define clearly-understandable parameters that are sensitive and accurate for detection of lameness.

First and foremost is to understand that lameness in horses is most efficiently measured by tracking and evaluating vertical motion of the torso. Vertical motion of the torso follows and therefore mimics the reduced ground reaction forces that occur (and are understood on physical first principles) with lameness. Limb movement, especially during the swing phase of the stride, and pelvic rotations, are highly dependent on “other” factors besides lameness, most notably physical anatomy and conformation. There is a potential for many “false negatives” and “false positives” when using limb movement and pelvic rotation to detect and evaluate lameness in horses.

The concept of using vertical motion of the torso as the primary indicator of lameness in quadrupeds is relatively straight forward to understand. It is logical. To reduce force on a painful limb during weight bearing the torso will fall less, more specifically it will fall with less downward acceleration, since $force = mass \times acceleration$. The torso will also rise less, with less upward acceleration during the second half of the stance phase of the stride. If the horse were an inanimate bouncing ball (and I realize that it is not) the sound horse would simply bounce up and down more than the lame horse. In fact, simply explained, this is indeed what happens. On closer inspection, however, by evaluating both the upward and downward movement the entire pelvis, more information about the lameness, besides which hind limb is involved and the amplitude of lameness, can be acquired. The trajectory of vertical pelvic movement also contains information relating to the timing of lameness within the stride cycle.

There are many descriptions of what motion parameters are good for picking up hind limb lameness in horses in textbooks, but I personally have found them either to be too difficult to understand and remember or misleading. As with the forelimb there are many movement parameters that are purported to indicate hind limb lameness, including joint flexions, how the limb swings forward, and especially pelvic rotational movement (which encompasses the phenomenon of “hip hike” and “hip dip”).

However, similarly to looking at vertical head movement to detect forelimb lameness, all the information that is needed to detect hind limb lameness can be found in the pattern of vertical movement of the entire pelvis. Other methods including limb movement and, more importantly, pelvic rotation are less sensitive and, in certain circumstances, may give false positive (looks lame but is not) or false negative (does not look lame but is) evaluations.

The two methods that are most used by practicing equine veterinarians are the pelvic rotation method, which is sometimes explained as “hip hike” and sometimes as “hip dip”, depending on what you are looking at, and the vertical pelvic movement method. Experimental evidence and clinical experience suggests that vertical movement of the entire pelvis is less prone to error than the pelvic rotation method. Comparing these two methods of evaluating pelvic movement to detect hind limb lameness in horses is instructive.

Let us first outline each method. First the vertical pelvic movement method observes the vertical movement of the pelvis as if it were one big ball. Disregarding pelvic rotation the observer looks at the vertical movement of the pelvis over time. Instead of seeing the entire pelvis as a large ball, which is difficult, the observer could, alternatively, observe a spot on the dorsal midline of the pelvis. With this method the observer observes for both less downward movement coming down onto the lame limb and less upward movement coming off the lame limb. This can be easily explained as either less impact (less downward movement of the pelvis) on the lame limb or decreased propulsion from the lame limb. So the pelvis “ball” either reaches a higher minimum during weight bearing or a lower maximum during swinging of the limb forward. The higher minimum occurs during stance and the lower maximum occurs right after stance of the lame hind limb.

The second method, the pelvic rotation method (“hip hikes” and “hip dips”), is easier to see since the total excursion of movement is greater, but conceptually it is more difficult to explain. With this method the observer actually evaluates amplitude of vertical movement of the tuber coxae (not really the “hip”) on the left side and compares it to that of the right tuber coxae, with the lame side either moving up more (a “hip hike”) or down more (a “hip dip”) than the sound side. The first fact to note when observing vertical tuber coxae movement is that, even in the sound horse, the trajectory is asymmetric. You cannot simply look at the pattern of tuber coxae movement in isolation (as you would evaluate head movement for forelimb lameness or vertical pelvic movement for the first method of detecting hind limb lameness) and determine lameness, you must compare amplitude from side to side. The second fact to

note is the timing of pelvic rotations. The pelvis is even, i.e. not rotated, with approximately equal height of each tuber coxae relative to the ground, right before impact of one hind limb (which is the same time as right after pushoff of the other hind limb). Essentially the pelvis is not rotated when the horse is airborne with no hind limbs touching the ground. The begins to rotate during weight bearing with maximum pelvic rotation occurring at about midstance of each hind limb and the rotation is toward the weight bearing hind limb. Thus, viewed from behind the horse, the pelvis is rotated clockwise when the right hind limb is on the ground, and counterclockwise when the left hind limb is on the ground. Also, highest vertical positions of the tubera coxae occur during the airborne phase of the hind limb stride and lowest positions occur during the weight bearing phase of the hind limb stride. “Hip hike” and “hip dip”, despite what some have suggested, are not the same events, since they do not occur at the same time within the stride cycle. “Hip hike” occurs right before impact of the lame hind limb and “hip dip” occurs right after pushoff of the lame hind limb. Why is this?

The horse uses its ability to rotate the pelvis with hind limb lameness similarly as it uses it head in forelimb lameness when landing on painful forelimb. Right before impact of the lame hind limb the horse will rotate its pelvis away from the painful limb that is about to impact the ground. Thus the tuber coxae is rising as the pelvis is falling. This is “hip hike”. If the pain of lameness is greater during propulsion (pushoff) the horse will simply not push off the affected hind limb with as much force as normal. The pelvis will subsequently rise (and move forward) less. It will be closer to the ground after pushoff of the lame limb. In order for the horse to bring the affected limb forward during the subsequent swing phase of the stride without dragging it on the ground (remember the pelvis is closer to the ground than it should be), and in fact sometimes it still does, the horse will have to flex the entire limb more than usual. This limb flexing rotates the pelvis towards the lame side and the tuber coxae moves down more than normal. This is “hip dip”.

However, which method is better, the vertical pelvic method or the rotation method? Experimental evidence suggests that, although more difficult, the vertical pelvic movement method is better. It is better because it is more sensitive, plagued less with false positives, and more robust. The vertical pelvic movement method mimics, actually is the direct result of, hind limb ground reaction forces. By contrast, the pelvic rotation method is more dependent upon anatomy and conformation, both of which may be asymmetric despite the horse landing and pushing off left and right hind limbs equally. Lastly, the vertical pelvic movement method is robust because it can be observed from any vantage point. The pelvic rotation method is difficult to use when viewing perpendicular to the horse’s direction of motion. You really must be behind the horse to adequately assess left to right asymmetry, and unless you are going to run behind the horse (or view the horse on a treadmill, which has its own difficulties), spatial resolution decreases quickly as the horse moves away.

Core information in support of these proceedings can be found in the following manuscripts and text chapters

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How to Use Lunging and Flexion Tests to Assist, but not Deduct from your Lameness Evaluation

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Veterinarians evaluate the horse at the lunge and perform flexion tests during lameness and pre-purchase evaluations. Lunging and flexion tests are thought to expose or exacerbate lameness that may not be seen with the horse trotting in a straight line. Many veterinarians also believe that lunging and flexion tests help localize lameness within the limb. Horses with bilateral lameness may not appear lame when trotting in a straight line, but the lameness becomes visible, sometimes on the outer limb, but more frequently on the inner limb, when the horses in lunged. There is a valid biomechanical explanation for this. Moving in a circular path alters type and amplitude of limb forces. Lunging is also (if the horse lunges easily and well) an efficient method to evaluate a horse for lameness when you are alone, or if you do not have someone physically capable of trotting a horse on a lead shank.

However, lunging a horse or performing flexion tests is not always safe or helpful. These activities have potential to distract the veterinarian, causing him/her to proceed incorrectly, unnecessarily prolonging the lameness evaluation.

Lunging

When a horse is lunging, additional centripetal force is active, “pulling” the horse to the center of the lunging circle. This force is caused by the horse changing direction. Changing direction generates transverse ground reaction forces and shear stresses, especially within the distal limb. Also, the torso of a horse trotting in a small circle is tilted, relative to the ground, towards the center of the circle. This tilt can be up to 18° for a 10 m diameter circle. Larger horses, smaller circles, and faster trotting speeds may increase this tilt. Surface characteristics, like evenness (more precisely unevenness) or hardness, also affect the amplitude of tilt. Because the torso is tilted, inside and outside limbs experience different compressive load patterns, with the abaxial half of the inside limb and the axial half of the outside limb experiencing greater compressive load, and the axial half of the inside limb and the abaxial half of the outside limb experiencing greater tensile forces. Thus, pain from lameness conditions with some lateralization of pathology within the limb can be worse with the horse moving in a circle. Examples include conditions such as collateral ligament desmitis, or carpal arthritis, since carpal arthritis is commonly localized on the axial half of the joint. Horses with carpal arthritis can be expected to be worse during the lunge when the most affected limb is on the outside of the circle.

Because the horse is tilted when lunging, movement of the torso and limbs, even in the sound horse, will not be the same in each half cycle (left and right) of the stride. Height of torso from the ground is shorter for the inside limb, so the inside limb must flex more during the swing phase of the stride. Greater flexion of the inside hind limb as it swings forward rotates the pelvis toward the inside of the circle. Comparatively, the outside hind limb flexes less when swinging forward and the pelvis rotates less to the outside. Hypothetically, these asymmetries, if seen when the horse was trotting in a straight line, would appear to be like movement in a lame horse. This exposes two weaknesses in the logic of evaluating horses for lameness at the lunge. First, the “thresholds” for asymmetric movement between right and left sides of the body that indicate lameness are necessarily larger for the lunge than for straight line trot. Second, it will be more difficult (if not impossible) to detect lameness at a “snapshot” in time when the horse is lunging in the first direction. You must at least evaluate the horse lunging in the other direction before the decision for the existence of lameness is declared.

The asymmetric patterns of vertical torso movement when horses are lunging have been studied extensively through experiment using objective measures of movement, especially using body-mounted inertial sensors. From these studies it is clear that the asymmetric patterns in normal horses (and therefore not indicative of lameness) depend much on ground surface hardness. Horses lunging on hard ground will frequently display more downward movement of the head and pelvis when the outside forelimb and hind limb are weight bearing. Also, the tuber coxae will move up more during the swing phase of the inner hind limb compared to the outer hind limb, giving the movement the appearance of a “hip hike” on the inner hind limb. Therefore, on hard surface even normal horses sometimes may appear to be lame on the inner forelimb and hind limb.

By contrast, on soft ground a horse will frequently raise the head up more when the outside forelimb is in the second half of stance. It will then fall a large vertical distance during the subsequent first half of opposite (inner) forelimb stance. The horse uses this upward vertical head movement to assist in the directional change (toward the left lunging left and to the right when lunging right), and the ability to accomplish this is slightly reduced with the outside limb sinking into the soft surface. In a 2-component model of head and “rest-of-body” movement in a lame horse, this normal movement would appear to be an outside forelimb pushoff type lameness, which is exactly the opposite effect as seen on hard surface. In the hind limbs the effect of soft surface on vertical pelvic movement is also different than on hard ground. The horse does not have a heavy counter-weight on a long lever arm attached to the hind part of the torso (like the head in the front of the torso), a counter-weight with which to use to assist in changing direction. Changing direction is therefore primarily accomplished by changes in the forces of hind limb impact and pushoff. On soft ground,

when the outside hind limb pushes off at the end of stance, the foot sinks into the soft surface. As a result the pelvis rises less relative to the ground, which is equivalent to an apparent outside hind limb lack of impulsion or pushoff type lameness. However, the pelvis still falls less on soft ground when the inside hind limb is in stance, giving the appearance (as on hard ground) of an inner hind limb impact type lameness.

Summary

On hard ground many normal horses appear to have inner forelimb impact type lameness and inner hind limb impact (hip hike) and pushoff (hip dip) type lameness. On soft ground many normal horses appear to have outer forelimb and hind limb (hip dip) pushoff type lameness and inner hind limb impact (hip hike) type lameness. The asymmetries should be taken into consideration when evaluating horses for lameness at the lunge.

Based on biomechanical considerations, it is more likely that many forelimb lameness conditions will be worsened more significantly than hind limb lameness during the lunge, and that many hind limb lameness conditions will be somewhat masked during the lunge. In a horse that is trotting in a straight line at moderate speed (4 m/s) the forelimbs act primarily as struts, braking the forward movement of the torso, but with very little propulsion imparted to the torso. The hind limbs also brake, but most of the work of propulsion to advance the torso forward is supplied by the hind limbs. The needed propulsive force to move the horse forward in a straight line is greater than that needed during the lunge, since at the lunge the horse is primarily changing direction. So, the braking effect of both the forelimbs and hind limbs is biomechanically more important during the lunge, but the need for propulsion, which is supplied by the hind limbs, is less important during the lunge. Experimental findings with natural and induced lameness seem to support this.

It is uncommon for horses to show lameness in only one limb during the straight line trot, but then to show lameness in only one limb opposite to that seen in the straight line trot. It is, however, common for horses to show multiple limb lameness, either compensatory (or false) lameness and secondary lameness, during the lunge. Thus, lunging the horse can complicate the clinical appearance of lameness in the horse. Agreement between veterinarians for detection of lameness when allowed both evaluation of straight line trot and lunging is less than between veterinarians when allowed only evaluation with the horse trotting in a straight line. Additional complexity and confusion can arise when horses are evaluated for lameness trotting straight on one surface and then while lunged on a different surface. Because of these complicating factors I do not recommend evaluating horses for lameness at the lunge, unless the lameness cannot be definitively detected in the straight line trot, or unless there is no other way (you are by yourself). If the lunge is needed it is important to use the same, or similar surface, as that used in the straight line trot evaluation, and to have a patient who is practiced and lunged regularly. Mixing surfaces, activities (lunge, straight), size of lunging circles, besides being time consuming, rapidly complicates the lameness evaluation and increases the likelihood of confusing compensatory or secondary lameness for the primary problem. Lunging should be considered an extra step, an advanced examination, to be employed only if needed.

Flexion tests

The use of flexion tests by veterinarians in both lameness and pre-purchase evaluations is traditional and common. Attempts at logical explanation of the apparent increase in lameness following flexion range from flexion-induced stress on soft tissue structures to an increase in intra-articular pressure. However, there is little objective evidence of the effectiveness of these tests to 1) help isolate the focus of lameness within a limb, or 2) to bring out lameness as a clinical sign indicative of existing but subtle orthopedic dysfunction. Evaluation of response to flexion tests varies greatly depending on the individual evaluator (some are more prone to indicate positive response), the “strength” of the flexion (amount of pressure applied to the flexion of the joint), time of flexion, and horse. Many horses with no history of lameness that display positive response to flexion do not develop lameness later on. There is no association between response to flexion and pathology. Objective measurements seem to indicate that a positive response to proximal hind limb flexion is limited to decreased pushoff of the hind limb, regardless of whether the horse has a primary impact or pushoff type hind limb lameness before flexion. Responses to flexion tests frequently complicate the lameness picture and make it difficult to unequivocally evaluate nerve and joint blocks. What does it mean if a horse seems improved after a block when trotting in a straight without flexion, but then appears worse after flexion, and *vice versa*, a horse that does not appear better but has less lameness after flexion?

Conclusion

Flexion tests are useful for some lameness evaluations but with some caveats. Care should be given to overzealous interpretation of response to flexion tests during pre-purchase evaluations. There is little objective evidence to support the use of flexion test to localize lameness within a limb. Flexion tests are most useful to “bring out” lameness that is not visible. When performing flexion tests use short time durations and do not flex too “firmly”.

Core information in support of these proceedings:

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Evaluation of Lameness under Saddle: Effect of the Rider

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Evaluation of horse under saddle is performed routinely by some veterinarians and almost not at all by others. Some of the former strongly feel that a lameness evaluation is not complete without evaluation of the horse under saddle. The true lameness may be missed. In opposition, the latter may feel that it is either simply not necessary, a waste of time, or, worse, because of potential the influence of the rider, a distraction, leading the veterinarian on a wild-goose chase, hunting down asymmetric motion thought to be lameness but really only an effect of the rider. Which is more often correct?

Regretfully, there is only scant objective evidence in support of either opinion, but the early consensus supports the view that the rider can strongly influence the appearance of lameness, both in a positive and negative way. With this in mind, let us attempt to “keep a score” on the question of whether “a horse should be routinely ridden during lameness evaluations”, which we will designate as answer A, and “a horse should not be routinely ridden during lameness evaluations”, designated answer B. As preface, let us assume that the lameness evaluation begins with evaluation not under saddle. Notwithstanding possible unique situations, this is generally true.

- I. A good rider can adjust their position and balance skillfully (better than unskilled riders) to be in concert with the movement of the horse. So, a lameness that is seen without a rider may be covered up under saddle. If the horse was truly lame, an incorrect assumption could be made that the horse just needs another rider, which would be unfortunate for the horse. A = 0, B = 1.
- II. A bad (i.e. unskilled rider) rider increases the variability of the horse’s normal movement. So, consistent asymmetric movement due to lameness will be harder to separate from asymmetric movement due to rider variability. This is a noise problem. Separating the true signal quality (lameness) from the noise (rider induced variability) is more difficult. A = 0, B = 2.
- III. Specific rider activity, e.g. sit trot, posting, 2- or 3-point stances, will influence the symmetric movement of the horse’s head and torso, a sign of possible forelimb and hind limb lameness, respectively. Asymmetric movement of the rider can then either exacerbate a true lameness (a vote for A), create an apparent but false lameness (a vote for B), or mask (a vote for B) the true asymmetric movement of the horse due to lameness. A = 1, B = 4.
- IV. Adding weight increases forces on the limbs and can shift (depending on rider position) majority force to either front or hind limbs. If it is true, that an increased force on a lame limb will render it more visible, a logical first principle, then a true lameness will be amplified. This is a vote for A = 2, B = 4.
- V. Horses under saddle are more excited. Increased excitement (more adrenaline) covers up small discomforts. Mild lameness becomes invisible. This is not fact, just my opinion. So, no vote is given here. It is still A = 2, B = 4.

It seems the votes go for B. It does not support the routine requirement of evaluating the horse for lameness under saddle.

Most of the studies concerning this question were based on data collections from small numbers of normal horses and/or under rather controlled conditions. Larger studies specifically measuring effect on natural lameness are lacking. I am now going to briefly present, in broad strokes to protect intended future publication, an analysis of results of an in-depth study on a large number of horses (sound and with natural forelimb and hind limb lameness), the effects of a rider on the appearance of lameness. Appearance of lameness was objectively measured with inertial sensors attached to the horse’s head and pelvis, and rider activity was objectively measured with inertial sensors attached to the horse.

Horses were evaluated for forelimb and hind limb lameness under the following conditions and activities. First evaluations, to serve as baselines, were with the horse trotting in a straight line, saddled and bridled but without a rider. Subsequently, horses were evaluated for lameness under saddle with the rider, riding in circle of two different sized (small and large), first with the rider sitting the trot then posting on the correct limb (on the right forelimb riding to the left and on the left forelimb riding to the right). Lameness in the forelimb was measured with amplitude of asymmetric vertical head movement taking into consideration both the upward and downward movement.

Results

With the rider sitting the trot the majority of horses showed lameness in the same limb that was indicated when trotting without a rider in a straight line. Horses in which a different limb was found to be lame during the sit trot had a very mild lameness when evaluated trotting in a straight line without a rider. Most switching of apparent lameness was to the opposite half of the body and not to the contralateral limb in the same half of the body. The only movement parameter that was definitely changed during the sit trot was downward movement of the pelvis, which was less during the stance phase of the hind limb towards the inside of the circle in which

the horse was being ridden. This affect was amplified with smaller circles. This could be interpreted as the potential for the appearance of a false, inner hind limb, impact-type hind limb lameness. This finding, however, is identical to the potential effect of a horse simply trotting in a circle without a rider.

When the rider was posting several movement adjustments by the horse could be interpreted as lameness, but the most definitive and predictable was upward movement of the pelvis as the riding was falling into the saddle. The rider falling into the saddle during posting reduced the upward movement of the pelvis. Thus, posting on the right forelimb (moving in a left circle) caused the horse to move with an apparent, but false, left hind limb pushoff-type lameness (less left hind limb propulsion), and posting on the left forelimb (moving in a right circle) caused the horse to move with an apparent, but false, right hind limb pushoff-type lameness. Natural right hind limb lameness during the right forelimb post was masked, and *vice versa*, natural left hind limb lameness during the right forelimb post was exacerbated. There was a real and predictable capability of the posting of the rider to falsely affect the appearance of lameness.

The reader is left to make his/her own decision about the utility and necessity of evaluating lame horses under saddle. Objective evidence indicates that only in cases in which the lameness without a rider is equivocal will evaluation under saddle not distract from the analysis. I do not evaluate horses for lameness under saddle except; 1) when no consistent lameness is visible or measurable with the horse trotting in a straight line, lunging, or after flexion tests, 2) when the history indicates that the lameness is only detectable under saddle, and 3) when the owner insists.

Note: I do not know what happens to the horse when the rider adopts the 2- or 3-point stance. My guess is that it is similar to the sit trot, but possibly with less intense effect on the horse.

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Drink Up! Fluid Therapy Considerations for Exotic Pets

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The majority of the exotic pet cases presented to veterinarians are dehydrated as a result of a chronic disease. Animals primarily lose moisture through the gastrointestinal and respiratory tracts, although the integument and eye (non-spectacle) are also sites where moisture is lost. Diseases associated with the gastrointestinal tract (e.g., diarrhea) or traumatic injuries to the integument (e.g., thermal burns) can increase the amount of moisture lost in our patients.

Characterizing the extent of dehydration and providing appropriate fluid replacement is necessary to successfully rehabilitate the patient. An understanding of the “water” make-up of these patients should be considered before selecting a fluid. For example, reptiles have higher total body water than mammals and the extracellular space of reptiles contains higher sodium and lower potassium levels compared to mammals (the reverse is true for the intracellular space). Therefore, fluid selection should be based on both the type of dehydration and the physiological status of the patient. Hypertonic dehydration is common in animals that have limited access to water or do not drink. Isotonic dehydration generally occurs as a result of hemorrhage, diarrhea, and short-term anorexia. Hypotonic dehydration is a common sequella to prolonged anorexia. Characterizing the state of dehydration is important to ensure that the patient is re-hydrated correctly.

Historically, isotonic balanced fluids, such as lactated ringers solution (273mOsmol/l, pH 6.6)(Abbott Laboratories, North Chicago, IL) and Normasol® (294mOsmol/l, pH 6.6)(Abbott Laboratories, North Chicago, IL) have been used when large fluid volumes are required. These fluids generally expand the extracellular space without a significant shift into the intracellular space. Prolonged usage of these fluids can lead to hypokalemia. In mammals, physiologic saline (0.9%)(308mOsm/l, pH 5.6) is preferred when there is a need for a rapid expansion of the circulatory volume, or to correct hyponatremia or alkalosis. Hypertonic solutions, such as 5% dextrose (252 mOsm/l, pH 4.3), are used when fluids are required to expand both the intracellular and extracellular spaces. The caloric input from the glucose is probably negligible and veterinarians should use appropriate enteral sources of nutrition to provide essential calories and nutrition. Combination fluids, such as 0.45% saline and 2.5% dextrose (280 mOsm/l, pH 4.3), are also commercially available.

Maintenance fluids should be provided to those animals not consuming sufficient fluids, in addition to correcting their fluid deficit. In general, the fluid maintenance rate for rabbits and small exotic mammals is 80-100 ml/kg/day. For birds there is a wide range of recommended fluid rates (50-100 ml/kg/day), although the author always bases the maintenance level on the high end of the range (100 ml/kg/day). The maintenance fluid rate of reptiles is 10-30 ml/kg/day.

Fluids can be given per os (PO) in patients that are mildly dehydrated (<5%) and have a functional gastrointestinal tract. The PO route is less invasive than other techniques. Per os fluids are not recommended in cases where patients are regurgitating, vomiting or have diarrhea, as the administration of fluids by the PO route could potentiate an osmotic diarrhea. The patient must be restrained properly to ensure safe administration of fluids. Fluid administration generally requires two individuals, one to restrain the animal and one to deliver the fluids. Attempting to administer fluids PO using inappropriate techniques could lead to fluid aspiration. Fluids can be administered PO using a stainless steel gavage tube or red rubber feeding tube. The required tube length can be determined by measuring the distance between the snout and the midbody, which is the approximate location of the stomach.

Subcutaneous (SC) fluids can also be used to rehydrate mildly dehydrated patients (<5%). In severe cases of dehydration (>8%), other routes of fluid administration, such as intracoelomic, intraosseus, and intravenous fluids, should be used. There are a number of advantages to using SC fluids, including ease of administration and an ability to deliver large volumes of fluids. The primary disadvantage of using SC fluids is that the subcutaneous space in most animals is relatively avascular, leading to variable absorption rates. The most common site to administer SC fluids in snakes and lizards is the lateral body wall. In chelonians, SC fluids are generally administered in the inguinal/femoral space. In birds, the inguinal and scapular areas are the most common sites of SC fluid administration. In mammals, the dorsal thoracic (scapular) and lateral body walls are the preferred sites for SC fluid administration.

Intraosseus (IO) fluids can be used in cases with moderate to severe dehydration. The IO route may be used when peripheral vasoconstriction limits intravenous access. Intraosseous catheters are clinically advantageous and appropriate in small and fractious patients due to ease of placement, catheter stability and clinical response. The femur, tibia, and humerus may be used for IO catheter placement in reptiles. In birds, the ulna and tibiotarsus are preferred. The femur and humerus should never be used because they may be associated with air sacs. In mammals, the proximal femur and tibia are preferred sites for IO catheters. A local anesthetic, such as lidocaine, should be used to reduce the pain associated with catheter placement. The author prefers to use spinal needles for IO catheters, as they have a stylet that prevents plugging the needle with a bone core.

Intracoelomic (ICo) fluids can be administered to reptiles and mammals with moderate to severe dehydration; however, this route should never be used in birds as it can lead to accidental drowning. The large serosal surface area of the viscera and the

coelomic/peritoneal membranes of reptiles and mammals serve to resorb the fluids. Irritating compounds should not be administered ICo. Intracoelomic fluids are not recommended in reptile patients that have respiratory compromise, as they may place an additional burden on the animal. Intracoelomic fluids should be given in the caudal coelomic cavity.

Intravenous fluid administration is the preferred route of fluid administration in moderately to severely dehydrated patients. The jugular vein can be used for lizards, chelonians, and snakes. Placement of the jugular catheter in the snake and lizard requires a surgical cut-down. A local anesthetic, such as lidocaine, should be used to reduce discomfort. The cephalic vein is another site for catheterization in the lizard, whereas the heart may be directly catheterized in severely moribund snakes. In birds, the jugular, basilic or medial metatarsal veins can be used to place IV catheters. The medial metatarsal vein is generally large (and approachable) in waterfowl, raptors, and large psittacines. In smaller psittacines, the basilic vessel is preferred. In mammals, the jugular, cephalic and lateral saphenous sites can be used for IV catheters. When collecting blood samples from exotic pet patients, it is important to consider possible IV sites prior to sample collection. For example, the author never collects a blood sample from a rabbit cephalic vein, preferring to save the site for IV catheterization.

Anesthetic Considerations for Exotic Pets: It's about More Than Just Passing Gas

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Clinicians working with exotic pets should establish consistent anesthetic and analgesic protocols to manage cases that require diagnostic or surgical procedures. Unfortunately, there are still cases where patients are being managed using “bruticaine” or analgesic limited protocols that aren’t taking into account the potential pain that develops or continues after a procedure (e.g., only using isoflurane anesthesia with no other long term management plan). Advances in domestic animal anesthesia have provided safer, consistent compounds that may be used to anesthetize exotic pets and provide long term analgesia.

A patient should receive a thorough examination, including auscultation of the heart and lung(s), prior to any anesthetic procedure. In those cases where auscultation is limited, such as with reptiles, an ultrasonic Doppler may be used to assess the heart. Pre-surgical blood work, which is commonly performed in domestic species, can provide insight into the physiological status of an animal. A complete blood count and plasma chemistry panel should be performed when possible. In cases where blood volume or owner finances are limited, a packed cell volume, total solids, and blood smear can be performed to provide important information regarding the animal’s status.

Ectotherms, such as reptiles and amphibians, should be provided supplemental heat during an anesthetic procedure that is consistent with their preferred environmental temperature. Endotherms, including birds and mammals, should also be provided supplemental heat during these procedures. Hypothermia in endotherms can result in the loss of essential energy to maintain an appropriate core body temperature. Animals maintained at an inappropriate temperature will experience a prolonged recovery. Water-circulating heat pads and forced air heating units provide good results and are unlikely to cause thermal burns. Radiant heat from an incandescent light can also be used to provide supplemental heat.

Variability in the physiology of exotic pets often results in variable responses between classes of animals. For example, anesthetics that provide surgical anesthesia in a mammal or bird may provide little to no anesthesia in a reptile or amphibian. Differences in anesthetic responses within animal classes have also been described. The anesthetic agents that have been found to provide the most reliable results in exotic pets include the dissociatives, benzodiazepines, alfaxalone, alpha-2 agonists, propofol, and inhalant anesthetics.

Benzodiazepines, such as midazolam, are excellent for sedating exotic pets for diagnostic procedures or as part of a pre-anesthetic protocol. The author routinely uses midazolam to sedate exotic small mammals for diagnostic imaging. Doses for rabbits range from 0.5-1 mg/kg, while for rodents may range from 0.5-2 mg/kg). Combining the midazolam with an opioid, such as buprenorphine (0.03-0.05 mg/kg), is useful if any painful procedures are expected (e.g., orthopedic manipulation for radiographs).

Dissociative agents are routinely used to anesthetize exotic pets. The most common dissociative agents used are ketamine (Ketaset, Ft. Dodge Laboratories, Ft. Dodge, IA, USA) and tiletamine (Telazol, Fort Dodge Laboratories, Ft. Dodge, IA, USA). Reported dosages for ketamine are quite varied. When a short, painless procedures (e.g., examination) or pre-anesthetic is required (e.g., facilitate intubation) for reptiles, a dose between 10-30 mg/kg IM is sufficient. Ketamine provides minimal analgesia and should be combined with an analgesic when a painful procedure is performed. A dose of 55-88 mg/kg IM has been recommended for surgical anesthesia in reptiles, but ketamine is inappropriate as a sole anesthetic in a surgical procedure. Ketamine is generally used in combination with alpha-2 agonists in mammals. If used alone, a dose from 15-30 mg/kg may be used, whereas the dose can be reduced when the drug is used in combination with an alpha-2 agonist. Side effects reported with ketamine usage include respiratory arrest, bradycardia, skin depigmentation, and prolonged recoveries. These side effects are usually associated with the administration of high doses (>80 mg/kg). Tiletamine is more potent than ketamine and provides similar results at a lower dose in reptiles (3-8 mg/kg). The addition of zolazepam is of benefit because it improves muscle relaxation and is an anticonvulsant. Tiletamine has been used in snakes, lizards and crocodylians with some success, but recoveries are still prolonged. Tiletamine should only be used for short, painless procedures or as a pre-anesthetic as it provides limited analgesia. The dissociatives have been used in birds, but generally result in violent recoveries.

The alpha-2 agonists, including xylazine and dexmedetomidine, have been used with good success in exotic pets. In general, they are used in combination with other drugs. Of the two drugs, dexmedetomidine is used more frequently because of its greater effect and potency. Dexmedetomidine provides muscle relaxation, analgesia and is reversible with atipamezole. The primary side effect associated with this drug is cardiopulmonary depression.

Propofol is a non-barbiturate anesthetic agent that can be used to provide general anesthesia. Propofol is readily metabolized, has no cumulative effect, and provides approximately 10-45 minutes of anesthesia. To be effective, propofol must be administered intravenously (IV) or intraosseously (IO). The author has been able to anesthetize amphibians using the intracoelomic route, but the dose is much higher (35 mg/kg) than the IV dose. A dose of 10-15 mg/kg IV will provide general anesthesia in birds, mammals, and

reptiles. Additional boluses of propofol may be necessary during a procedure. Because propofol is a respiratory depressant, the patient should be intubated and ventilated.

Inhalant anesthetics are still considered the gold standard for anesthesia. The primary advantage of the inhalant anesthetics is that delivery is controlled via a precision vaporizer. The most common inhalant anesthetics used in veterinary practice are sevoflurane and isoflurane. Exotic pets, like domestic species, should be intubated to ensure consistent delivery of the anesthetic. Birds, chelonians, and crocodylians have closed tracheal rings and should be intubated with a non-cuffed endotracheal tube. Intubating a reptile or bird is a simple procedure because the glottis is located on the floor of the mouth. Intubating lagomorphs can be very difficult because of their long, narrow oral cavity. Birds and reptiles under general anesthesia may become apneic during the procedure and should be ventilated using intermittent positive pressure. Typically, 4-6 breaths per minute at a pressure less than 12 cm of water is satisfactory. Non-rebreathing systems are appropriate for animals under 5 kg.

Exotic pets should be monitored during an anesthetic procedure using standard procedures. Breathing can be monitored by observing contraction of the body wall, or with the assistance of an audible respiratory monitor. Auscultation of the heart is difficult, if not impossible, in reptiles. Esophageal stethoscopes may be used to monitor the heart rate in larger species, but are impractical in smaller animals. An ultrasonic Doppler produces an audible sound that insures cardiac function. An electrocardiogram (ECG) can also be used to monitor heart rate and rhythm. The pulse oximeter is a monitoring device that continues to gain popularity in veterinary medicine because it enables the anesthetist to monitor both heart rate and oxygen saturation. There are a number of different monitoring probes that can be purchased with these systems. Although these devices simplify anesthetic monitoring, placement and re-positioning may be required during the procedure. Mucous membrane color and hydration status of the patient should also be monitored during the surgical procedure. Any animal that experiences significant blood loss during a procedure should be given fluids (e.g. intravenous or intraosseous). Recovery from an anesthetic procedure should take place in a warm, dark, quiet area.

Ring the Bell, Dinner's Served: Nutritional Considerations for Captive Reptiles

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Reptiles may be herbivorous, omnivorous, or carnivorous, depending on the species. An ideal diet for captive reptiles should mimic their natural diet as closely as possible and provide a diversified selection of food. Some herbivorous species will often readily eat an omnivorous diet, but eventually these animals will reveal signs of nutritional deficiencies. Therefore, it is important to remember that food preferences do not always correlate with appropriate nutrition.

Herbivorous reptiles

Herbivorous reptiles are primarily classified as hind-gut fermenters, with microbial fermentation occurring in the large intestine. Consequently, the bulk of the diet of herbivorous reptiles should be vegetable fiber. The vegetable fiber offered should be rich in vitamins A and D3 and should have more available calcium than phosphorous. An ideal Ca:P ratio of at least 1.5-2:1 should be present. The diet should also be low in fats, oils, proteins, thiocyanates, and oxylates. In captivity, reptiles are typically fed weeds, flowers, and grasses on a daily basis. Herbivorous reptiles housed outdoors will forage for themselves if provided with an appropriately planted enclosure, but additional food is usually required. It is important to periodically peruse the yard and rule-out the presence of any poisonous plants. A variety of foods should be offered and can be mixed with calcium, iodine, vitamin D3, and vitamin A supplementation. It is important to remember that grocery greens are generally higher in protein and lower in fiber and may have an inverse calcium: phosphorus ratio when compared to natural forage. Spinach, cabbage, and beet greens should not be fed in excess due to their high oxylate content. The majority of foods designed for dogs, cats, humans, and other mammals should not be fed to herbivorous reptiles. Debilitated herbivorous reptiles requiring force-feeding or tube-feedings should be fed a critical care diet designed for their specific needs.

Omnivorous reptiles

It has been suggested that omnivorous reptiles do best when offered plant and animal matter in proportions that range from 75:25 to 90:10. Dietary requirements in these species tend to change with age, with most juveniles requiring a diet comprised of a higher proportion of animal matter. As the juveniles mature, their dietary requirements shift to a more herbivorous diet. The primary animal proteins offered should mimic a natural diet, including earthworms, slugs, snails, millipedes, pupae, and maggots (mealworms). It is essential to monitor the diets of captive invertebrates in order to avoid nutritional deficiencies in the reptiles eating them. Offering the invertebrates a diet rich in minerals and vitamins will help to ensure that the prey is "gut-loaded". Mammalian diets should generally be avoided as they may be too potent (e.g., excess protein and vitamins) for a reptile. Liver and yellow or dark orange colored vegetables (squash, carrots, sweet potatoes) are excellent sources of vitamin A, and Swiss chard, kale, beet greens, escarole, parsley, watercress, and green beans all have a positive Ca:P ratio.

Carnivorous reptiles

Carnivorous reptiles are generally the easiest group to provide food for in captivity, as there is a range of invertebrate and vertebrate prey species that can be offered. As was mentioned previously, however, those carnivores that specifically hunt invertebrates do need to have their prey species "gut-loaded". Most carnivorous aquatic species are piscivorous. If frozen fish are offered, then the diet needs to be supplemented with thiamine, as frozen-thawed fish can produce thiaminases.

Nutritional diseases

Nutritional disorders in reptiles commonly present as a chronic problem, and the diet is often times centered around limited food sources or human convenience. In most cases, deficient diets are comprised of limited numbers of food items and/or are not supplemented with calcium and vitamin powders.

Hypovitaminosis A

Vitamin A is a critical component in the production and maintenance of epithelial cells, and is also intimately associated with several structures related to vision. Hypovitaminosis A is a common clinical entity in reptile medicine, especially in chelonians fed predominately vitamin A deficient foods. The most obvious clinical abnormality associated with hypovitaminosis A is squamous metaplasia, which results in the degeneration of epithelial surfaces (e.g., conjunctiva, gingiva, pancreatic ducts, renal tubules, skin, and lung faveoli). Due to the multiple epithelial surfaces of the body, squamous metaplasia can manifest itself in several different ways. Blepharospasm, conjunctivitis, blepharodema, blindness, rhinitis, blepharitis, lower respiratory tract disease (nasal discharge, depression, dyspnea, open-mouth breathing), and/or cutaneous abnormalities may be observed. Middle ear infections and aural abscesses have also been linked with hypovitaminosis A. The diagnosis of hypovitaminosis A can be met via dietary history, clinical

signs, measuring vitamin A levels, or histopathology of tissue samples (squamous metaplasia of the epithelia surfaces). Supportive treatment should be utilized concerning the clinical manifestations of vitamin A deficiency, and appropriate husbandry and dietary changes should be instituted. Vitamin A deficiency can be corrected by oral supplementation with vitamin A products, or by offering small amounts of liver once per week. Injectable vitamin A should be used very cautiously, as hypervitaminosis A can occur with a single injection.

Secondary nutritional hyperparathyroidism (metabolic bone disease)

Metabolic bone disease (MBD) is defined as any metabolic defect that alters the morphology and functioning of bones. MBD is usually related to low levels of calcium or excessive levels of phosphorus, which consequently bind to calcium and render it physiologically unavailable. Decreased calcium availability results in increased parathyroid activity and mobilization of stored calcium from the shell and bone cortices. Factors predisposing reptiles to the development of MBD include: dietary deficiency of calcium and/or suitable vitamin D3, inappropriate calcium: phosphorus ratio of the diet, lack of exposure to ultraviolet light (ultraviolet B radiation increases activation of vitamin D precursors and facilitates gastrointestinal absorption of calcium), dietary excess of protein during rapid growth periods, anorexia, or abnormal vitamin D3 metabolism secondary to renal, hepatic, intestinal, or parathyroid disease. MBD is commonly observed in rapidly growing juvenile reptiles and reproductively active females. Clinical signs consistent with MBD vary depending on the age and species of the patient. The most common clinical finding in reptiles with MBD include muscle tremors/fasciculations, seizures, soft-shell, pathologic fractures and acute death. A thorough history is required before a diagnosis of MBD can be met. Diagnostically, radiographs and blood work can provide insight into the reptile's disease state. Radiography may reveal fibrous osteodystrophy and pathologic fractures. Low blood calcium levels are highly suggestive of MBD, but calcium blood levels are frequently not low in cases of MBD because of hyperparathyroid activity. It must be remembered that blood levels of calcium are not reflective of physiologically available levels of calcium. Ionized levels of calcium are more indicative of the availability of calcium, but, unfortunately, published reference levels are difficult to find in the literature. Treatment of MBD is dependent upon the correction of inappropriate husbandry. An unsuitable calcium: phosphorus ratio of the diet should be corrected, the proper provision of ultraviolet light should be instituted, and oral supplementation of calcium and vitamin D3 should be initiated. Supplemental calcium during the treatment period is also strongly recommended.

Gout

Gout is defined as the deposition of uric acid and urate salts within visceral tissues and on articular surfaces. Gout occurs as a result of hyperuricemia, which arises secondary to increased production or decreased excretion of uric acid. Increased production of uric acid may occur secondary to the ingestion of excessive amounts of protein (e.g., an herbivorous chelonian that is regularly offered animal protein). Decreased excretion of uric acid may occur secondary to reduced perfusion of renal tissues, which may be a result of dehydration, hemoconcentration, water deprivation, or renal disease. Reduced glomerular filtration eventually leads to a decrease in the overall excretion of urate salts, which results in hyperuricemia. Hyperuricemia, in turn, leads to the precipitation of urate complex microcrystals within tissues. These deposits are known as "gout tophi". Common sites of deposition of uric acid include articular joints and viscera. Clinical signs associated with gout include joint swelling and pain, depression, and dehydration. Affected animals are also commonly anorectic and lethargic. The diagnosis of gout may be done with blood work and radiographs/ultrasound. The mainstay of therapy is rehydration to correct the hyperuricemia, and the correction of any dietary imbalances or other predisposing causes of gout. Allopurinol, a urase inhibitor, is commonly used in hyperuricemic animals to reduce uric acid production. It must be mentioned that studies concerning the efficacy of this drug and the possible long-term effects of the drug in reptiles have not been conducted. Probenecid, which increases the renal excretion of uric acid, should not be used until the glomerular filtration rate is considered acceptable. Any concurrent infections in affected joints or organs that occur secondary to gout deposition should be treated appropriately. Surgery is occasionally indicated when uric acid deposits are compromising joints.

What's Your Diagnosis? Interactive Reptile and Exotic Small Mammal Cases

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Veterinarians working with reptiles and exotic mammal patients are routinely presented with challenging cases. The purpose of this presentation is to provide attendees with a series of actual reptile and exotic mammal cases in an interactive forum and discuss different diagnostic and treatment approaches.

A thorough physical examination should be performed on every reptile and exotic mammal patient. If the animal presents in respiratory distress, the physical examination should be postponed until the animal is stabilized. Placing the animal into an oxygen chamber or delivering oxygen via a facemask or endotracheal tube should be done to reduce the likelihood of hypoxia in the animal. The physical examination can be used to develop an initial prognosis regarding the case. Veterinarians must be realistic when considering the potential outcome for a case.

Diagnostic tests can be invaluable in confirming a specific etiology associated with a case. A complete blood count (CBC) can be used to evaluate the likelihood of an inflammatory response within the animal. In general, reptile and exotic mammal cases presenting with white blood cell counts (WBC) > 15-20,000 cells/ml are the result of an inflammatory response. However, stress leukograms can occur in animals with WBC counts in this range too; therefore, it is imperative that a differential count be done to determine the most likely cause of a leukocytosis. With stress, neutrophilia (heterophilia), monocytosis, lymphopenia and eosinopenia are common. In general, inflammatory leukograms are characterized by neutrophilia (heterophilia), monocytosis, and a lymphocytosis. Inflammatory leukograms can occur as a result of an infectious disease, toxin, neoplasia, trauma, or foreign body. In many cases, veterinarians attempt to associate inflammatory leukograms with an infectious etiology, when the etiology may not be infectious. The CBC also provides information regarding the erythron. If anemia is suspected, then attempts to classify the anemia (regenerative, non-regenerative) should be made.

Reptile and exotic mammal patients are stoic animals that can mask their illness. Serum/plasma biochemistry analysis can be used to evaluate physiologic disturbances in these animals. Veterinarians may find it difficult to find reference data for many of the species being presented to their facilities. Fortunately, the values for many of the biochemistries are similar to those described for domestic species. Veterinarians should become familiar with the physiologic differences between different reptile and exotic small mammals (e.g., herbivorous rabbits versus carnivorous ferrets) to help with interpreting results.

Radiographs are necessary to characterize the extent of injury associated with a fracture. When evaluating a fracture, it is important to consider which bone is affected, the location of the fracture (e.g., metaphysis, epiphysis, diaphysis), type of fracture (e.g., transverse, spiral, oblique), whether the fracture is open or closed, and whether there is soft-tissue and joint involvement. Evaluating the extent of soft-tissue injury associated with a fracture is necessary to estimate the convalescence period that will be required for the patient. A minimum of two high-quality images is required to fully evaluate an injury. Radiographs can also be used to evaluate the extent of disease associated with non-traumatic injuries too. Ultrasound imaging may also be used to assess the exotic pet patient. The author finds ultrasound especially useful for characterizing the reproductive status of animals.

Microbiological culture is an important diagnostic tool for veterinarians. Historically, veterinarians managed most infectious diseases as a primary bacterial disease. We now realize that bacterial infections, at least in some cases, are secondary opportunists that occur following viral and fungal infections. When submitting microbiological samples it is important to consider not only bacterial microbes, but fungi too. Performing a cytological examination prior to submitting a sample is strongly recommended, and may be useful in guiding a diagnostic laboratory.

The advancement of serological and molecular diagnostic assays has improved the veterinarian's chances of making an ante-mortem diagnosis for an infectious disease. Currently, hemagglutination inhibition (HI) assays are available to characterize exposure to a variety of viral pathogens. Because these assays are subject to misclassification, other more specific assays should be pursued to characterize specific viruses. Enzyme-linked immunosorbent assays and serum neutralization assays are considered more sensitive and specific than HI assays. When using serological assays, serial tests are necessary to characterize active infections. Polymerase chain reaction-based assays enable veterinarians to characterize active infections in exotic pet patients.

Necropsy, and subsequent histopathology, is often necessary to confirm a diagnosis in a case. This is especially important in the face of an epizootic. Veterinarians should take appropriate precautions when performing a necropsy on an exotic pet patient. Because many infectious diseases can be transmitted via aerosolization, necropsy should be performed under a negative pressure hood. Veterinarians should submit samples to a pathologist that is familiar with exotic pet pathology.

Success with exotic pet cases requires a thorough and well thought out diagnostic plan. Historically, exotic pet cases were approached by performing few diagnostics and administering empirical therapeutics. By practicing the same good standard-of-care expected for domestic pets, veterinarians will find improved success with their exotic pet cases.

Diagnostic Imaging in Reptiles: Am I Supposed to See What's in that Image?

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Diagnostic imaging is an underutilized resource in herpetological medicine. Survey radiographs and ultrasound can be used to evaluate many different systems simultaneously, and provide insight into possible problems in a case. To be successful with diagnostic imaging, veterinarians need to acquire a basic knowledge of anatomy regarding the species of interest, methods used to restrain reptiles to collect the images, and the most appropriate techniques used to collect and interpret the results.

There are a variety of resources available to the veterinarian that is trying to learn more about reptile diagnostic imaging. Mader's *Reptile Medicine and Surgery* (Elsevier/Saunders, 2006) provides an excellent review on the subject. Expert opinions can be obtained either via phone consults or via the internet (e.g., Veterinary Information Network). There are also board certified radiologists that offer consultation services. Regardless of the source, veterinarians have many options when attempting to interpret the findings of a diagnostic image.

With over 9,000 different species of reptiles, it is impossible to become comfortable with the anatomic peculiarities of all the reptiles. Fortunately, reptile anatomy is highly conserved among the orders. For simplicity, the reptiles can be categorized into one of four groups: chelonians, lizards, snakes, and crocodylians. The tuatara is not mentioned because it is not considered a common captive reptile. Reptile morphology texts are excellent resources for learning the anatomy of these animals. Short descriptions can also be found in *Reptile Medicine and Surgery* (Mader, Elsevier/Saunders, 2006) and *Clinical Anatomy and Physiology of Exotic Species* (O'Malley, Elsevier/Saunders, 2005).

The quality of the equipment used to take radiographs is an important consideration. A radiographic machine to be used for reptiles should be capable of taking a range of images, which might include day geckos (*Phelsuma* spp.) to varanids (komodo dragons, *Varanus komodoensis*). A machine capable of such a range should have a short exposure time. 1/60th of a second or shorter is recommended. The machine should also have a high milliamperes capacity (>300). This is important because of the variability in detail that might be expected among different sized animals. The killovolt peak range should also be large, 40-100 killovolt peak, to accommodate the different sized patients a veterinarian may encounter. The ability to alter the killovolt peak by small increments (e.g., 2 killovolt peak) is important because it will enable the veterinarian to review small details between images. A machine in which the tube can be rotated to provide a horizontal beam is preferred. This will enable the veterinarian to take lateral images on animals in sternal recumbency. This is especially important with large chelonians.

For small patient, dental radiograph machines can be used. The author has used this type of equipment to take "whole body" radiographs of small lizards (e.g., juvenile bearded dragons). The detail from these images, although not always refined, does provide more detail than standard films.

Selecting the correct type of cassette or film is as important as using the correct machine. High-detail, rare earth cassettes are preferred. These cassettes should be used in combination with slow speed, single emulsion (gray) films. This combination provides the best detail for small lizards. Double emulsion (black) films can be used for larger reptiles when small detail is not required. Selecting the correct size cassette and film combination is also an important consideration.

When taking radiographs it is important to always collect at least two images. The most common images are a lateral and dorsoventral or ventrodorsal image. These two, two-dimensional images will provide the most insight into interpreting the anatomy of a three-dimensional reptile. Care should be taken when positioning an animal to ensure that the area of interest can be evaluated.

A reptile must be still to collect the "perfect" image. Taking radiographs on un-anesthetized or restrained reptiles can lead to motion and a loss of detail. The author has found that reptiles can be restrained manually for images or anesthetized. Manual restraint does result in increased radiation exposure for the handlers, so it should be kept to a minimum. Placing blinders over the eyes of a lizard can also be done to minimize movement. The author has found this technique to work well with iguanas, bearded dragons, and varanids. An ophthalmic eye lube is placed in the eyes of the animal and the head is wrapped with vet-wrap (3M products, St. Paul, MN). Dimming the lights and minimizing human movement and speaking in the room will also help reduce the stimuli on the reptile.

Interpreting reptile radiographs is more challenging than in mammals or birds. Lizards do not store their fat in a mesentery like mammals. This absence of fat between the internal organs reduces the contrast between the tissues, leading the viscera to appear as a single soft tissue structure. The absence of a diaphragm also limits the radiographic interpretation of the coelomic structures. The bone of reptiles is less radio opaque than mammals, which can make the interpretation of the cortical densities more difficult. To reduce the likelihood of misclassifying a case of secondary nutritional hyperparathyroidism, the author always evaluates the cortical densities of the long bones instead of the digits. The best way to become comfortable with interpreting radiographs is to practice, practice, and practice.

As veterinarians have become more familiar with ultrasonography, its application in reptile medicine has greatly expanded. When considering an ultrasound machine for a veterinary hospital, it is important to consider the range of patients the machine will be used on. If exotic species are going to be regularly screened using ultrasound, a machine with a fine transducer is recommended. The author has found that 7.5 and 10.0 MHz transducers are generally best for evaluating reptiles; however, 3 and 5-MHz transducers have also been used in larger species. One of the problems with using these lower MHz transducers is the loss of detail associated with upper surface lesions. Because of the relative small size of many of our reptile patients, the author also prefers the transducer to have a small footprint.

Capturing a high detail ultrasound image requires intimate contact between the transducer and the animal. There are two different methods for obtaining high quality ultrasound images: direct contact via a non-irritating coupling gel or direct/non-direct contact via an aquatic medium (e.g., water). Coupling gel is the most common method used for collecting ultrasound images in mammals. In reptiles, this technique can also be used, but it is important to spread the gel between the scales to reduce the loss of detail associated with trapped air bubbles. The transducer can also be placed against a water-filled examination glove that is directed against the reptile's body. This method is the least productive in the author's opinion. Another technique that many reptiles are tolerant of involves placing the animal and the transducer into water. The water acts as an excellent contact medium. The author works with a number of herpetoculturists that use this method for assessing the reproductive status of their reptiles.

Ultrasound can be used to evaluate any number of systems in a reptile. This diagnostic technique is primarily used by the author to assess the reproductive status of reptiles. Follicles can be measured to predict whether an animal is likely to ovulate. For some species this information can be used to determine the best time for introducing a male and female. Images of the ovaries are best obtained by placing the transducer on the lateral body wall just caudal to the last rib. Each ovary should be evaluated individually, as one gonad may be active while the other is not.

Ultrasound can also be used to evaluate the heart of reptiles. The heart of most lizards is located in the pectoral girdle, with varanids being an exception. Their heart is located more caudally in the body cavity. The snake heart is located approximately 1/3 the distance from the head. The chelonian heart is located dorsal to the thoracic scutes of the plastron. Access to the heart with ultrasound can be obtained via the axillary region in lizards and chelonians, and direct placement over the beating heart of a snake. Lizards, snakes, and chelonians have a three-chambered heart, while crocodylians are the only reptiles with a four-chambered heart. Rotating the transducer should enable the ultrasonographer to evaluate all three (or four) chambers.

Ultrasound can also be used to evaluate the viscera in the caudal coelomic cavity. The author generally uses ultrasound to assist with the collection of fine-needle aspirates or biopsies of different coelomic organs. Kidney disease is a common problem in captive, adult green iguanas. Iguana kidneys are located in the intra-pelvic canal in normal animals, but enter the coelomic cavity when enlarged. Ultrasound can be used to collect a percutaneous biopsy of these organs without the need for an exploratory coeliotomy.

Infectious and Parasitic Diseases of Captive Reptiles: What is Lurking Under Those Scales?

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In the past two decades, there has been a rise in the number of emerging and re-emerging infectious diseases reported in reptiles. Emerging infectious diseases include newly identified pathogens, while those characterized as re-emerging include those that may have been previously characterized but are being reported with increased frequency. Veterinarians play an important role in the diagnosis of infectious diseases in herpetological collections and should closely monitor the literature to keep abreast of new findings and current research.

The rise in emerging infectious diseases in reptiles may be attributed to several factors, including the increased number of reptiles being imported into the United States and Europe, poor quarantine and sanitation programs, and improved diagnostic assays. The popularity of reptiles in the United States remains high, with millions of reptiles being imported annually. The popularity of reptiles has led to the growth of reptile swap meets, where herpetoculturists have the opportunity to select from a large number of different reptile species. At these swap meets large numbers of reptiles are maintained in relatively small areas with minimal/no biosecurity. Herpetoculturists routinely handle different specimens without washing their hands, possibly introducing and disseminating pathogens through the reptiles. The sanitation methods used to control or eliminate pathogens in reptile collections may also be suspect. Inappropriate use of disinfectants may lead to the development of resistant strains of microbes.

The number of diagnostic tests available to the clinician treating reptiles has increased dramatically over the past ten years. Historically, clinicians treated all “infections” in reptiles as bacterial diseases. However, over the past ten years, there have been an increased number of reports of viruses and fungi being isolated from diseased reptiles. The advent of molecular diagnostic testing has led to the development of highly sensitive and specific enzyme-linked immunosorbent assays, polymerase chain reaction (PCR), and reverse-transcriptase PCR.

The incidence of herpesvirus infections in chelonians has been on the rise since originally being isolated from sea turtles in 1975. Herpesvirus infections have been identified in freshwater, marine, and terrestrial species of chelonians. Transmission of the herpesvirus is believed to be via the horizontal route, although it has been suggested that a vertical route of transmission is also possible. Affected animals may present with rhinitis, conjunctivitis, necrotizing stomatitis, enteritis, pneumonia, and neurological disease. Molecular diagnostics, electron microscopy, and viral isolation have been used to diagnose herpes infections in chelonians. Affected animals should be provided appropriate supportive care (e.g., fluids, enterals, and antibiotics) to control clinical signs. Acyclovir has been used with some success by reducing viral replication. However, there is no effective treatment for this virus. Affected animals should not be released into the wild to prevent translocation of the virus to naïve chelonians.

Mycoplasmiasis is a bacterial infection that has been associated with severe disease in chelonians. Affected animals may present with nasal and ocular discharge, conjunctivitis, palpebral edema and pneumonia. Mycoplasmosis has also been identified in squamates and crocodylians. There are several diagnostic tests available to confirm mycoplasmosis in reptiles, including culture, an ELISA and a PCR assay. Microbiologic culture can be used to confirm an infection, but it is difficult to isolate this bacteria and time consuming. Currently, parallel testing using both the ELISA and PCR assays provides the highest degree of sensitivity. Treatment may be attempted using tetracyclines and flouroquinolones. Mycoplasmosis has been associated with declines in native tortoise populations in the United States and treatment of wild specimens is not recommended.

Cryptosporidium serpentis is considered a “plague” of captive snake collections. This apicomplexan parasite has been associated with both high morbidity and mortality in captive collections. Affected snakes commonly regurgitate their meals, have a mid-body swelling, and are dehydrated. A variety of methods may be used to diagnose cryptosporidiosis in snakes. Acid-fast cytology of a regurgitated meal or fecal sample is often diagnostic. Because there is currently no effective treatment, affected animals should be culled. *Cryptosporidium saurophilum* is a more recently diagnosed species associated with lizards. Whereas *C. serpentis* is associated with the stomach, *C. saurophilum* is associated with the intestine. Currently, no consistent treatment is available for *C. saurophilum* or *C. serpentis*.

Bearded dragon adenovirus was first reported in Australia in the early 1980's. The virus was not characterized in the United States until more than a decade later. Since that time, the virus has spread through the bearded dragon population in the USA and should be considered endemic. Transmission of the virus is primarily by the direct route (fecal-oral), although vertical transmission may also be possible. Affected animals may present with anorexia, weight loss, limb paresis, diarrhea and opisthotonus. Concurrent dependovirus and coccidial infections have also been observed in neonatal bearded dragons. Biopsies of the liver, stomach, esophagus, and kidney may be collected to confirm diagnosis (ante-mortem). On histopathology, basophilic intranuclear inclusion bodies are strongly suggestive of adenoviral infection. Currently, there is no non-invasive ante mortem diagnostic test to confirm adenovirus in the reptile; however, the author is currently working on a polymerase chain reaction (PCR) assay to detect adenovirus in the feces of affected

animals. There is no effective treatment for adenoviral infections, although supportive care (e.g., fluids, enterals, antibiotics) may be useful in stemming the secondary effects of the disease. Again, very little is known regarding the epidemiology of this virus; therefore, special precautions should be taken when working with affected animals. Because there is no effective treatment, affected bearded dragons should be culled from breeding populations.

Coccidiosis is a major cause of morbidity and mortality in reptiles. A species of special concern, *Isospora amphiboluri*, is found in bearded dragons. These endoparasites are especially problematic in neonatal dragons, often resulting in stunting, diarrhea, and death. Whereas most coccidial infections in higher vertebrates are self-limiting, these infections often persist in bearded dragon colonies. Historically, eliminating coccidia from bearded dragons was difficult because most of the therapeutics used to eliminate the parasites were coccidiostatic. Penazoril (30 mg/kg per os once with a second treatment 48 hours later) is coccidiocidal and has excellent therapeutic value against *I. amphiboluri*. Quarantine and environmental disinfection/sanitation should also be done to eliminate coccidia from dragon colonies.

Microsporidians are obligate intracellular parasites. The life cycle of these parasites includes both merogonic and sporogonic phases. These parasites are common in lower vertebrates (e.g., fish), but have also been implicated as a concern in humans with acquired immunodeficiency virus. Bearded dragons infected with these parasites can present with a similar clinical picture as adenovirus or coccidiosis. Affected dragons are anorectic, unthrifty, cachectic, and may die acutely. Diagnosis is generally made at post-mortem. Hepatic and renal necrosis is common, although other organ systems (e.g., intestine and gonads) may also be affected. There is no effective treatment. To limit the likelihood of introducing this parasite into a collection, herpetoculturists should only acquire animals from reputable breeders and quarantine any new arrivals for a minimum of 60-90 days.

Ranavirus is an emerging disease of chelonians. This virus has a high morbidity and mortality. It has been isolated from both captive and wild chelonians. Affected animals typically develop upper respiratory signs (e.g., palpebral edema, conjunctivitis), lower respiratory signs, oral ulcers, cervical edema, and gastrointestinal signs. Diagnosis can be done using PCR. There is currently no effective treatment for affected animals.

Burned! Ultraviolet B Radiation for Exotic Pets: The Good, the Bad, and the Photokeratitis

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Because the majority of exotic pets are being housed indoors, it is important that they are provided lighting that mimics natural light. In addition to the provision of light, the amount of light provided in captivity should also mimic natural patterns. Photoperiods in the wild are generally between 12-15 hours a day, depending on season. To have success with exotic pets in captivity, it is important that we make recommendations to our clients that can ensure their long term success with their pets/breeding animals. The purpose of this presentation is to provide attendees an overview of the different types of lighting available for exotic pets held indoors, and how we can best use these lighting systems to provide the best captive environment for our patients.

Artificial lighting is provided in two different forms: incandescent and fluorescent lighting. Many of us are familiar with the standard forms of these lighting types, although there are some exceptions we may be less familiar with. One of the confusing aspects of lighting comes when manufacturers make claims about their light bulbs that are not true. The following review is meant to help clarify any misconceptions regarding the different types of lights.

Incandescent lighting is represented by the standard screw-in light bulb. This type of light has dominated the lighting scene for the provision of light in standard lighting fixtures in human domiciles. This type of light can generate a great deal of heat, especially at higher wattages, and requires a large amount of energy to run. There is a current movement to replace these bulbs for the more energy conserving fluorescent light bulbs. The primary benefits associated with the incandescent bulbs are that they are inexpensive, can be used to generate heat, and can be made in different colors (e.g., red, black green, clear) and lighting spectrums (e.g., black light). To the author, incandescent lighting remains the best method for providing and regulating the environmental temperature within an exotic pet's enclosure. Incandescent lighting, with few exceptions, functions to provide visible light and infrared light (or heat). Although many manufacturers make a claim that their infrared lights are "full-spectrum" and can provide ultraviolet B radiation, it is not true. Two exceptions are the black lights and mercury vapor bulbs. Black lights do produce ultraviolet radiation, but it is not in the spectrum considered important for the photochemical stimulation of vitamin D. Some mercury vapor bulbs do provide ultraviolet B radiation within this spectrum, as well as heat. Actually, many of the mercury vapor bulbs can produce a significant amount of heat, making them only ideal for large vivariums.

Fluorescent light bulbs are sold in two forms, the original tube style and the more recent coiled screw-in type. Historically, when people discussed "full spectrum" light bulbs they were talking about the fluorescent tube light bulbs. The first to be sold as "full-spectrum", the Vita-light, was popular among hobbyists. It wasn't until later that research showed that this bulb did not produce an appreciable amount of ultraviolet B radiation in the appropriate range. This is an important point to consider, as there are a number of different manufacturers offering these bulbs and making claims regarding their value. It is important to research the bulbs prior to making the recommendations. The more recent coiled fluorescent bulbs appear to have the potential to produce even higher amounts of ultraviolet B radiation (in the appropriate range) than the tube bulbs. Again, the bulbs that can do this are specifically manufactured to do so. A fluorescent light bulb from the local hardware store is not the same bulb as one produced specifically for reptile enclosures. The primary advantages associated with these bulbs is that they can provide ultraviolet B radiation in the appropriate range (290-310 nanometers) and provide high quality visible light. The primary disadvantages are that these bulbs produce little heat, requiring an additional bulb to generate infrared light heat, and can be expensive.

Ultraviolet light is produced by electromagnetic radiation. The wavelengths for ultraviolet radiation are shorter than those for visible and infrared light. Ultraviolet radiation is generally discussed in relation to those categories important to vertebrates: Ultraviolet A, B, and C. Ultraviolet C radiation represents the shortest wavelengths of the three classes (<280 nanometers). This range of ultraviolet radiation is germicidal, and is commonly used to control pathogens in aquatic systems. Ultraviolet B radiation provides the medium range ultraviolet radiation (280-315 nanometers). Ultraviolet A radiation represents the longest rays of the group and is characterized as "black light" (> 315-380 nanometers). Ultraviolet B radiation represents the range considered important in the synthesis of vitamin D3. Vitamin D3 is an essential hormone that plays many different important physiologic roles. Its role in calcium metabolism is probably its most recognized function, where it helps to ensure the development and maintenance of healthy bones. In some exotic pets, maintaining appropriate levels of vitamin D3 has also been found to be associated with increased reproductive success. Ultraviolet C is not generally discussed at any great extent, although it is considered important in regulating behavior in vertebrates.

There are two primary methods for obtaining vitamin D3: synthesizing it from exposure to ultraviolet B radiation or consuming a vertebrate that has synthesized the hormone through exposure to the sun. The production of vitamin D occurs as a result of the photosynthetic conversion of 7-dehydrocholesterol to pre-vitamin D3. Pre-vitamin D3 is converted to vitamin D3 via a temperature

dependent process. At this stage the hormone is transported to the liver where it is hydroxylated to 25-hydroxyvitamin D3. The kidneys serve as the site for the final conversion of the hormone to 1, 25-hydroxyvitamin D3, which represents the active form.

Vitamin D is considered important in vertebrates because it plays many different roles in the body. Because captive exotic pets are generally maintained indoors and derive no unobstructed sunlight, the use of “full spectrum” lighting has become an important consideration for ensuring that captive, non-carnivorous species can obtain vitamin D3. Until recently, studies evaluating the importance of full spectrum lighting in exotic pets have been limited to species of lizards. However, recently published original research from the author’s laboratory has shown that 25-hydroxyvitamin D levels in a snake, *Elaphe guttata*, and chelonian, *Trachemys scripta elegans*, could be significantly increased after exposure to appropriate full spectrum lighting. Similarly, research evaluating these lights in rabbits and rodents has shown similar results. It has generally been accepted that these animals obtain their vitamin D through their diet; however, the results of these studies suggest that in these species, they can generate endogenous vitamin D, like humans, from direct stimulation to appropriate artificial lighting. Coiled fluorescent screw-in light bulbs were used for the study. The bulbs were placed within 6-9 inches of the study animal’s basking spot. The findings of these studies confirm the importance of using full spectrum lighting for captive exotic pets.

When making recommendations regarding lighting that provides good quality ultraviolet B radiation it is important to recognize that not all bulbs are created equal. Although “full-spectrum” lights may appear similar, they can produce vastly different quantities of ultraviolet B radiation. To confirm the quantity of ultraviolet B radiation being produced by a bulb, it is important to measure the intensity of the radiation using an appropriate radiometer/photometer. The distance the bulb is placed to a basking reptile can also have an effect on the quantity and intensity of light reaching an animal. “Full-spectrum” lights should not be shown through glass, as it can deflect the ultraviolet B radiation away from the pet. Historically, only fluorescent tube light bulbs produced any significant quantity of ultraviolet B radiation; however, some coiled fluorescent bulbs and mercury vapor bulbs can also produce appropriate to high levels of ultraviolet B radiation.

Visible light

Visible light is provided in the mid-light spectrum. The quality of visible light provided by different bulbs can vary. Some light bulbs provide poor-quality visible light across the color spectrum. In these cases, the light within the enclosure may have a “yellow” quality and the vibrant colors of the pet won’t be apparent. Many exotic pets require high-quality visible light to identify the colors of foods, predators, and potential mates, among other things. Color rendering index is an important parameter to evaluate in the light bulbs. Fluorescent bulbs generally provide the best visible light. Most of the high quality “full spectrum” fluorescent tube and coil bulbs available through the pet trade provide good quality visible light.

Infrared light

Infrared radiation is in the upper end of the light spectrum, and the area in which heat is generated. Although there are a variety of different heating elements for exotic pet enclosures, the author prefers to use radiant heat sources in the form of light. This is the most natural method of providing heat to exotic pets, and mimics the primary method they absorb heat in the wild. It is possible to use variable wattage incandescent bulbs to provide a gradient of temperature for a pet’s enclosure. The wattage for the bulbs will vary depending on the size and depth of the enclosure.

Conclusions

Artificial light is an important consideration for captive exotic pets being held indoors. It is important to use high quality light bulbs that meet the animal’s needs across all three forms of the light spectrum, including ultraviolet, visible and infrared radiation. The provision of high quality light will help to ensure our client’s success with their pet.

Ornamental Fish 101: Managing Pet Fish Without Getting All Wet

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There are two ways to approach a disease issue in fish: 1) ante-mortem tests and 2) post-mortem tests. Ante-mortem tests, or those done on live fish, are done when the aquarist is interested in saving a particular fish. The aquarist may pursue this route because of either personal (yes, the human-animal bond does occur with non-furry animals!) or financial (e.g., valuable breeding animal) reasons. Post-mortem tests, or those done on dead animals, are pursued when the aquarist is interested in saving a group of fish. A necropsy (animal form of an autopsy) can provide a great deal of insight into the disease condition of a particular fish, and therefore the population of animals that it originates from. The purpose of this presentation is to review the common diagnostic tests used to assess the disease status of a fish.

There are a number of different reasons that fish develop disease, including poor water quality, inappropriate husbandry, nutritional deficiencies, infectious disease (e.g., bacteria, viral, fungal), and parasitic disease. To determine which of these etiologies is responsible for disease in a particular fish (or fishes), diagnostic testing is required. Although the concept of performing these tests may appear overwhelming, with practice, diagnosing disease can become second nature.

The most common ante-mortem tests performed on fish are gill biopsies, skin scrapes, fin biopsies, complete blood counts, cultures, and fecal direct smears. Selecting which test to perform should be based on the clinical signs of the fish. Dyspnea (rapid breathing) in fish is suggestive of gill disease, and a gill biopsy would be appropriate. Lesions found on the skin (e.g., excessive mucous production) or fins (e.g., erosions) may be suggestive of infectious or parasitic disease, and a skin scrape or fin biopsy would be appropriate. Fish that are depressed, anorectic (not eating), or thin (muscle wasting) may have an internal disease (e.g., infectious or parasitic disease). A bacterial culture can be done to identify a specific bacterial pathogen. An antibiotic sensitivity profile can also be done to determine which antibiotic is best suited for eliminating the infection. A complete blood count can be used to interpret the animal's overall well-being or a fecal exam can be used to assess the potential for internal parasites. All of these tests can be done on alert or anesthetized animals, although the author prefers to anesthetize animals for the procedures. Tricaine methane sulfonate (MS-222; Argent Laboratories, Redmond, WA 98052)(100-200 mg/L) is the preferred anesthetic for anesthetizing fish.

Gill biopsies (clips) are an excellent method for assessing the quality of the gills. Teleosts, or bony fish, have 4 pairs of gills. The gills reside in the protective buccopharyngeal chamber under the operculum (gill cover). At the microscopic level, the gills can be divided into the primary and secondary lamellae. The primary lamellae represent the individual gill filaments that can be observed with the naked eye, while the secondary lamellae are comprised of a single layer of epithelial and endothelial cells and line the primary lamellae. The secondary lamellae are the site for gas exchange (e.g., oxygen absorption and carbon dioxide off-loading) and the excretion of wastes (e.g., ammonia). The surface area of the gills is vast, and allows for the rapid movement of water across the gill surface. Any damage to the gills can decrease the surface area associated with the secondary lamellae, and lead to dyspnea and death. Elevated levels of chlorine, ammonia, and nitrite, along with infectious and parasitic diseases, are the most common causes of gill disease in ornamental fish. To confirm which of these problems is associated with a specific case, diagnostic tests, such as a gill biopsy, should be done. If ammonia, nitrite or chlorine toxicity is suspected, than a water test should be done too. Elevated levels of any of these toxins, in combination with microscopic changes in the gills (e.g., excessive mucous production and a loss of respiratory surface area), are diagnostic. The presence of infectious (e.g., bacterial or fungal) or parasitic diseases with abnormal gills is also diagnostic. Once a diagnosis is made, an appropriate treatment plan can be devised. For example, water changes can be made to reduce the toxicity associated with ammonia or nitrite, sodium thiosulfate used to dechlorinate water, or an appropriate antibiotic or anti-parasitic given to treat infectious or parasitic agents.

A gill biopsy can be collected from an anesthetized or alert fish; however, the author performs this procedure on anesthetized patients. When handling fish it is best to wear latex exam gloves to minimize the likelihood of traumatizing the skin of the fish. The integument of fish is an important component of their innate (natural) immune system. Any damage to the skin can lead to an increased likelihood of opportunistic pathogens invading a fish. The gloves should also be moistened with the water from the animal's aquarium. The fish should be netted and removed from the aquarium. The thumb of your non-dominant hand should be inserted under the operculum, and the operculum raised slightly. Once elevated, a fine pair of scissors can be inserted under the operculum to collect the gill biopsy. A small cutting (4) of primary lamellae should be collected. A small amount of bleeding may occur, but generally ceases within seconds. The gill sample should be placed onto a glass microscope slide, a drop of water from the animal's aquarium placed on the sample, and a coverslip added to protect the sample. Water from the aquarium is preferred because it is isotonic (balanced) for any pathogens found on the gill. Adding water from another source that is not balanced can lead to the death of the organism and an inability to make a diagnosis. The sample should be reviewed immediately after collection to ensure best results.

A skin scrape should be done in cases where a fish has lesions on the skin. The skin scrape can be used to identify infectious or parasitic organisms. A glass microscope slide can be used to collect the sample. The slide should be held at a 45° angle and drawn in a cranial to caudal direction (e.g., from head to tail). The sample should be placed on a second microscope slide, mixed with a drop of water from the aquarium, and covered with a coverslip. Again, the sample should be read immediately for best results. If bacteria are a concern, than a Gram stain or Diff-quick stain can be done to evaluate the types of bacteria present. To prepare these slides, the sample and drop of water are mixed, the sample heat fixed using a match or lighter, and the sample stained according to the manufacturer's recommendation.

A fin biopsy should be considered in cases where lesions are found on the fins. Many times these lesions are associated with a bacterial, fungal or parasitic infection. A fine pair of scissors should be used to collect the sample. If the sample can be collected between fin rays, that is preferred; however, this is not always possible, and the fin will regenerate. The sample should be handled in a similar fashion to the skin scrape, and either be placed on a slide with a coverslip or stained.

Fecal exams for parasites can be done on free-catch samples (e.g., found in the tank) or via enema. The samples should be placed on a slide with a drop of water and a coverslip and reviewed.

Post-mortem examinations should always be performed immediately after the fish has expired. Autolysis, or tissue disintegration, can occur rapidly in fish, and can severely limit the value of a necropsy. Fish that have been dead in the water for even a couple hours, depending on the water conditions and temperature, may have limited value. Therefore, it is important to perform the procedure as soon as possible after death. In cases where this is not possible, the animal should be stored in a refrigerator in an air tight bag. Freezing a fish can lead to tissue crystallization and eventual autolysis with thawing and is not recommended. Storing a fish in water is also not recommended, again, because of the potential for autolysis.

A fish post-mortem can be divided into two major parts: the gross examination and the microscopic examination. The gross examination will provide a significant amount of information; however, this is not generally diagnostic. The microscopic examination requires a review of the tissues under a light microscope. This aspect of the post-mortem examination generally requires the assistance of a veterinary pathologist. Veterinarians interested in submitting samples can find individuals capable of reviewing a case by searching the internet or local/state diagnostic laboratory. The author sends his samples to Dr. Michael Garner at Northwest ZooPath (www.zoopath.com).

When performing a necropsy on a fish, it is important to protect yourself against potential zoonotic diseases (e.g., those diseases that can be transmitted from animals to humans). The author highly recommends wearing latex exam gloves (or nitrile gloves for those with allergies to latex) when performing a necropsy. There are a number of bacterial and fungal fish diseases that can cause localized or even systemic diseases in humans. The cuts and scrapes we have on our hands can serve as excellent sites of entry for these pathogens, and thus the reason gloves are important.

The gross post-mortem examination will be the primary focus of this article, as the histologic examination is beyond the scope of this article. The post-mortem examination should start with an external examination of the fish. The general appearance of the fish should be closely inspected. How is the musculing? Is the animal thin? This can usually be determined by evaluating the large (epaxial) muscles along the spine. Animals with chronic disease typically lose muscle in an attempt to generate energy to defend against an infectious disease (e.g., mycobacteriosis). Are there erosions or ulcers on the skin? How large are they? Are they full thickness (e.g., can you see the underlying muscles)? These types of lesions may be indicative of aggressive bacterial infections that may be contagious to other fishes (e.g., *Aeromonas* spp.). A close external examination can provide a significant amount of insight into the health status of the animal. Not fully evaluating the fish can result in misdiagnosis. Once the external examination is completed, a thorough internal examination should be done.

Prior to opening the coelomic cavity (abdomen), it is important to evaluate the oral cavity and gills. The operculum should be removed and the gross appearance of the gills recorded. If the fish is only recently expired, they should remain moist and red. If the fish has been expired for an extended period of time, then they may appear deteriorated. Excessive mucous production or a loss of color is suggestive of disease. A clip of the gills can be taken and reviewed (unstained) under a light microscope to identify potential pathogens.

The author prefers to open the fish on the left side for the internal examination, as it provides better access to the spleen. The initial incision should be made on the ventral surface of the fish, cranial (in front of) to the anus. The incision should then be extended cranially to the level of the operculum. The incision should then be extended dorsally towards the spine. At this point, the incision can be extended caudally towards the tail, parallel to the spine. Finally, the incision can be extended ventrally back to the level of the initial incision. Once the incision is completed, the entire lateral aspect of the body wall can be removed. With the body wall removed, it will be possible to visualize the internal organs. With over 20,000 different teleosts, it is impossible to describe the variation in organ position, size, color, and texture in a single article. For the most part, these things are similar, but you can expect to be stumped on occasion. provide a review of the general locations of these organs in two different species of cichlids. For a more complete review of fish anatomy, the readers are directed to Michael Stosskopf's *Fish Medicine* (1992, W. B. Saunders Publishing). With time and practice, a veterinarian can become quite adept at identifying organs and knowing what looks normal and what looks abnormal.

The gross examination of the organs can certainly provide some insight into the health status of the animal, but is generally limited without histopathology (microscopic review of the tissues). Again, this is when submitting samples to a pathologist can prove invaluable. For example, the gills of a fish may appear grossly abnormal, but it would require histopathology to confirm the presence of a mycobacteriosis.

To truly characterize a specific cause of disease in a fish or a group of fish, diagnostic tests must be performed. For many veterinarians, the idea of performing these tests may be daunting; however, with practice any veterinarian can become proficient at performing and interpreting these tests.

The Simple Tooth: A Review of Feline Skull and Tooth Anatomy

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Skull anatomy

The skull can be divided into the fused bones of the calvarium, the upper jaw, and the lower jaw. The cranial portion of the calvarium consists of the paired frontal bones, which articulate cranially with the nasal bones and maxillae, and caudally with the parietal bones. The nasal cavity contains an ethmoid bone and is bordered dorsally by the incisive, nasal and frontal bones, laterally by the incisive, maxilla, lacrimal, frontal and palatine bones, ventrally by the incisive, maxilla, and palatine bones and caudally by a single vomer bone which lies ventral to the ethmoid and dorsal to the hard palate. The lateral surface of the frontal bone shapes the dorsomedial and caudal aspect of the orbit. The medial and ventral part of the orbit is completed by articulation of the frontal bone with the lacrimal, ethmoid, maxilla, presphenoid and palatine bones. The zygomatic bone forms the lateral boundary of the orbit. The temporal process of the zygomatic bone articulates with the zygomatic process of the temporal bone, forming the zygomatic arch. Caudal to the frontal bones and forming the caudal portion of the cranial vault are the paired parietal bones, which articulate caudally with the occipital bone. Ventrally, the parietal bone joins the temporal and basisphenoid bones.

The upper jaw includes the incisive, maxillary, and palatine bones. The paired incisive bones form approximately one-sixth of the hard palate, and three incisors are rooted in each incisive bone. The incisive bones are bordered dorsally by the nasal bones, caudally by the vomer bone and laterally and caudally by the maxillae. The maxillae extend to the caudal border of the hard palate laterally, but are joined medially by the paired palatine bones to complete the hard palate. The roots of the canine tooth, three premolar teeth, and a single molar tooth are embedded within the alveolar process of each maxilla.

The lower jaw is composed of two mandibles, which are joined rostrally at the cartilaginous symphysis and form a synchondrosis. Each mandible consists of a body and a ramus. The three mandibular incisors, canine tooth, two premolars and single molar are anchored in the dorsal alveolar border of the body of the mandible. The ramus of the mandible contains three processes: the coronoid process, the condylar process, and the angular process. The coronoid process forms the most dorsal part of the mandibular ramus and the angular process is located at the caudoventral aspect of the ramus. The temporomandibular joint is formed by the condylar process of the mandible which articulates in the mandibular fossa of the squamous part of the temporal bone. The condylar process is bar-shaped in the cat, which is typical for carnivores. The mandibular fossa is bordered rostrally by the articular eminence and caudally by the retroarticular process. Both of these bony prominences are well developed in the cat, which creates a very deep mandibular fossa and normally prevents any movement of the mandibular condyle beyond these prominent bony processes.

The temporomandibular joint (TMJ) is a condylar synovial joint, which is separated into a dorsal and ventral compartment by a thin articular disk. The disc attaches around its entire periphery to the joint capsule which creates two separate articular spaces. Normally, when the mouth is opened, the medial aspect of the mandibular condyle is seated firmly in the mandibular fossa. The lateral aspect of the joint capsule is thickened in cats and tenses at maximum jaw opening which functions to limit lateral motion of the condyle. A caudal capsular reinforcement has also been demonstrated in the cat. Construction of the feline TMJ reduces rotary and lateral grinding movements.

Muscles of mastication

The muscles of mastication in the cat include the temporalis, masseter, medial and lateral pterygoids and rostral and caudal digastricus. The masseter, temporalis and pterygoid muscles close the jaw and the digastricus muscle opens the mouth.

Blood supply

The majority of blood supply to the feline oral cavity is provided by the maxillary artery. In the mandible the maxillary artery branches into the mandibular (inferior alveolar) artery which enters the mandibular canal through the mandibular foramen. The mandibular (inferior alveolar) artery courses rostrally within the mandibular canal and then exits laterally through the caudal, middle and rostral mental foramina. Blood supply to the maxilla is provided by the major palatine and infraorbital branches of the maxillary artery. The major palatine artery courses through the caudal nasal cavity, passes through the palatine foramen and courses on the ventral surface of the hard palate midway between midline and the maxillary arcade. The infraorbital artery branches from the maxillary artery and enters the infraorbital canal.

Innervation

Motor innervation to the muscles of mastication is supplied by the mandibular branch of the trigeminal nerve (except the caudal belly of the digastricus which is innervated by the facial nerve). Sensory innervation is received from the maxillary and mandibular branches of the trigeminal nerve. The maxillary nerve courses through the pterygopalatine fossa to enter the infraorbital canal. The

palatine nerves branch from the maxillary nerve prior at the caudal limit of the infraorbital canal. The caudal maxillary alveolar nerve branches from the maxillary nerve prior to it entering the infraorbital canal. The maxillary nerve becomes the infraorbital nerve when it enters the infraorbital canal. The middle and rostral maxillary alveolar nerves branch from the infraorbital nerve within the canal. The infraorbital nerve exits the infraorbital canal and innervates the lateral and dorsal cutaneous structures of the rostral maxilla and upper lip.

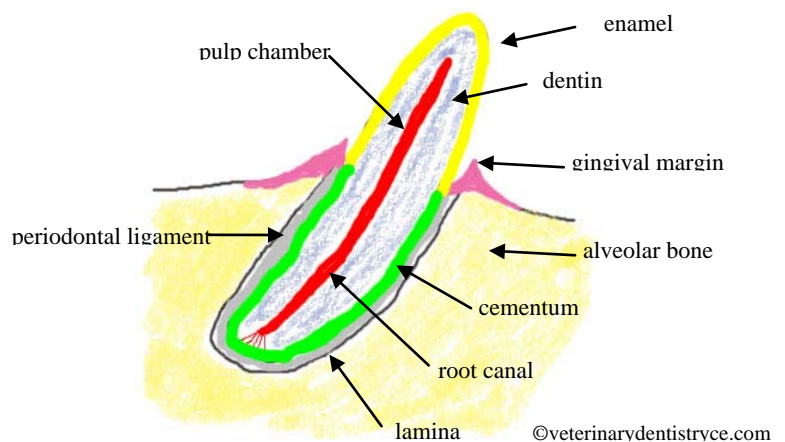
The mandibular branch of the trigeminal nerve enters the mandibular foramen on the lingual side of the mandible, travels in the mandibular canal and exits laterally as the caudal, middle and rostral mental nerves. The middle mental foramen is located in the diastema between the mandibular canine tooth and mandibular third premolar tooth halfway between the dorsal and ventral cortex of the mandible.

Salivary glands

The major salivary glands of the cat are the parotid, zygomatic, mandibular, and sublingual. The parotid salivary duct exits at the papilla which is located in the alveolar mucosa just caudal to the maxillary fourth premolar. The zygomatic salivary duct orifice opens in the alveolar mucosa near the maxillary first molar. The mandibular and sublingual salivary duct orifice opens on a small sublingual papilla located lateral to the rostral end of the tongue frenulum. There are two sets of molar salivary glands in the cat. The lingual molar glands are located linguodistal to the mandibular first molars. The buccal molar salivary glands empty into the oral cavity through several small ducts.

Tooth anatomy

- *Crown* is the portion of the tooth that is covered by enamel which is visible above the gumline.
- *Root* is the portion of the tooth that is covered by cementum located within the alveolus beneath the gingival tissue.
- *Apex* is the area of the root which is the deepest in the alveolar bone.
- *Enamel* is the hardest substance in the body which is the outer layer of the tooth crown. Enamel is formed by ameloblasts within the tooth bud prior to eruption. If enamel is damaged it is incapable of repair.
- *Cementum* is the outer layer of the tooth root which provides a surface for attachment of the periodontal ligament to the tooth.
- *Cementoenamel junction* is the neck of the tooth where the crown meets the root.
- *Periodontal ligament* is the fibrous connective tissue that surrounds the root of the tooth, separating it from and attaching it to the alveolar bone and serving to hold the tooth in place. The periodontal ligament also acts as a shock absorber.
- *Pulp cavity* is the central cavity of the tooth consisting of the pulp chamber and root canal containing blood vessels, nerves, lymph vessels and other cells (odontoblasts). The pulp chamber of the cat lies very close to the enamel surface, so any fracture in a cat's tooth requires endodontic or exodontic treatment.
- *Dentin* is the living tissue that comprises the bulk of the tooth surrounding the pulp cavity and covered by cementum and enamel. Dentin is 70% inorganic and 30% organic. Dentin is porous containing dentinal tubules which extend from the dentin-cementum or dentin-enamel surfaces of the tooth to the pulp and are responsible for transmission of painful stimuli if the dentin is exposed.
 - *Primary dentin* forms before tooth eruption.
 - *Secondary dentin* is produced by odontoblasts within the pulp after tooth eruption causing the dentin walls to thicken.
 - *Tertiary or reparative dentin* is morphologically irregular dentin that forms in response to an irritant.
- *Alveolar bone* is the thin layer of the mandibular and maxilla that comprises the 'tooth socket' and contains teeth.



- *Lamina dura* is a sheet of compact alveolar bone that lies adjacent to the periodontal ligament space. Radiographically it appears as a 'white line'.

Gingiva anatomy

- *Marginal gingiva* is the free gingival tissue that forms the gingival margin surrounding the crown of the tooth.
- *Attached gingiva* is located apical to the marginal gingiva and is tightly adhered to underlying alveolar bone. The attached gingival tissue is coronal to the mucogingival line. The attached gingiva is widest at the maxillary canine teeth in the cat.
- *Mucogingival line* is the junction between the alveolar mucosal tissue and the attached gingival tissue. The mucogingival line remains stationary although the gingival tissues around it may change in size or height (gingival enlargement or gingival recession).
- *Gingival sulcus* is the crevice surrounding the tooth located between the external tooth surface and the marginal gingival tissue. Normal sulcus depth in a cat is less than 1 mm.
- *Junctional epithelium* attaches to the enamel of the most apical portion of the crown. The floor of the gingival sulcus is on the most coronal portion of the junctional epithelial cells.
- *Interdental papilla* is the gingival peak between adjacent teeth.
- *Periodontium* consists of the tissues that surround and support the teeth, including the gingiva, periodontal ligament, cementum and alveolus.

Types of teeth

- *Incisors (I)* are small single rooted teeth located in the front of the mouth. They are utilized for cutting, picking up objects and grooming. Cats have six maxillary and six mandibular incisors.
- *Canines (C)* are large single rooted teeth, commonly called 'fang' teeth. They are utilized for holding prey, slashing and tearing. The lower canine teeth assist in holding the tongue in place. Cats have a right and left maxillary canine tooth and a right and left mandibular canine tooth.
- *Premolars (PM)* are located on the side of the mouth behind the canines. They are utilized for holding food and for breaking food into smaller pieces. Cats do not have a maxillary first premolar or mandibular first and second premolars. In each maxillary quadrant there is a single rooted second premolar, a two rooted third premolar and a three rooted fourth premolar. In each mandibular quadrant there is a two rooted third and fourth premolar.
- *Molars (M)* are in the back of the mouth and are used for grinding food. Cats have one maxillary first molar and one mandibular first molar.

Tooth eruption times

	Deciduous teeth (weeks)	Permanent teeth (months)
Incisor	2-3	3-4
Canine	3-4	4-5
Premolars	3-6	4-6
Molars		4-6

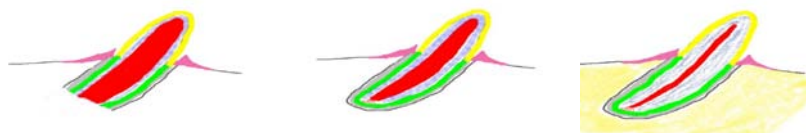
Remember there are no deciduous precursors for the molar teeth in a cat. The maxillary teeth usually erupt prior to their mandibular counterparts. The incisors generally erupt first, followed by the canine teeth then premolars and molars.

Feline dental formulas

Deciduous	$\frac{3 \ 1 \ 3}{3 \ 1 \ 2}$	total teeth = 26
Permanent	$\frac{3 \ 1 \ 3 \ 1}{3 \ 1 \ 2 \ 1}$	total teeth = 30

Permanent tooth development

At the time of permanent tooth eruption, the apex is incomplete and there is a very wide pulp cavity with primary dentin present. As the tooth continues to develop the apex closes and secondary dentin is produced by odontoblasts within the pulp cavity. As the cat continues to mature the pulp cavity continues to get smaller as the secondary dentin layer increases in thickness.



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Directional Nomenclature

- Mesial – toward the midline of the dental arch
- Distal – farthest away from the midline of the dental arch
- Vestibular – next to or toward the lips; buccal and labial are also acceptable
- Labial – next to or toward the lips
- Buccal – toward the cheek
- Lingual – next to or toward the tongue
- Palatal – toward the palate
- Apical – toward the apex (root)
- Coronal – toward the crown
- Rostral – anatomical term applicable to the head referring to a structure closer to the most forward structure of the head
- Caudal – anatomical term applicable to the head referring to a structure closer to the tail

Occlusion

Class 0 normal occlusion

- Scissors bite with the maxillary incisors overlapping, but touching the mandibular incisors in a scissor-type fashion. The maxillary incisors should be slightly rostral to the mandibular incisors. A level bite is also acceptable in cats.
- The mandibular canine teeth interdigitate in the interproximal space equidistant between the maxillary lateral incisor and canine tooth.
- The maxillary premolars interdigitate with the mandibular premolars in a “pinking shears” fashion.
- Cusp of the maxillary fourth premolar should be buccal to the mandibular first molar.

Class 1 malocclusion

- Neutroclusion, normal jaw lengths
- Individual teeth are malaligned
- Lingually displaced mandibular canine tooth, mesioversion maxillary canine tooth, rostral crossbite, caudal crossbite

Class 2 malocclusion (mandibular distocclusion)

- Mandible is shorter than the maxilla (mandibular brachygnathism) ‘overbite’ ‘parrot mouth’

Class 3 malocclusion (mandibular mesiocclusion)

- Maxilla is shorter than the mandible (mandibular prognathism) ‘underbite’

Class 4 asymmetrical malocclusion

- Can occur in a rostro-caudal, side-to-side, or dorso-ventral direction

Triadan tooth identification system

The modified Triadan system (3 numbers for each tooth) is considered to be the tooth numbering system of choice in veterinary dentistry.

The first number indicates the quadrant that the tooth is in and whether the tooth is a permanent or deciduous tooth

- Permanent tooth first numbers
 - 1 – Right maxilla
 - 2 – Left maxilla
 - 3 – Left mandible
 - 4 – Right mandible
- Deciduous tooth first numbers
 - 5 – Right maxilla
 - 6 – Left maxilla
 - 7 – Left mandible
 - 8 – Right mandible

The second and third digits indicate the tooth position within the quadrant with the sequence starting at the midline. So, 01 is the first tooth on the midline (the first incisor) and the numbering continues sequentially away from the midline.

- *Rules to remember* Rule of 4, 8 and 9
 - 04 is always the canine tooth
 - 08 is always the fourth premolar
 - 09 is always the first molar

Remember there is not a maxillary right or left first premolar in the cat (105, 205) and there is not a mandibular right or left first or second premolar in the cat (405, 406, 305, 306).

Knowledge of normal anatomy of the cat skull and oral cavity allows the veterinarian to properly evaluate and treat oral and maxillofacial diseases.

My Cat Can't Close its Mouth! How to Close the Case

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Oral and maxillofacial disorders in the cat can present as an inability to close the mouth and reaching an accurate diagnosis can be challenging if all of the differentials are not systematically considered. Differential diagnoses include: luxation of the temporomandibular joint, fracture of the temporomandibular joint, caudal mandibular fracture, impingement of the coronoid process of the mandible on the zygomatic arch, mechanical obstruction, and neuropathy. A complete intraoral examination and evaluation of a patient's occlusion often allows the clinician to identify the cause for a cat being unable to close the mouth. Periodontal disease causing tooth to tooth contact is a common and often unrecognized cause for open-mouth dental interlock and may be diagnosed without sedation or imaging.

Maxillofacial examination

Evaluation of a patient's occlusion is an essential component of all maxillofacial examinations. With normal occlusion, the maxillary and mandibular teeth should interdigitate perfectly. The maxillary incisors should be positioned slightly rostral to the mandibular incisors and the mandibular canine teeth should be positioned in the interdental space between the opposing maxillary third incisor tooth and canine tooth. The maxillary premolars interdigitate with the mandibular premolars in a "pinking shears" fashion. The buccal surface of the mandibular molar occludes with the palatal surface of the maxillary fourth premolar.

A malocclusion describes an abnormal interdigitation between the upper and lower teeth. This may be due to malposition of one or more individual teeth, where the normal relationship between the dental arches is maintained. An example of this type of malocclusion is a lingually displaced permanent mandibular canine tooth secondary to a persistent deciduous mandibular canine tooth. A malocclusion may also be caused by a skeletal abnormality. Skeletal malocclusions are often due to discrepancies in jaw lengths, as seen in mandibular mesiocclusion in brachycephalic breeds. Skeletal malocclusions may also occur secondary to deviation of bones which support the dentition, as occurs with luxation of the temporomandibular joint. Skeletal malocclusions may be symmetrical or asymmetrical. Symmetrical skeletal malocclusions are described as either class 2 (mandibular distocclusion) or class 3 (mandibular mesiocclusion). An asymmetrical skeletal malocclusion can occur in a rostro-caudal, side-to-side or dorso-ventral direction. When evaluating for normal occlusion, the teeth should interdigitate normally, the midlines of the maxillae and mandibles should align and the right and left mandibular arcades should be at the same height.

Clinical history

Cats with a history of trauma (vehicular trauma, a fight, or a fall from a height) may present with an inability to close the mouth. Differentials include luxation of the temporomandibular joint, fracture of the temporomandibular joint and mandibular fracture. Open jaw locking secondary to impingement of the coronoid process on the zygomatic arch should be considered as a differential in a cat that has a history of intermittent episodes of being unable to close the mouth without history of trauma or in a cat that acutely cannot close its mouth without previous history of any oral issues. Trigeminal neuropathy should be considered as a differential if a cat presents with a flaccid open mouth with or without history of trauma. Cats with dental interlock secondary to mechanical obstruction (secondary to neoplasia, foreign bodies, or tooth to tooth contact due to periodontal disease) do not usually have a history of trauma.

TMJ luxation

Luxation of the condylar process in a rostro-dorsal direction may occur without mandibular fracture or symphyseal separation. Physical examination of a unilateral rostro-dorsal luxation reveals an asymmetrical malocclusion with the mandibles deviated away from the side of the TMJ luxation. Bilateral rostral luxation results in slight rostral protrusion of the mandibles. Unilateral caudal luxation is rare but results in shifting of the mandibles toward the side of luxation. This often occurs with a fracture of the retroarticular process.

TMJ fractures

Fractures of the TMJ may be true intra-articular fractures of the squamous portion of the temporal bone or condylar process of the mandible, or they may be extra-articular fractures of the condylar process or retroarticular process. The degree of displacement of these fractures will often determine whether or not a malocclusion is present. One of the more common maxillofacial injuries in the cat is fracture of the condylar process. This will often cause collapse of the mandibles towards the side of the fracture, resulting in an asymmetrical malocclusion.

Mandibular fractures

Fractures of the mandibular ramus and coronoid process also frequently result in malocclusions as they are the location of insertion of the muscles of mastication. These asymmetrical malocclusions may occur in a side-to-side, dorso-ventral, and/or rostro-caudal direction. The cat's inability to close the mouth is often secondary to tooth-to-tooth contact as a result of the asymmetrical malocclusion in a side-to-side direction. Deviation of the mandibles prevents normal interdigitation of the teeth which may cause the maxillary canine tooth to contact the mandibular canine tooth, or the mandibular canine tooth to contact the palate. Fractures of the zygomatic bone or zygomatic process of the temporal bone less commonly cause a malocclusion in cats due to the wide curvature of the zygomatic arch. Bilateral caudal mandibular body fractures may also cause a cat to not be able to close the mouth. In these cases, depending on the location of the fractures, manual closure of the jaws may be accomplished if the fractures are rostral to the insertion of the adductor muscles. There may or may not be an asymmetrical malocclusion depending on the degree of displacement of the fractured segments.

Diagnostic imaging

Dorsoventral, lateral, and right and left lateral oblique skull radiographs are the standard recommended views to diagnose maxillofacial trauma but skull radiographs may be difficult to interpret due to the presence of overlapping structures. Intraoral radiography is superior to traditional skull radiographs for evaluating the dental arches. Advanced imaging such as computed tomography (CT) should be considered with maxillofacial trauma in a cat as studies have shown that trauma often results in multiple maxillofacial injuries. Computed tomography should be considered for any cat with maxillofacial trauma to allow for more accurate diagnosis, treatment planning and prognosis.

Treatment

Treatment for TMJ luxation or mandibular fractures causing a cat to be unable to close their mouth is dependent on the type of injury. Closed reduction of a TMJ luxation following acute injury should be attempted to avoid formation of fibrous tissue within the joint space. Nonsurgical versus surgical treatment of TMJ and mandibular fractures depends on whether or not the articular surface is involved, the degree of stability and/or displacement, and the presence of ankylosis. Maxillomandibular fixation is often the treatment utilized for stabilization of caudal mandibular fractures, fractures involving the temporomandibular joint and TMJ luxations if they are unstable after reduction.

Open mouth jaw locking secondary to impingement of the coronoid process on the zygomatic arch

Impingement of the coronoid process of the mandible on the zygomatic arch is a relatively uncommon cause for a cat to be unable to close the mouth. Rotation of the mandibles and subsequent lateral flaring of the coronoid process allows the coronoid process to engage the zygomatic arch after the mouth is opened wide. The most dorsal portion of the coronoid process is then lateral to the zygomatic arch, preventing closure of the mouth.

Clinically, these patients present with intermittent episodes of being unable to close the mouth without a history of trauma. These episodes often resolve spontaneously by opening the mouth wider, allowing the coronoid process to disengage from the zygomatic arch and move medially into a normal anatomic position.

Physical examination during an open-mouth locking episode reveals an asymmetrical malocclusion in a side-to-side direction with the mandibles deviated towards the side where the coronoid process is contacting the zygomatic arch. There may also be an asymmetrical malocclusion in a dorso-ventral direction with the affected mandible displaced slightly ventral compared to the contralateral mandible due to rotation of the mandibles. A palpable and visible bulge lateral to the zygomatic arch where the coronoid process is displaced may be detected. Physical examination after the locked jaw has been reduced, either manually or spontaneously by opening the mouth wider to disengage the coronoid process, may be normal, or there may be discomfort on palpation or manipulation of the head and jaws. Manipulation of the mandibles under general anesthesia in a rotational manner can recreate the displacement of the coronoid process to engage the ventral or lateral aspect of the adjacent zygomatic arch. This should be attempted on both sides as bilateral TMJ laxity with alternating right and left locking episodes is possible. If the joints are normal, locking cannot be recreated, although it is possible that manipulation of the mandibles even in patients with TMJ laxity may not result in open-mouth jaw locking.

Diagnostic imaging

Skull radiographs during a locking episode may reveal contact between the coronoid process and zygomatic arch. Skull radiographs may also show evidence of the associated structural abnormalities possible with TMJ dysplasia or widened joint spaces of either the ipsilateral, contralateral, or bilateral joints. When radiographs are normal, CT should be considered to detect abnormalities of the TMJ as CT of the TMJ has been shown to be more sensitive than conventional radiography.

Treatment

Treatment options for lateral impingement of the coronoid process on the zygomatic arch include partial ostectomy of the ventral margin of the zygomatic arch, coronoidectomy, partial resection of the rostral portion of the zygomatic arch in combination with partial resection of the coronoid process, temporary maxillomandibular fixation, imbrication-plication of the lateral aspect of the TMJ capsule, and mandibular condylectomy. Partial coronoidectomy alone has been 100% successful in the three reported cases, is

reportedly easier to perform and less invasive. If the jaw locking is secondary to excessive laxity of the mandibular symphysis, symphysiotomy, symphysiectomy and intermandibular arthrodesis has been successful in one cat.

Trigeminal neuropathy

Animals with bilateral neurologic dysfunction of the mandibular branch of the trigeminal nerve, or trigeminal neuropathy, may present with an inability to close the mouth. To the authors' knowledge, trigeminal neuropathy in cats has not been previously reported, although the authors have seen one such case in a six year old cat. Clinical signs reported in dogs and in the cat observed by the authors include an acute onset of a dropped jaw, difficulty prehending, messy eating and drooling. The mouth hangs down passively, can be closed by manually lifting the mandibles, and falls back into its former dropped position when released. Unlike cases of bilateral caudal mandibular fractures, animals with trigeminal neuropathy are not painful when the mouth is manipulated.

The mandibular branch of the trigeminal nerve supplies both motor and sensory innervation to all of the muscles of mastication responsible for closing the mouth. The mandibular nerve and its branches to the muscles of mastication are closely related to the joint capsule of the TMJ and stretching of the nerve during wide opening of the mouth has been postulated to be a cause of interference with nerve function. The cat treated by the authors was fed through an esophagostomy tube and continued on pain medications without other treatment. The cat regained most voluntary jaw movement after 15-20 days and full control returned after 32 days. Electromyography can be used to confirm the diagnosis, although practically, a flaccid paralysis of the mandibles without evidence of caudal mandibular fractures can be sufficient to make a presumptive diagnosis of trigeminal neuropathy. Central neurologic lesions and rabies should also be considered if there is evidence of other cranial nerve deficits or systemic weakness.

Open mouth dental interlock

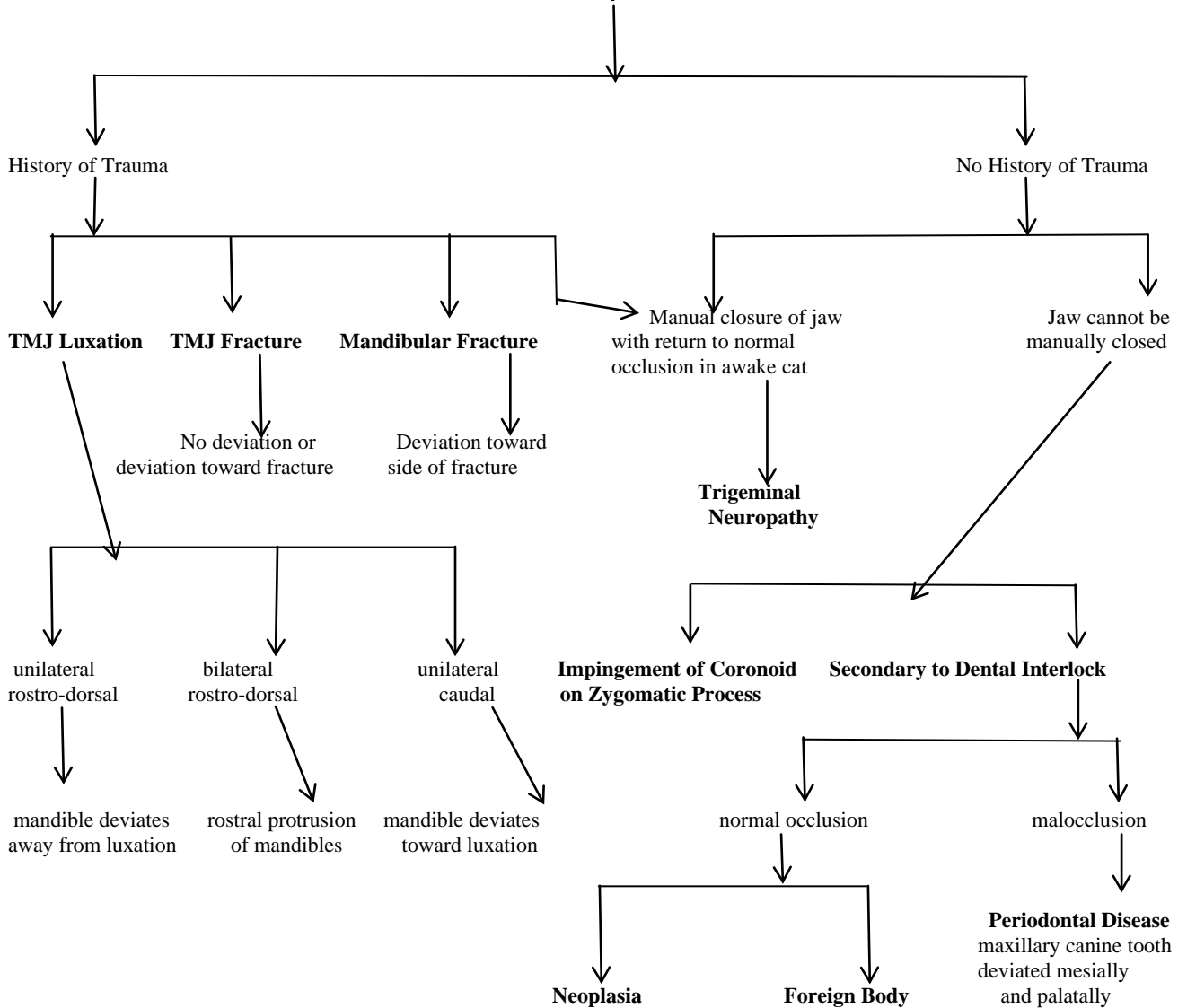
Mechanical obstruction independent of the temporomandibular joint is a common cause for open-mouth jaw locking in cats. Mechanical obstruction may be caused by oral foreign bodies, soft tissue swelling, neoplasia, or tooth-to-tooth contact. Tooth-to-tooth contact may be secondary to trauma resulting in displacement of a tooth, but is often seen in cats as a result of periodontal disease associated with a maxillary canine tooth. Periodontitis is inflammation of the periodontium, or tissues that support the tooth (gingiva, periodontal ligament, alveolar bone and cementum) and results in loss of tooth attachment. Advanced periodontitis may lead to significant bone loss, deep periodontal pockets and tooth mobility. Periodontal disease affecting the canine teeth in cats may be associated with alveolar osteitis and extrusion of affected teeth. Clinically, there may be expansion of the buccal alveolar bone making the bone appear "wider" than normal and supraeruption making the tooth appear "longer" than normal. With enough attachment loss, extrusion and mobility, the maxillary canine tooth may deviate mesially and palatally to occlude lingual to the mandibular canine tooth resulting in open-mouth dental interlock secondary to the tooth-to-tooth contact.

A complete intraoral examination, including observation of the occlusion in an awake cat, allows the clinician to differentiate open-mouth dental interlock secondary to periodontal disease from lesions of the temporomandibular joint without sedation or imaging. If general anesthesia is necessary, tooth mobility is confirmed, and dental probing as part of the clinical oral examination detects deep periodontal pockets. Intraoral radiographs may reveal vertical bone loss around the tooth root and expansile buccal alveolar bone. Temporary replacement of the affected mobile maxillary canine tooth into the normal position results in a return to normal occlusion. Definitive treatment is oral surgery to extract the periodontally diseased maxillary canine tooth.

Despite the numerous differential diagnoses for a cat that is unable to close the mouth, a complete physical examination including a thorough intraoral examination and observation of the occlusion may eliminate some of the conditions prior to sedation or imaging. A combination of skull radiographs and skull CT may be necessary for accurate diagnosis and treatment planning. An understanding of the anatomical structures of the head, in combination with a complete extraoral and intraoral examination and observation of the patient's occlusion, allows the clinician to quickly and efficiently obtain a diagnosis when presented with a cat who is unable to close the mouth.

References available upon request.

Cat Presents with Inability to Close Its Mouth



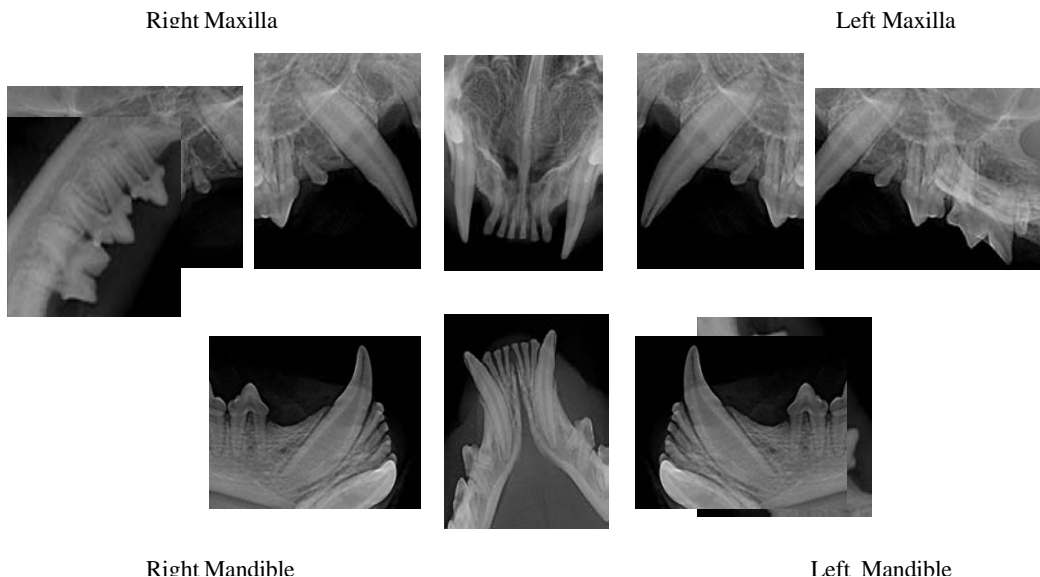
Shades of Gray: Interpretation of Feline Dental Radiographs

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As with any new piece of equipment in veterinary hospitals, there is a learning curve associated with dental radiography – both in obtaining diagnostic dental radiographs and interpretation of dental pathology.

With digital images, the image appears on the computer screen. When obtaining intraoral radiographs the following tips will help you orient the image in the same way each time for evaluation. Some veterinary software programs will label the images with the tooth number or tooth as you expose them. First, if the tooth being imaged is a maxillary tooth the tooth crowns should point down and if the tooth being imaged is a mandibular tooth the tooth crowns should point up. Remember that all three rooted teeth are located in the maxilla. The presence of the palatine fissures, nasal passages and sinuses indicate the tooth is in the maxilla. Visualization of the mandibular canal or ventral cortex of the mandible confirms that the tooth is a mandibular tooth. After determining if the tooth is in the maxilla or mandible then determine if you are viewing the right or left side. When viewing the right side of the mouth the anterior teeth are on the right side of the image and when viewing the left side of the mouth the anterior teeth are on the left side of the image. Depending on the imaging software the images may appear on the computer screen in the correct orientation.

When mounting full mouth radiographs, the patient's right maxilla and right mandible are on the viewer's left side and the patient's left maxilla and left mandible are on the viewer's right side. (Remember that the viewer is standing on the outside of the patient's mouth looking at the patient.)



Knowledge of normal anatomy of the tooth, mandible and maxilla is essential for the proper evaluation of dental radiographs. The components of the tooth and its supporting structures are usually well defined on dental radiographs. These structures include the following:

- *Enamel*: the outermost layer of the crown of the tooth
- *Cementum*: the outermost layer of the root of the tooth
- *Cementoenamel junction*: area where the cementum and enamel meet
- *Dentin*: radiopaque layer between the outermost surfaces of the crown and root and the radiodense pulp cavity
- *Pulp cavity*: radiodense area within the tooth and roots including the pulp chamber, pulp horns and root canal.
- *Periodontal ligament space*: thin radiolucent area between the root of the tooth and the lamina dura
- *Lamina dura*: the cribiform plate and dense alveolar bone surrounding the root which appears as a radiopaque line adjacent to the periodontal ligament space
- *Alveolar bone*: encases and supports the tooth structure
- *Alveolar margin*: most coronal portion of the alveolar bone, located between teeth, composed of dense cortical bone
- *Furcation*: the anatomic area of a multi-rooted tooth where the roots diverge
- *Periapical*: the area around the tooth apex

The mandibular canal is visible as a radiolucency of uniform width in the mandible parallel to the ventral border of the mandible. The caudal, middle and rostral mental foramen may be mistaken for periapical pathology in the area of the mandibular premolars. The middle mental foramen is located distal to the apex of the canine tooth in the cat. (To distinguish the foramen versus a periapical lucency, change the horizontal angle of the tubehead. If the lucency remains associated with the apex of the tooth it is indeed a periapical lucency. The foramen will move relative to the root as the horizontal angle of the tubehead is changed.) The mandibular symphysis appears as a linear radiolucent line between the central incisors.

In the maxilla the symmetrical radiolucent structures which appear distal to the maxillary incisors are the palatine fissures. The junction of the vertical body of the maxilla and its palatine process is visualized as a radiopaque line that crosses the midroot section of the maxillary canine tooth.

Radiographs should include the entire crown and root of the tooth being imaged and 3 mm of alveolar bone around the tooth apex. The following generalizations can be made about dental radiograph interpretation.

Radiographic signs of feline tooth resorption include defects present at the cemento-enamel junction and/or roots with evidence of root replacement. Clinically, there are two types of tooth resorption in cats. Tooth resorption type I lesions have normal root density and a well-defined periodontal ligament space around the tooth root. Often these teeth have associated horizontal or vertical bone loss. Tooth resorption type II lesions have root replacement resorption with no discernible periodontal ligament space and the roots appear to blend in with the surrounding bone. Both types of tooth resorption can be found in the same cat and even in the same tooth. Differentiation between type I and type II tooth resorption in feline patients is important to determine the appropriate treatment for these teeth. Type I tooth resorption is treated by extraction of the entire tooth and root. Type II tooth resorption is treated by crown amputation with intentional root retention.

Radiographic signs of periodontal disease may include: widening of the periodontal space; resorption of the alveolar crest; decreased alveolar bone density and horizontal, vertical, angular or furcation bone loss. Remember that 30-60% of the bone must be lost before it is visible radiographically. Horizontal bone loss involves the buccal, lingual and interdental portions of bone and appears as decreased alveolar marginal bone around the tooth. Vertical bone loss usually appears as an area of decreased bone density surrounding the tooth root and may appear to as a 'V' shape adjacent to the tooth root. It is important to recognize that clinical examination in combination with dental radiographs is necessary to properly diagnose periodontal disease. Mild bone loss, stage 1 furcation exposure, vertical bone loss on the palatal side of the maxillary canine teeth may not be visible radiographically, only clinically. In addition, proper exposure is necessary to evaluate the alveolar bone margin. Overexposure of the dental radiograph may result in 'burnout' of the alveolar bone margin and interdental bone.

Radiographic signs of endodontic disease include changes associated with the bone surrounding the tip of the root (periradicular area) and changes within the pulp cavity or tooth itself. Radiographs to evaluate a tooth for endodontic disease should include the entire root tip and the surrounding bone. The characteristic radiographic lesion of endodontic origin (LEO) involves changes in the periapical radiodensity (often appearing as a radiolucency) or detail that results from apical periodontitis. Lesions of endodontic origin can also develop along the lateral aspect of the root at the site of a lateral canal. Remember that lack of radiographic lesions does not rule out endodontic disease.

Radiographic signs of endodontic disease that are associated with the tissues around the tooth may include: increased width of the periodontal ligament space, loss of the radiopaque lamina dura, diffuse periapical lucency, well defined periapical lucency, or a diffuse area of radiopacity.

Radiographic changes within the tooth are often associated with endodontic disease. When a permanent tooth first erupts, the apex is open, the pulp canal is very wide and the primary dentin layer is thin. Next, the apex closes and then as the tooth continues to mature, the odontoblasts within the pulp canal continue to lay down dentin (secondary dentin). As the tooth continues to mature, the secondary dentin becomes thicker as the pulp canal decreases in width. Radiographically, a tooth that became non-vital during the maturation process will have a pulp canal larger than the contralateral tooth indicating arrested tooth maturation. A seemingly narrow pulp cavity can result from pulpitis that is generalized over a section of the root canal.

Internal root or crown resorption, caused by inflammation in the pulp, appears as an irregularly shaped root canal system. Internal root resorption results from removal of dentin from the wall of the pulp cavity. An internal resorption lesion does not move with change in horizontal angle of the beam of the radiograph (it stays associated with the root canal system).

External resorption resulting from inflammation in the periodontal ligament appears as an irregular defect in the external surface of the tooth root. An external root resorption that is overlying the root canal system will move relative to the root canal system with a change in horizontal angulation of the beam of the radiograph.

- Radiographic signs of aggressive jaw lesions include:
 - Lytic areas of variable size or uniformly pinpointed
 - Indistinct margins
 - Lysis of the cortex
 - Layers of varied opacity or sunburst effect

- Teeth in position, floating in space
- Bone is moth eaten in appearance
- Root structure is irregular
- Increased tooth mobility
- Radiographic signs of non-aggressive jaw lesions include:
 - Well defined areas of lysis
 - Distinct regular, smooth or sclerotic margins
 - Expanding or thinning of cortex
 - Uniform opacity or lamellar onion skin pattern
 - Displaced teeth
 - Tooth mobility may be affected

Dental radiography is an essential part of the evaluation of oral and maxillofacial diseases. In combination with a complete extraoral and intraoral examination, including the use of a dental probe and explorer, intraoral radiography makes dentistry a science based on fact and provides veterinarians with the tools to properly evaluate and treat oral disease.

Feline Gingivostomatitis: What We Know and How We Treat It

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Stomatitis is a term used to describe widespread inflammation of the oral cavity. Gingivostomatitis means inflammation of the gingival tissues and oral cavity. Cats with stomatitis may have inflammation or ulceration and/or proliferative lesions anywhere within the oral cavity. The lesions may involve the gingival tissues, alveolar mucosal tissues, caudal buccal mucosal tissues, the area lateral to the palatoglossal folds in the caudal oral cavity, the sublingual tissue and/or the oropharyngeal tissues.

Terms used to describe oral and oropharyngeal inflammation in the feline oral cavity include:

- Gingivitis: inflammation of the gingiva
- Periodontitis: inflammation of the non-gingival periodontal tissues (periodontal ligament and alveolar bone)
- Alveolar mucositis: inflammation of the alveolar mucosa (mucosa overlying the alveolar process and extending from the mucogingival junction without obvious demarcation to the vestibular sulcus and floor of the mouth)
- Sublingual mucositis: inflammation of the mucosa on the floor of the mouth
- Labial / buccal mucositis: inflammation of the lip / cheek mucosa
- Caudal mucositis: inflammation of the mucosa of the caudal oral cavity, bordered medially by the palatoglossal folds and fauces, dorsally by the hard and soft palate and rostrally by the alveolar and buccal mucosa
- Palatitis: inflammation of the mucosa covering the hard and soft palate
- Glossitis: inflammation of the mucosa of the dorsal and/or ventral tongue surface
- Cheilitis: inflammation of the lip (including the mucocutaneous junction area and skin of the lip)
- Osteomyelitis: inflammation of the bone and bone marrow
- Stomatitis: inflammation of the mucous lining of any of the structures in the mouth; in clinical use the term should be reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues (i.e. marked caudal mucositis extending into submucosal tissues may be termed caudal stomatitis).

Etiology/pathogenesis

It is thought that stomatitis is a multifactorial disease where the cat's immune system responds inappropriately to chronic oral antigenic stimulation of various origins. Antigens may include plaque bacteria, feline calicivirus and food proteins. Periodontal disease, tooth resorption, as well as viral infections (FIV, Feleuk, calici, herpes) have been suggested to play a role. Genetic predisposition, food allergies, and bacteria may also play a role in feline oropharyngeal inflammation. Current thought is that cats with feline chronic gingivostomatitis have an inappropriate response or 'hyper' immune response to the dental plaque bacteria. Specific bacteria, as seen in periodontal disease, have been reported in these cats. *Pasteurella* and *Prevotella* species are more highly represented than others. Calici virus is present in 97% of cats affected by chronic oropharyngeal inflammation when compared to a control group (25%); however no cause and effect has been established. Some cats with stomatitis test positive for *Bartonella*, but again a cause and effect has not been established. We do not know for sure what causes the disease which makes treatment of the disease challenging.

Cats with chronic gingivostomatitis most often have bilateral disease. Differential diagnoses include eosinophilic granuloma complex, periodontitis, neoplasia (squamous cell carcinoma, fibrosarcoma), uremic stomatitis, caustic chemical ingestion, plant irritation, electrical cord burn, food allergies, and systemic autoimmune diseases (lupus, pemphigus).

History and clinical signs

A thorough history is the first step in evaluation of any patient with oral disease. Factors to be considered include the patient's diet, age at onset of clinical signs, onset and duration of clinical signs, environmental hazards, chronic illness, and / or systemic disease. The median age of affected cats is seven years. No gender predilection has been reported.

Clinical signs may include anorexia, weight loss, hypersalivation, pawing at the face, pain when opening the mouth or yawning, dropping food, and/or reluctance to eat hard food. The patient's haircoat may be matted and unkempt due to the decrease in self grooming that occurs secondary to oral pain. Halitosis and blood tinged saliva may also be present.

The second step in patient evaluation is a complete physical exam to evaluate all organ systems. A complete intraoral examination will help to determine the extent of disease and identify any teeth with tooth resorption or periodontal disease. A complete examination under general anesthesia including full mouth radiographs is the only way to determine the true extent of oral pathology.

Laboratory tests should include a CBC, biochemistry profile, thyroid panel and urinalysis to rule out concurrent systemic disease. A feline leukemia and FIV test should be completed to rule out concurrent viral disease. Many cats with stomatitis will have elevation

of total protein and globulins. Other tests that may be included in the patient evaluation are toxoplasmosis titer, Bartonella screening, viral testing for calici and herpes virus, immune profiles (ANA) and serum protein electrophoresis.

Treatment

Feline stomatitis is often a frustrating disease to treat. As there is no known single etiology, treatment success varies with every case. The goal of treatment is to restore the balance between the cat's immune response and the oral antigen burden. Currently there is no known medical protocol that consistently has positive *long term* results. Treating with medications usually is only masking the underlying issue of a hyperimmune response to plaque. Extraction of teeth in the vicinity of the alveolar mucositis and caudal stomatitis and extracting teeth with periodontal disease or tooth resorption in order to suppress any chronic oral antigenic stimulation has shown the best results.

The extent of disease at the time of presentation determines the appropriate first stage of treatment. If the patient presents with *very mild* disease, initial treatment includes periodontal therapy, full mouth radiographs and extraction of any teeth affected by periodontal disease or tooth resorption. The goal of treatment is to remove the bacterial plaque and bacterial byproducts that are toxic to the periodontal tissues with thorough supragingival and subgingival scaling and polishing. It is imperative to remove all inflammation within the oral cavity. Biopsy of affected tissue should be obtained to rule out neoplasia. Histopathology of the mucosa and submucosa reveals dense infiltrates of plasma cells with lesser numbers of lymphocytes, neutrophils and macrophages which is consistent with virtually any inflammation in a cat's mouth. After the procedure, daily home care is required to maintain a plaque free environment. A chlorhexidine gel applied daily may assist with plaque control. Daily brushing, if the cat will allow it, remains the most effective way to control plaque. In addition to daily brushing, use of Veterinary Oral Health Council (VOHC) accepted diets, treats and/or water additives to control plaque is recommended.

If the owner is unable or unwilling to provide homecare, or if the inflammation persists in spite of home care, or if the inflammation in the oral cavity is moderate to severe, then oral surgery to extract the premolars and molars and/or canines and incisors is recommended. The purpose of extraction is to lower the chronic antigenic stimulation from the plaque bacteria. Traditional medical therapy usually does not control the disease and resolve clinical signs. If there is no visible inflammation in the caudal buccal mucosal tissues or around the canine teeth and incisors then extraction of all of the premolars and molars is recommended. If there is periodontal disease or tooth resorption affecting the canine teeth and/or incisors they are extracted in addition to the premolars and molars. If there is inflammation involving the gingival tissue surrounding the canines and incisors or if there is inflammation in the caudal buccal mucosal tissues then initial oral surgery should be completed to extract *all* of the teeth.

With oral surgery it is essential to remove the entire tooth root. Full mouth radiographs *must* be obtained preoperatively. In each quadrant, a mucogingival flap is elevated and buccal bone is removed to expose the furcation of multi-rooted teeth. Each tooth is sectioned and the tooth roots are elevated and extracted. The alveolar bone should be smoothed with a diamond bur (alveoplasty). Each alveolus should be debrided and cleaned with either a diamond bur or hand curette to ensure removal of all tooth, root, and periodontal ligament and bone particles. Following extraction radiographs are obtained to confirm extraction of all tooth roots. NO tooth roots, root fragments or tooth remnants may remain. The periosteum of the flap is released and the alveolar gingival tissue is sutured to the lingual or palatal mucosal tissue utilizing absorbable sutures.

Pre-, intra- and postoperative analgesia is very important in these patients. Utilization of a multimodal preemptive pain management protocol is recommended.

If clinical symptoms persist after extraction of premolars and molars then the author recommends extraction of the remaining incisors and canine teeth to eliminate *all* plaque retentive surfaces. If inflammation still persists, then adjunctive medical treatment is recommended. Remember, most of these patients have had inflammation for a long time prior to presentation, so the inflammation within the oral cavity is not likely to resolve quickly after surgery. Medications may be necessary for an interim period while the patient's immune system responds. Frequent periodic monitoring of these patients is required to adjust medications and treatment based on each individual's response. There are no current studies to support the use of one particular medication over the others as the 'best' medical option.

Medical management of refractory cases

The primary goal of any treatment for a cat with gingivostomatitis is to decrease inflammation, pain, infection, and to modulate the host's immune response. Medical treatment is sometimes necessary *after* oral surgery to control disease in resistant cases.

Anti-inflammatory drugs

Use of these drugs as a sole treatment for cases with stomatitis is *not* recommended. Use of long term steroids can lead to diabetes mellitus and can decrease the body's ability to resist the inflammatory process. Often with long term use of steroids, cats seem to develop 'resistance' and their response to the drug decreases.

Prednisolone - 2 mg/kg daily for a week, then 1 mg/kg daily for a week then a maintenance dose of 0.5-1 mg/kg every other day (goal is to decrease to the lowest effective dose)

Oral triamcinolone - 1.5 mg per cat once daily for a week, then every other day for a week, then every 3 days. Then leave at twice a week for a few months and occasionally try weaning off medication. The pill can be crushed to a powder and suspended in water for administration.

Methylprednisolone acetate 15-20 mg/cat SQ every 3-6 weeks as needed

Antimicrobials

Use of antimicrobials will decrease the bacterial load in the oral cavity, but should *not* be utilized alone in cases of stomatitis. The most commonly used drugs include amoxicillin-clavulanic acid, clindamycin, doxycycline and metronidazole. Azithromycin has been suggested for use in Bartonella positive cats with gingivostomatitis. Studies by Dower and Quimby did not find any correlation between cats with gingivostomatitis and Bartonella and found treatment with azithromycin unrewarding. Chlorhexidine gluconate oral rinses have a bacteriostatic action, though most cats with a painful mouth resist oral rinses. Doxycycline has an inhibitory effect on the secretion of matrix metalloproteinases (which destroy collagen and other matrix components) by gingival PMNs. Use of a submicrobial dose may result in a decrease of gingival collagen destruction. This author has used a dose of 10 mg/cat twice daily for two weeks, then once daily for two weeks, then every other day if the patient shows clinical response. Some patients may require doxycycline at the lowest effective dose forever.

Immune modulating drugs

Cyclosporine is an immunosuppressant that focuses on cell mediated immune responses. While the exact mechanism of action is unknown, it is believed that it acts by a specific, reversible inhibition of immunocompetent lymphocytes in the G₀ or G₁ phase of the cell cycles. T-helper lymphocytes are the primary target, but T-suppressor cells are also affected. Lymphokine production and release (including interleukin-2, T-cell growth factor) are also inhibited by cyclosporine. Potential side effects include vomiting, diarrhea, hepatic dysfunction, impaired renal function, anemia, hypertrichosis, and gingival hyperplasia. Monitoring with complete blood counts and biochemistry profiles is recommended. Adjunct treatment with corticosteroids may be necessary.

Feline recombinant omega interferon (Virbagen Omega^R, Virbac) are immune modulating cytokines labeled for use in Europe to treat FeLV and/or FIV. It may also be of benefit in acute feline calicivirus infections and FIP. Its principle action is not as a direct anti-viral, but by acting on virus infected cells inhibiting mRNA and translation proteins, thereby inhibiting viral replication. Feline omega interferon has more antiviral effects against certain viruses than human alpha interferon. Virbagen Omega^R has been used in cats that are refractory to traditional treatments for gingivostomatitis. The therapeutic effect of interferon after oromucosal administration is due to the immunomodulatory activity through the oropharyngeal lymphoid tissues and via paracrine activity as this glycoprotein is destroyed during transit through the digestive tract. A randomized double blinded multicenter study was conducted studying calici positive cats presenting with persistent caudal stomatitis after dental extractions. The study showed that treatment with oral feline omega interferon resulted in significant clinical improvement and was found to be at least as good as short term prednisolone therapy in the treatment of calici virus positive cats presenting with caudal stomatitis after dental extractions. Virbagen Omega^R is not currently licensed for use in the US.

Other medical options

Lysine 250 - 500 mg/cat PO BID Lysine is an amino acid that is thought to compete with arginine for incorporation into many herpes viruses. As it is believed that arginine is required for producing infective virus particles, when lysine is incorporated the virus becomes less infective.

Niacinamide 500 mg ¼ tablet twice daily Used in canine medicine in combination with tetracycline to treat immune mediated skin conditions. It blocks IgE induced histamine release and degranulation of mast cells. When used with tetracycline it may suppress leukocyte chemotaxis secondary to complement activation by antibody antigen complexes. It also inhibits phosphodiesterases and decreases the release of proteases.

Esterified fatty acids

Esterified fatty acid complexes are administered orally and work transmucosally to modulate local inflammation.

Laser treatment

There is only one case study reporting the use of CO₂ laser treatment in a cat with gingivostomatitis. The study concluded that laser therapy is a viable adjunct, but should not be considered as a stand-alone modality or replacement for full mouth or nearly full mouth extractions. The goal of laser treatment is to remove the proliferative tissue to resolve the self-induced trauma and entrapment of food and debris in the tissue pockets; stimulate fibrosis to make the tissues less prone to continued inflammation and proliferation; and reduction of opportunistic bacteria. Laser treatment may also provide some pain relief as the surface nerve endings are cauterized.

Prognosis

Hennet studied the effectiveness of dental extractions: 60% of cats were clinically cured; 20% showed significant improvement with minor flare ups; 13% showed only little improvement and required continued medications; and 7% were refractory to treatment showing no improvement. A study of treatment outcome following full mouth extraction published by Girard in 2005 showed 50% resolved without further treatment, 37% improved but required continuing medical treatment and 13% did not improve. There is

continuing discussion regarding which teeth should be extracted - all premolars and molars only or extraction of all teeth (including canine teeth and incisors). There is currently no published data to support either treatment modality.

Owners of cats with stomatitis should understand that not all cats respond to treatment and this disease is often frustrating to treat. It requires consistent treatment and frequent monitoring of the cat's response to treatment.

Feline Oral Tumors: Diagnosis and Treatment

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Oral tumors account for 7- 12% of all feline tumors and 90% of oral tumors in cats are malignant. They may be of dental (odontogenic) or non-dental origin. Squamous cell carcinoma is the most common oropharyngeal cancer in cats accounting for 60-80% of all oral tumors, followed by fibrosarcoma which accounts 13-22% of feline oral tumors.

History and clinical signs

Cats with oral tumors may present with drooling, exophthalmos, facial swelling, epistaxis, sneezing, weight loss, dysphagia, anorexia, decreased appetite, reluctance to eat hard food, decreased activity, hiding and less interactive, halitosis, an unkempt haircoat due to poor grooming, and/or pain when opening the mouth. Beware that loose teeth in a cat with otherwise good dentition could indicate an underlying neoplastic process causing bone lysis.

Clinical staging

Clinical staging of the tumor should be completed utilizing the TMN system which involves assessment of the primary tumor (T), assessment for metastasis to distant sites (M) and to regional lymph nodes (N).

Evaluation of the primary tumor (T)

Evaluation of the primary tumor should include a clinical examination, diagnostic imaging and histopathological evaluation. The size and location of the tumor, the presence of any ulceration or necrosis, and any abnormal mobility of associated teeth should be noted. Clinical features suggestive of a malignancy include rapid growth, fixation to underlying tissue, displacement of teeth, facial deformity, ulceration, and poorly defined margins. Clinical features suggestive of a benign oral mass include and expansile, fluid filled mass.

Diagnostic imaging of the tumor

Dental radiographs should be obtained of the affected jaw to evaluate the extent of involvement of adjacent teeth and alveolar bone associated with the mass. Bone lysis is not radiographically apparent until more than 40% of the cortex of the bone is demineralized. Therefore, radiographs usually underestimate the extent of the tumor. Computed tomography is a valuable and more sensitive diagnostic tool for evaluation of bone invasion and possible extension of the oral tumor into the nasal cavity, caudal pharynx and orbit. CT imaging should be utilized for maxillary tumors and caudal mandibular tumors.

Incisional biopsy

An incisional biopsy is the procedure of choice for most oral soft tissue tumors. Punch biopsy has been shown to produce fewer artifacts than scalpel biopsy. Biopsies should be at least 4-6 mm in diameter with a depth of at least 2 mm. For incision of a hard tissue mass, consider the use of a Michel trephine. It is important to obtain the biopsy from within the oral cavity and not through the lip to avoid seeding the tumor cells into normal skin. Keep in mind the planned definitive surgical resection when obtaining biopsies. The biopsy should always be obtained within the the worst part of the lesion. Multiple biopsies may be obtained. Avoid necrotic and infected areas of the tumor and do not sample at the margin of the mass. When obtaining the biopsy consideration should be given to the plan for definitive surgery so the biopsy site is included in the definitive surgery.

Evaluation for distant metastasis (M)

Three view thoracic radiographs or thoracic CT should be evaluated for distant metastasis. CT is significantly more sensitive than thoracic radiographs for detecting soft tissue nodules. The lower size threshold is 1 mm to detect pulmonary nodules on CT images and 7-9 mm to reliably detect pulmonary nodules on radiographs. Cats less frequently develop the classical well defined appearance of lung metastasis. Metastatic disease can appear as ill-defined mass lesions or diffuse alveolar, interstitial or mixed patterns.

Lymph node evaluation (N)

Lymph nodes may be assessed by palpation to evaluate size, mobility, firmness, single vs multiple nodes, ipsilateral vs contralateral and bilateral distribution. Lymph node size is not a reliable predictor of metastasis. Remember that the lymph nodes that drain the oral cavity in the cat include the mandibular, parotid and medial retropharyngeal. Ruling out mandibular lymph node metastasis does not rule out metastatic disease. Lymph node evaluation may include fine needle aspirate of mandibular lymph nodes and/or evaluation of the other lymph nodes during CT evaluation of the oral mass.

Squamous cell carcinoma (SCC)

Squamous cell carcinoma is the most common oral tumor in cats accounting for approximately 65% of all oral tumors. Affected cats tend to be older, but may be as young as 5 months to as old as 21 years of age with a median age of 12 years. There is no gender

predilection. Various studies have shown an increased incidence of squamous cell carcinoma in cats that wear flea collars, cats that are exposed to environmental smoke, and cats with high canned food intake.

Squamous cell carcinoma in cats most often affects the frenulum and ventral surfaces of the tongue. The gingival tissue adjacent to the maxilla and mandible is second most common site. It is uncommon for the tonsil in the cat to be the primary location for a squamous cell carcinoma. Most squamous cell carcinomas occur caudal to the canine teeth. Squamous cell carcinoma is very invasive into the gingival tissue and underlying bone and may extend to involve the palate, pharynx or ramus of the mandible.

Bone invasion in feline squamous cell carcinoma is usually extensive and radiographically these cancers cause an intensely sclerotic, periosteal proliferation in the mandible. Marked osteolysis can also occur. In a study of cats with mandibular swellings only 50% had a tumor and osteomyelitis could not be differentiated from cancer based on radiographic appearance.

Nodal metastasis is seen in about 10% of affected cats. When lymph node metastasis is present the mandibular and retropharyngeal lymph nodes are most commonly affected. Lung metastasis in cats is rare, though it is not possible to determine a true metastatic rate since so few cats have their local disease controlled.

Squamous cell carcinoma in cats is very frustrating to treat as most cases are diagnosed at a late stage in the disease process, leading to few viable treatment options. There is no known effective treatment that consistently yields disease control or survival. If the tumor is located in the rostral mandible and discovered early in the course of disease a mandibulectomy and/or radiation treatment might be considered. Radiation therapy in conjunction with surgery or used alone still results in local recurrence of the tumor. Chemotherapy alone or in combination with radiation therapy has done little to improve survival times in cats with squamous cell carcinoma. The best treatment for squamous cell carcinoma has yet to be determined. Unfortunately palliative care is the most common method of treatment due to poor prognosis and extensive tumor involvement at the time of diagnosis. Palliative treatment may include tube feeding, analgesics and anti-inflammatory drugs. Overall median survival time in cats with squamous cell carcinoma is 44 days. Cats with squamous cell carcinoma have a poor prognosis with a one year survival of less than 10%.

Fibrosarcoma

Oral fibrosarcoma is the second most common oral tumor in cats and does not have a site predilection. Age of affected cats ranges from 1 to 21 years with a mean of 10.3 years. These tumors are locally invasive and metastasis is rare. The tumor arises from the submucosal stroma and is accompanied by local tissue destruction and invasion of skeletal muscle and bone. The preferred treatment is surgical excision with wide margins. As with squamous cell carcinomas, surgical excision is usually not possible due to the advanced disease at the time of diagnosis. Palliative radiation can be considered.

Osteosarcoma

Feline osteosarcoma accounts for 2.4% of all oral tumors and occurs most commonly in older cats with a median age of 10.5 years. Mandibulectomy alone or in combination with radiation or chemotherapy was associated with a 1-3 year survival rate and progression free rate of 83%.

Treatment of fibrosarcoma and osteosarcoma with mandibulectomy showed more than 80% of cats with osteosarcoma and 66% of cats with oral fibrosarcoma were alive three years after surgery. Radiation was used in some of these cases with incomplete surgical margins. Remember to support cats with feeding tubes after mandibulectomy.

Melanoma

Oral melanoma is rare in cats (less than 3% of oral tumors). Metastatic disease is common in cats with oral melanoma. In a small study, median survival of cats with oral melanoma was less than 5 months and no cat lived longer than 8 months.

Lymphoma

Oral and tonsillar lymphoma has been reported in cats, with 11 (2.9%) of a total of 371 cats affected. The appearance was described as single or multiple raised submucosal masses composed of unencapsulated sheets of neoplastic lymphoid cells. Radiation treatment alone or in combination with chemotherapy has been used to treat cats with oral lymphoma.

Salivary gland tumors

Salivary adenocarcinomas originate from the major (parotid, mandibular, sublingual, zygomatic) or minor salivary glands. Minor salivary glands include the lingual molar salivary gland and other salivary glands that can be found in the lip, cheek palate, gingival, tongue and floor of the mouth. Salivary adenocarcinomas can be very invasive. Up to 80% of cats have lymph node metastasis at the time of diagnosis. Pulmonary metastasis is less common. Surgical excision is the treatment of choice. The tumors are often very invasive extending into surrounding skin and musculature. With surgical excision, regrowth and lymph node metastasis are common. Combination treatment with surgical excision, radiation treatment and chemotherapy is recommended.

Osteoma

Osteoma is an uncommon benign bone tumor in cats composed of mature compact or cancellous bone that generally grows continuously and at a slow rate. Osteomas occasional occur in the oral and maxillofacial region. Treatment is recommended early in the course of the disease and involves debulking and recontouring of the affected area. When diagnosed at an advanced state of disease a more aggressive surgical resection may be required. There is debate regarding the etiology and pathogenesis of the osteoma. Some suggest that it is a true neoplasm whereas others classify it as a developmental anomaly triggered by infection or trauma and exacerbated by muscle traction.

Odontogenic tumors

Odontogenic tumors originate from the remnants of the embryonic tissues destined to develop into teeth and associated structures and account for 2.5% of all feline tumors. They are classified as inductive tumors when they retain the ability to induce reactive proliferation of connective tissue. Inductive odontogenic tumors include feline inductive odontogenic tumor (FIOT), dentinoma and ameloblastic, complex and compound odontomas. Non inductive tumors in cats include ameloblastomas and calcifying epithelial odontogenic tumors (CEOT).

Odontoma

An odontoma is an odontogenic tumor containing epithelial and mesenchymal cells which results in formation of all dental tissue types. The tumor is benign and slow growing but they can be expansile and can create a mass like effect in the oral tissues. Clinically an odontoma will appear as an unerupted tooth or a partially erupted tooth with an associated swelling. A compound odontoma contains rudimentary tooth like structures. An odontoma in which the conglomerate of dental tissues bears no resemblance to a tooth is called a complex odontoma. Treatment for an odontoma is removal of the mass and associated tooth like particles and curettage of the defect.

Dentigerous cyst

A dentigerous cyst is a benign, non neoplastic, well circumscribed, cystic lesion associated with an impacted tooth. The fluid filled cyst forms around the tooth crown and is attached to the neck of the unerupted tooth. The resulting lesion is an expansile lesion and can cause a significant bone loss and destruction. Dental radiographs show a unilocular radiolucent area associated with the crown of the unerupted tooth. During normal adult tooth development the inner and outer enamel epithelium are responsible for the production of enamel. After the enamel is formed these tissues fuse to become the reduced enamel epithelium which is a tight sac around the enamel. As the tooth erupts this tissue becomes the junctional epithelium. When tooth does not erupt normally, the ameloblasts persist and form a sac lined with epithelium which may lead to formation of a dentigerous cyst. Treatment for a dentigerous cyst is surgical removal of the tooth and associated cyst lining.

Feline inductive odontogenic tumor (FIOT)

Feline inductive fibroameloblastomas is a raised submucosal soft tissue mass typically located in the rostral maxilla in young cats 8-18 months of age. The tumor is locally invasive and metastasis has not been reported. Intraoral radiographs show bone lysis, production and expansion of the maxillary and mandibular bones, and areas of mineralization within the tumor. Wide surgical excision is the treatment of choice and complete excision is considered curative.

Amyloid producing odontogenic tumors (APOT)

Although previously referred to as a calcifying epithelial odontogenic tumors, it has been determined that the amyloid producing odontogenic tumor is not equivalent to the human calcifying epithelial odontogenic tumors. The amyloid producing odontogenic tumors appear as a gingival enlargement which grows by expansion. Clinically the tumors appear similar to a squamous cell carcinoma as they are friable, ulcerated and often bleed easily. Some APOTs are darkly pigmented. It is locally invasive but not metastatic. They occur most commonly in older male cats with a median age of 9 years. It often has a cystic appearance on radiographs. Wide surgical excision is recommended. Complete surgical excision is considered curative.

Peripheral odontogenic fibroma

Peripheral odontogenic fibromas now include tumors that were previously classified as fibromatous and ossifying epulides. Peripheral odontogenic fibromas are uncommon in the cat. They can be pedunculated or sessile and may contain osseous material. Complete excision is usually curative.

Non neoplastic proliferative oral lesions

Eosinophilic granuloma

Eosinophilic granuloma can be located on the hard palate, soft palate or base of the tongue. Eosinophilic granulomas are more commonly found in young cats, 2-6 years of age. The etiology is rarely determined and it is often considered idiopathic. Treatment is usually steroids, hypoallergenic diets, RT, surgery, immunomodulation or cryosurgery. The prognosis for complete recovery is fair.

Eosinophilic ulcer

Eosinophilic ulcer is typically a well circumscribed lesion with raised edges and ulceration most frequently located on the upper lip. It is found in cats of all ages and breed, with a higher incidence in middle aged female cats.

Pyogenic granuloma

Pyogenic granuloma is a benign solitary nodules resembling granulation tissue. They are raised, friable and easily bleed. They most commonly occur at the vestibular mucogingival tissues of the mandibular first molar teeth. A pyogenic granuloma can resemble a squamous cell carcinoma clinically.

It is important to keep in mind the less common malignant oral tumors, odontogenic tumors and non-neoplastic proliferative oral lesions in the differential diagnosis list for oral masses as they are often clinically indistinguishable from common malignant oral tumors. A complete evaluation of the patient and the tumor allows the clinician to determine the appropriate treatment recommendations for oral tumors in cats.

Diagnosing and Treating Urinary Tract Infection in Cats

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Urinary tract infection (UTI) exists when bacteria colonize portions of the urinary tract that are normally sterile (i.e., kidney, ureter, bladder, proximal urethra). UTI most commonly affects the bladder. Bacterial colonization may be superficial along the mucosa, or deeper within the mucosa or submucosa. Bacterial UTI is far less commonly diagnosed in cats compared to dogs and is estimated to affect 1-3% of cats in their lifetime. Dogs with no identifiable anatomical, metabolic, or urinary functional problems of the urethra or bladder can acquire UTI, which is quite different for UTI that develops in most cats. Cats that develop UTI are by definition considered “complicated” since healthy cats have exquisite urinary tract defense systems that simply do not allow a “casual” development of UTI. Cats with bacterial UTI will most often be discovered to have anatomical, metabolic, or functional problems of the bladder or urethra, or have undergone urinary tract instrumentation (e.g. urinary catheterization) that facilitate bacterial ascent and colonization of the urinary tract.

Diagnosis

Various combinations of hematuria, pyuria, and bacteriuria are observed in urinary sediment from cats with LUT signs associated with a positive quantitative urine culture (clinical UTI). In cats without LUT signs evaluated for other reasons, a positive urine culture in substantial quantity can be documented (occult or asymptomatic UTI – discussed later). The isolation of bacteria in large quantities does not determine whether the UTI is located in the upper or lower urinary tract, if the UTI is chronic or acute, or if the infection is deep within tissue or superficial along the mucosa.

It is important to remember that many particles in urinary sediment from cats, more so than dogs, resemble bacteria – lipid droplets, small crystals, cellular fragments, mucus, stain precipitates. Dry-mount examination of urinary sediment following either Wright’s-Giemsa or Gram stain to further identify bacteria in urinary sediment from cats increases the certainty that UTI really exists or it does not.¹ Urinalysis and aerobic quantitative urine culture reported in colony-forming units per milliliter (cfu/mL) should be conducted in all cats suspected of having a UTI. Isolation of organisms in large quantitative growth (cfu/mL) from a properly collected and handled sample is the gold standard for definitive diagnosis. The number of cfu/mL needed to definitively confirm the existence of UTI varies depending on how the urine is collected and whether clinical signs are present. Lower cfu/ml are often considered clinically significant in patients with increased voiding frequency in which organisms may be eliminated from the bladder before they have time to replicate to higher numbers.

Do not submit sterile swabs soaked or dipped in urine since quantitative culture methods cannot be performed on this type of sample. Culture of urine following cystocentesis is the method of choice to most easily establish a definitive diagnosis of UTI as this bypasses potential contamination with organisms from the distal urethra or genital tract.^{2,3} Far less contamination with bacterial organisms occurs during collection of voided or catheterized urine samples from cats compared to dogs. In 24 samples from healthy cats of both sexes, no growth occurred when urine was collected by cystocentesis. Minimal cfu/ml of bacterial growth occurred from samples collected by urinary catheter. In 9 of 12 samples from male cats no growth occurred; 3 samples grew between 10 and 100 cfu/ml. No growth occurred in 11 of 12 samples from female cats in samples collected by catheter; in 1 sample between 100 and 1,000 cfu/ml growth occurred. Quantitative growth (cfu/ml) was much greater in both male and female cats from urine samples collected by voiding. Organisms grew from all 11 urine samples collected by voiding from male cats. Quantitative growth ranged from 100 to > 100,000 cfu/ml in these samples; in 6 of 11 samples, growth exceeded 1,000 cfu/ml (> 10,000 cfu/ml in 2 samples). No growth occurred in 5 of 12 samples collected by voiding from female cats; in 4 of 7 positive cultures, growth was 1,000 to 10,000 cfu/ml and in 1 > 100,000 cfu/ml. In samples with positive growth, more than one organism was frequently isolated. *Escherichia coli*, *Staphylococcus* spp, *Streptococcus* spp, *Corynebacterium* spp, *Pasteurella* spp, and *Flavobacterium* spp were the organisms isolated in decreasing frequency from the urine of these normal cats.⁴

True bacterial UTI is likely in cats when $\geq 1,000$ cfu/ml of organisms are isolated from urine collected by cystocentesis; < 1,000 cfu/ml is more likely to be from contamination during the collection process. Low-level growth from cystocentesis samples is possible in cats with true UTI when antibacterial treatment has been given recently. UTI is likely to exist when $\geq 1,000$ cfu/ml are isolated from urine collected by urinary catheterization from either male or female cats; < 1,000 cfu/ml is most likely associated with contamination. Some criteria state that UTI is likely in cats isolating $\geq 10,000$ cfu/ml from voided urine⁵, but this may not always be true since high level contamination occasionally occurs in both male and female cats using this method of collection.⁴ Culture of voided urine is not recommended since high level growth can occur from contamination rather than indicating true UTI, though no growth on voided urine samples does provide meaningful information.

The Uricult[®] Vet dip paddle system (LifeSign, Skillman, NJ) can be a useful in-house screening tool for identification of bacterial growth.⁶ Quantitative results (cfu/mL) determined by comparing growth on the paddles with a standard illustration of organism

density provided by the manufacturer were not always accurate. Inaccuracy in identification of isolated organisms sometimes occurred when paddles were used, particularly when multiple uropathogens were present. This paddle system provides no method for susceptibility testing of isolated organisms, although the bacteria can be categorized into gram-positive or gram-negative status. When growth occurs, paddles or a fresh urine sample should be submitted to a commercial microbiology laboratory for identification and antimicrobial susceptibility testing. Veterinary hospitals should determine whether their referral microbiology laboratory will accept organisms already growing on paddles for definitive identification and minimum inhibitory concentration (MIC) testing. This paddle system for organism isolation appears most clinically useful as an in-house method to identify urine samples that are sterile or samples with low quantitative growth compatible with contamination during the sample collection.⁶

The Accutest Uriscreen® is an in-house color reaction based test designed to rapidly detect catalase from bacteria and from cells in the urine sample from dogs and cats. A negative test supports that UTI does not exist but there are false positives for UTI, so a positive test necessitates a follow-up quantitative urine culture.⁷

Organisms isolated from cats with UTI

Twenty-five percent of urine cultures from cats not biased toward those diagnosed with urinary disease were positive for bacterial growth considered indicative of a UTI in one report from a teaching hospital. The criteria to establish a UTI included any growth in a cystocentesis sample, $\geq 1,000$ cfu/ml in catheterized samples, and $\geq 10,000$ cfu/ml in voided urine. The number of cats with true UTI is likely overestimated in this study due to the entry criteria. Eighteen bacterial species were isolated in this study. *E. coli* accounted for 47% of the isolates, *Staphylococcus* spp for 18%, and *Streptococcus* spp for 13%. A single bacterial isolate occurred in 85%; > 1 isolate occurred in 15% of the positive cultures. The USG of cats infected with *E. coli* tended to be < 1.025 whereas those infected with Staph or Strep were usually > 1.025 . Older female cats were over represented, as were Siamese cats.⁸ *E. coli* and gram positive cocci were also the most commonly isolated organisms from Australian cats with UTI in other reports. Older female cats were also more likely to have a positive urine culture as in the previously mentioned study. *E. coli* was isolated in 37% of the positive cultures, *Enterococcus* species in 29%, *Staphylococcus felis* in 20% and *Proteus* species in 5%. *Enterococcus faecalis* accounted for 95% of enterococci spp with the remainder by *enterococcus faecium*.^{9,10} *Enterococcus* accounted for 19% of positive urine culture from cats evaluated at the OSU CVM.¹¹ *Staphylococcus felis* is a coagulase-negative organism that has traditionally been considered a normal commensal organism from healthy cats present on the skin, eyelid margins, conjunctival sac, and in saliva, but appears that this organism can be a uropathogen for the cat.⁹

Occult UTI was documented in 38 of 132 urine specimens (44 isolates) collected by cystocentesis from cats without LUT signs, inappropriate urination, or previous UTI – these samples were submitted as part of other diagnostic workups for a variety of conditions including CKD, hypothyroidism, and diabetes mellitus. Hematuria and pyuria were common in the urinalyses from urine culture-positive cats and culture-positive urine specimens were more likely to come from older female cats. *Enterococcus faecalis* was the most common isolate (19 of 44 total isolates) followed by *E. coli* (17 of 44 isolates). A few isolates of *Proteus mirabilis*, *Staphylococcus felis*, and *Streptococcus bovis* were also documented in this group of cats. Heavy growth of bacteria at $\geq 100,000$ cfu/mL was documented in 39 of 44 isolates and moderate growth at 10,000 to 100,000 cfu/mL was found in 5 of 44 isolates.¹² Occult bacteriuria that is either persistent or transient has been described in apparently healthy dogs or those presented for elective surgical procedures^{13,14} but this has not been reported in healthy cats. Urine was collected by cystocentesis from 108 healthy cats (53 males and 55 females) with a median age of 4.0 years without previous or current LUT signs. Both urine and urine sediment underwent quantitative culture resulting in no growth in 107 of 108 samples. In the remaining sample $>100,000$ cfu/mL of 2 organisms was isolated, likely the result of contamination.¹⁵

A unique form of relapsing UTI is caused by *Corynebacterium urealyticum*^{16,17} or *corynebacterium jeikeium*¹⁸ in which encrustations of urinary tissue and struvite (so-called “encrusting cystitis”) prevent eradication of the organism with medical treatment alone. These organisms are rarely isolated as a cause for UTI in cats but may be under-diagnosed. These organisms are often reported as “diphtheroids” thought to be contaminants that are not further characterized. These organisms are often slow growing and require special media to facilitate their growth and identification. These organisms are highly resistant to commonly prescribed urinary antibacterials and the prognosis for cure is generally poor even with surgery and long-term antibiotics.

Conditions associated with UTI in cats

UTI occurs with increased frequency in special populations of cats that include those with metabolic disease (CKD, hyperthyroidism, diabetes mellitus), prior instrumentation of the urinary tract with urinary catheterization, urinary incontinence, acquired anatomical abnormalities (stones, tumors, perineal urethrostomy), and congenital anomalies. Chronic kidney disease (CKD), hyperthyroidism, and/or diabetes mellitus all increase the risk for cats to acquire a true bacterial UTI,¹⁹ though clinical signs of UTI may not be present (asymptomatic bacteriuria). In one study 10–15% of cats with hyperthyroidism, diabetes mellitus or chronic renal disease had a bacterial UTI,¹² similar to findings of other studies.¹⁹⁻²¹

In a report comparing 155 cats with UTI to 186 cats without UTI, significant risk factors to acquire UTI were identified for cats with urinary incontinence, transurethral procedures, gastrointestinal diseases, decreased body weight, and decreased urine specific gravity. In this study, 35.5% of cats had no clinical signs associated with their UTI (asymptomatic bacteriuria). UTI in this study was defined as any growth from samples collected by cystocentesis and $> 10^3$ cfu/mL from samples collected by urethral catheterization²². Decreased urinary specific gravity was not identified as a risk for UTI in cats of another study.¹⁹

An early report drew attention to the apparently high rate of UTI in cats with azotemic CKD. Five of 15 CKD cat urine samples without obvious bacteriuria in urinary sediment grew organisms and 12 of 19 CKD cats with bacteriuria grew organisms. Whether or not these CKD cats had LUT signs associated with a positive urine culture was not addressed.²³ The finding of a positive urine culture in cats with CKD could be associated with infection within the kidneys but often this cannot be proven to exist. In a study of 42 female and 44 male cats with CKD undergoing routine urine culture surveillance, positive urine cultures in samples collected by cystocentesis were identified 31 times from 25 cats over a period up to 3 year of their CKD. Eighteen of the 25 cats (72%) were classified as having occult UTI. Eighty-seven percent of cats with positive urine cultures were found to have active urinary sediment. Increasing age was a significant risk factor to acquire occult UTI in female CKD cats. The presence of UTI was not associated with the severity of azotemia or survival in these cats²⁴.

The frequency of UTI in reports of young cats with non-obstructive LUT signs is quite low (often reported at less than 2%) in most studies in North America, the UK and Europe.²⁵⁻³¹ Idiopathic/interstitial cystitis accounts for 60 to 70% of diagnoses in cats presenting for some form of urinary urgency. In cats older than 10 years, UTI appeared to be quite common (>50%) in those evaluated for signs of urinary urgency; idiopathic cystitis accounted for only 5% of cases in this group of cats.^{32,33}

A study in 2007 of cats from Norway with a variety of obstructive and non-obstructive causes of LUT signs³⁴ found a surprisingly high number of cats with positive urine culture in large quantitative growth, far more so than in other reports. Findings from this study are difficult to interpret since many of the cultures were from voided midstream (46%) or catheterized urine samples (21%) rather than from the gold standard of cystocentesis (21%); in 10% the method of urine collection was not recorded. 44 of 118 samples cultured on the same day isolated bacteria $> 10^3$ cfu/ml. In 33 of these 44 samples, growth was $> 10^4$ cfu/ml and in 20 growth was $> 10^5$ cfu/ml. Quantitative growth from midstream voided samples from healthy cats is sometimes substantial as was shown in 55% of males and 40% of females that grew $> 10^3$ cfu/ml in another study⁴.

Congenital anomalies of the urinary tract are occasionally the cause of UTI in young cats. Any condition associated with non-urge related incontinence can be expected to be associated with UTI. A common urogenital sinus malformation was found as the underlying cause for UTI and incontinence in 3 young female cats that were evaluated for recurrent lower urinary tract infections and incontinence (Ohio State University CVM 2014 – publication in preparation). Fusion of the vagina to the proximal urethra created a single vaginourethra. No vestibule existed as the vulva and urethra appeared as a continuous structure that allowed easy fecal contamination. Cystoscopy was the diagnostic tool used in these cases to confirm the abnormal anatomical status. Partial invagination of the urinary bladder was diagnosed in one cat with clinical signs of hematuria, stranguria, and inappropriate urination associated with UTI. This diagnosis may be made on the basis of detection of invaginated tissue in the bladder apex during abdominal ultrasonography.³⁵

Treatment

Antibacterial susceptibility testing on isolated organisms is recommended to guide the best treatment selection. Results can reveal the presence of resistance organisms that can predict treatment failure and the need for greater surveillance following treatment. A change in urinary antimicrobial may be needed based on the results of susceptibility testing after the initial treatment was started at the time of submission of the culture.

The Working Group of the International Society for Companion Animal Infectious Diseases (ISCAID) recommends treatment with urinary antibacterial drugs that are likely to be effective against more than 90% of the urinary isolates when this information is available. In general, ISCAID recommends initial therapy for uncomplicated UTI with amoxicillin (11–15 mg/kg PO q8h) or trimethoprim–sulfonamide (TMP-sulfa; 15 mg/kg PO q12h); the group does not recommend amoxicillin–clavulanate for initial treatment in these cases because of lack of evidence for the need for clavulanate in addition to amoxicillin.³⁶ Additional detail and a free PDF download of this work published by Veterinary Medicine International is available at <http://www.hindawi.com/journals/vmi/2011/263768/>.

Amoxicillin/clavulanic acid was recommended for Gram-negative infections and amoxicillin for Gram-positive infections in one review of cats with UTI. Variation in bacterial prevalence and susceptibility patterns should also be taken into account when prescribing antibacterial treatment¹⁰ Most isolates of *E.coli* in one study showed susceptibility to the 14 antimicrobials tested. *Staphylococcus felis* was susceptible to all antimicrobial agents tested. Enterococcus was universally sensitive to amoxicillin/clavulanate and penicillin/amoxicillin in 2 studies of UTI in cats by the same group.^{9,12} *Enterococcus faecalis* can vary greatly in its susceptibility pattern to antimicrobial agents and so may require higher dosage, longer duration or a combination of therapeutic agents in some patients with overt LUT signs. A high proportion of *Enterococcus* isolates were resistant to clindamycin

(97.3%) and cephalothin (72.3%). *Enterococcus* had intermediate susceptibility to enrofloxacin, (61.1%) and marbofloxacin (80.5%).⁹ All cephalosporins, potentiated sulfas, and aminoglycosides are notoriously ineffective against *Enterococcus* even when the susceptibility test results return as sensitive for those drugs. *Enterococcus* is usually susceptible to imipenem and meropenem BUT use of these drugs should be restricted to those cases that have LUT signs and have failed treatment with amoxicillin or amoxicillin-clavulante. Current recommendations are to NOT treat asymptomatic UTI associated with *enterococcus* since this infection can come and go without treatment. Aggressive treatment for asymptomatic UTI runs the risk that the original *enterococcus* will become more resistant and then become symptomatic when it was not before. There is also the possibility that the *enterococcus* will be eradicated, but UTI with a more virulent and symptomatic organism will take its place.

Resistance patterns were reported for isolates of *E. coli* mostly from urine of dogs (301) and cats (75) in various regions of the United States. Resistance to amoxicillin was 46%, amoxicillin-clavulanate 37%, cefpodoxime 22%, doxycycline 22%, enrofloxacin 21%, trimethoprim-sulfa 19%, and gentamicin at 12%. This pattern for *E. coli* resistance suggests that empirical treatment for UTI may have limited success in this geographic location. Treatment of *E. coli* with amoxicillin or with amoxicillin-clavulanate may be less likely to be effective than commonly believed.³⁷

An early report documented the effectiveness of enrofloxacin treatment of UTI in cats. In this study all isolates were considered susceptible to enrofloxacin and post treatment sterility was documented in 21 of 23 cats.³⁸ As noted above, there are concerns for increasing resistance patterns for *E. coli* in the United States; there are no recent reports of UTI in cats treated with enrofloxacin. The total daily dose of enrofloxacin in cats should be limited to 5 mg/kg either once daily, or divided in order to limit retinal toxicity. Retinal toxicity is a fluoroquinolone class risk, especially for those that achieve the highest retinal concentrations and can result in mydriasis and blindness.^{39,40} It appears that cats as a species have developed a limited efflux mechanism to remove fluoroquinolones from the retina compared to other species.⁴¹ High-dose short-duration protocols prescribing enrofloxacin to treat UTI have been developed for use in dogs with uncomplicated UTI⁴² but these protocols should NEVER be used in cats due to retinotoxicity that predictably develops at high doses. Administration of the 3rd generation fluoroquinolone pradofloxacin at 6 to 10 times the recommended dose was shown to have no retinal toxic effects in cats based on rod and cone function evaluated with ERG. Retinal histopathology was unaltered during high dose pradofloxacin treatment. Cats treated with high doses of enrofloxacin showed diffuse retinal degeneration and poor rod and cone function.⁴⁰

Cefovecin is an extended spectrum semi-synthetic 3rd generation cephalosporin approved in Europe for use in cats with UTI caused by *E. coli*, but not approved for this indication in the United States. It is designed to have a 14-day dosing interval after a single subcutaneous injection. Post treatment urine cultures revealed sterile urine in 75.9% of all cats treated with a single injection of cefovecin. *Escherichia coli* was eliminated in 76.7 per cent of cefovecin-treated cats compared with 62.5 per cent of cephalexin-treated cats. Cefovecin demonstrated statistical non-inferiority compared with cephalexin for bacterial elimination in this study.⁴³ Efficacy of cefovecin to sterilize the urine in cats with UTI was less than that reported by the same group in dogs with UTI.⁴⁴

Client-owned cats with bacteriologically confirmed UTI were treated with either pradofloxacin, doxycycline, or amoxicillin-clavulante.⁴⁵ Urine culture revealed growth following treatment in 0 of 27 cats treated with pradofloxacin, 3 of 23 cats treated with doxycycline, and in 3 of 28 cats treated with amoxicillin-clavulante.⁴⁵ Pradofloxacin undergoes more hepatic excretion than does enrofloxacin but still achieves urinary concentrations that can be highly effective in the eradication of uropathogens. Pradofloxacin may be the preferred fluoroquinolone to prescribe for use in cats with UTI and impaired renal function due to the hepatic pathway for its excretion and its retinal safety profile should high concentrations of pradofloxacin accumulate in cats with decreased renal function. Pradofloxacin is FDA approved for soft tissue infections in cats; it can be considered for off-label treatment of UTI in cats.

Study of canine and feline *E. coli* isolates that were considered highly resistant to standard antimicrobial agents showed susceptibility to fosfomycin at concentrations well below the susceptible breakpoint. This finding makes it attractive to consider fosfomycin as a treatment for resistant *E. coli*.⁴⁶ Fosfomycin is considered a nephroprotectant in some species but in cats this drug can be highly nephrotoxic. When given to experimental cats for as little as 3 days, severe tubular lesions were evident and renal function declined as BUN and serum creatinine increased.⁴⁷

The recommendation of 7 to 14 days of an appropriate antimicrobial for treatment of an uncomplicated lower UTI has been based on conventional experience over the years, but surprisingly little data exist to support or refute these protocols. Ultimately, antimicrobials should be given for as long as is necessary to effect a bacteriologically sterile urine during administration of the medication and for a protracted time following discontinuation of treatment.

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Managing Cats with Idiopathic/Interstitial Cystitis (Parts 1 and 2)

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What is Pandora syndrome ?

Is this terminology more helpful than FUS or FLUTD or IC ?

Results of studies over the past 20 years indicate that idiopathic/interstitial 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. A recent review emphasizes that many cats with a diagnosis of FIC have lower urinary tract- predominant clinical signs that are part of a larger systemic disorder referred to as “Pandora Syndrome”¹. Clinical problems outside the lower urinary tract are common in those with a diagnosis of FIC and include signs related to the GI tract, respiratory system, skin, central nervous system, cardiovascular system and the immune system. It has been traditional to refer to cats that have obvious LUT signs as those having “feline urological syndrome”, “feline lower urinary tract disease”, or “feline interstitial cystitis” but this method of naming the disease focuses on the organ with the predominant clinical sign rather than a thorough evaluation of the entire cat and all of its organ systems. A diagnosis of Pandora Syndrome would apply to those cats that exhibit clinical signs in other organ systems (in addition to the LUT), waxing and waning of clinical signs associated with stressful events that presumably activate the stress response system, and undergo resolution of severity of clinical signs following effective environmental enrichment. Currently available evidence suggests that many cases of chronic idiopathic LUT signs presently diagnosed as having FIC actually do have a “Pandora” syndrome. The syndrome might result from early adverse experiences that sensitize the neuraxis to sensory input, increasing the frequency and duration of activation of the stress response system (SRS) when the individual is housed/living in a provocative environment. The chronic “wear and tear” of persistent activation of the SRS can upregulate the inflammatory response in a variety of tissues including the bladder.

Are there different types of presentations for cats with idiopathic/interstitial cystitis ?

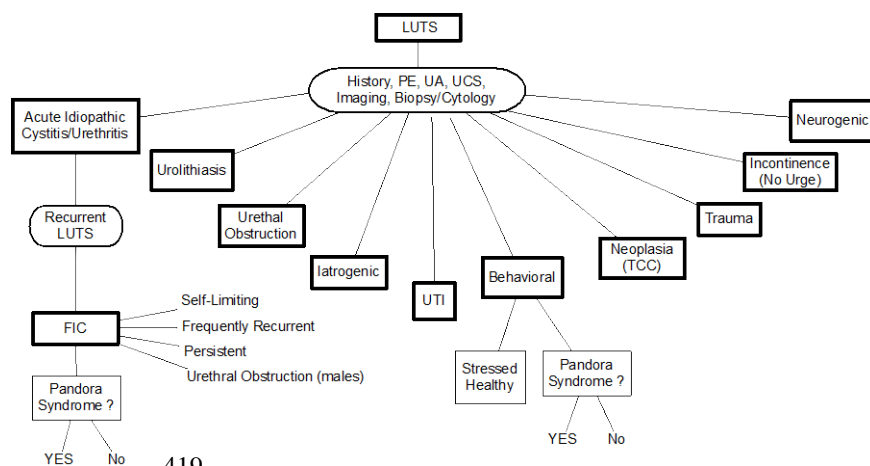
There are four possible urinary presentations associated with FIC. An acute seemingly self-limiting episode of FIC is thought to be the most common condition presenting to primary care practitioners with an estimated relative prevalence of 80 to 95% (Lulich ACVIM Forum Proceedings Anaheim 2010) – recurrence is likely if stressful situations become severe enough in the future. Frequently recurrent episodes of clinical signs related to FIC is next in occurrence (2 to 15%), followed by persistent forms of FIC (2 to 15%) in which the clinical signs never abate. The fourth possibility is for urethral obstruction to develop in male cats suffering from FIC (15 to 25%). These 4 types of presentations may represent a spectrum of signs from the same disease process, but this hypothesis has not been tested. Most publications reflect data from cats with frequent recurrences or persistent clinical signs that are presented to university referral practices. Based on our data, a potential fifth category could be healthy cats, especially males, that develop LUT signs when exposed to sufficient stressors².

What are the differential diagnoses for cats with LUT signs?

Though FIC is the most common diagnosis associated with LUTS in young cats, it is important to exclude the diagnosis of bacterial UTI and urolithiasis in a population of cats with risk factors. Collection of a detailed history that includes queries regarding environmental issues and husbandry practices is an essential first step in deciding if the LUTS are related to irritative voidings or not, and how likely stress may be playing a role. In order to determine if Pandora Syndrome is part of the LUTS, the history and physical examination must be extended beyond that immediately related to the urinary tract. Quantitative urine culture and survey radiography are recommended in the evaluation of all cats with recurrent LUTS to exclude UTI and radiopaque calculi. Advanced imaging that includes contrast radiography, ultrasonography, and urethra-cystoscopy are useful for the exclusion of anatomical defects, radiolucent calculi, and proliferative lesions in some cats.

Figure 1.

Some possible causes of LUTS in cats after appropriate diagnostic evaluation. PE – physical examination; UCS- quantitative urine culture (cfu/ml); Imaging – some combination of radiography, contrast urography, ultrasonography, and/or uroendoscopy. Not all tests are appropriate for every cat, so diagnostic evaluations tailored to each individual cat are most likely to arrive at the correct diagnosis.



What diagnostic workup is needed for cats with LUTS signs?

Figure 2.

A diagnostic approach for cats with LUTS, emphasizing the distinction between those cats that are obstructed or not, and cats that do or do not have irritative voiding.

Can you summarize where we are in our understanding of the pathophysiology of FIC?

Though all the pieces are not completely understood, the basic centerpiece is one of neurogenic inflammation – this type of inflammation is quite different from the standard kind of inflammation classically involving infiltration of neutrophils.

Increased bladder permeability is an important part of

this process, as this allows constituents of urine to gain access to the bladder wall- these compounds stimulate sensory nerve endings to carry excessive pain signals to the brain. The increase in bladder permeability likely involves changes in the GAG layer and the integrity of the structure and function of the urothelium. The stress response system (SRS) becomes activated but is not adequately terminated by release of cortisol as it is in normal cats. Unrestrained outflow of sympathetic nervous system activity characterizes this disease. Excess effects of norepinephrine are known to upregulate a variety of inflammatory processes including that in the bladder. Infiltration with mast cells is important in some cats with FIC – degranulation of mast cells then contributes to the inflammatory process (vasodilation, edema, diapedesis of RBC, recruitment of sensory nerves with NGF). Local axon reflexes within the bladder wall can result in vasodilation directly, degranulation of mast cells, and detrusor muscle contractions. Certain constituents of urine that gain access to the bladder wall are more potent stimulators of pain than others; absence of some substances in urine can magnify the pain response. The “bottom up” theory emphasizes defects in the bladder wall (GAG and or urothelium that increase permeability) and then over-activation of the noradrenergic nervous system. The “top-down” theory emphasizes that stressors from the environment can be potent enough to directly activate the SRS and turn on neurogenic inflammation³. Another piece of the pathophysiology is that cats with FIC appear to have mild adrenal insufficiency based on a blunted increase in cortisol concentration following ACTH stimulation compared to normal cats. The adrenal glands of cats are also smaller than those of normal cats and do not contain histopathologic lesions⁴. One explanation proposes that these small hypofunctioning adrenal glands are the result of a maternal perception of threat from the environment that is transmitted to the fetus from hormones that cross the placenta to effect the development of the fetal adrenal gland at a critical time for its development.⁵ It should be emphasized that only adrenocortical steroid measured was that of cortisol, and that many other adrenocorticosteroids have the potential to also be deficient⁶, but this has not yet been studied in cats. Cats with idiopathic cystitis do not appear to experience long-term benefit from current glucocorticoid therapy regimens. The same in utero developmental story just described could also account for a fetal stress response that has been programmed toward enhanced vigilance that would then be manifested after birth by an intense SRS output when the cat faces provocateurs. FIC cats in colony housing have higher levels of circulating catecholamines and their metabolites compared to normal cats, especially when exposed to a stressful environment. A return to lower levels of circulating catecholamines occurred in stressed FIC cats following environmental modification, but this response was less complete and took longer than that which occurred in healthy cats⁷. FIC cats were recently reported to have a heightened response to sensory stimuli when measured by the acoustic startle reflex (ASR) compared to healthy cats⁸. The ASR is a defensive brainstem mediated response to sudden intense stimuli. Environmental enrichment led to a significant decrease in ASR in cats with IC compared to healthy cats. Habituation to new housing prior to environmental enrichment decreased ASR in female but not male cats with FIC⁸. Results of this study add to the concept that management of FIC benefits the cat when the patient’s perception of unpredictability in the environment is reduced. Urodynamic evaluation of female cats with FIC revealed no finding of spontaneous detrusor muscle contraction that can occur in overactive bladder (OAB) further separating FIC from OAB⁹. Consequently, drugs that target detrusor muscle contraction do not appear warranted in cats with FIC. High maximal urethral closure pressure (MUCP) was documented in female cats with FIC of the same study, suggesting that alpha-1 –adrenoceptor antagonists, alpha-2 agonists, or skeletal muscle relaxants could potentially be useful treatment⁹ but this has yet to be studied.

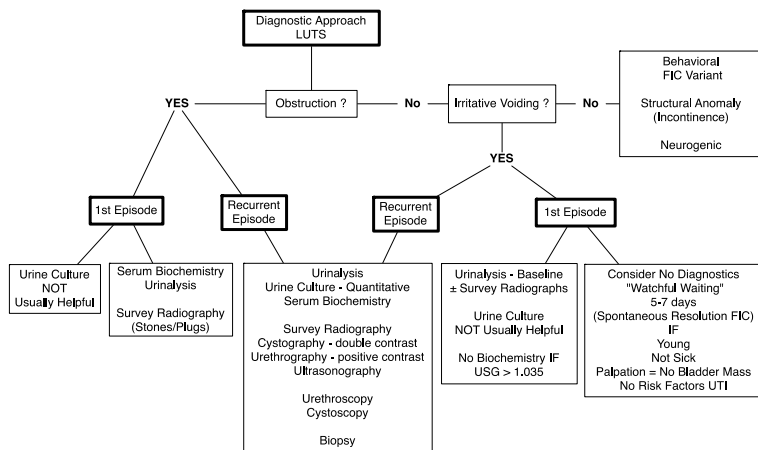


Figure 3. Neurogenic inflammation as it affects the urinary bladder in interstitial cystitis.

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.

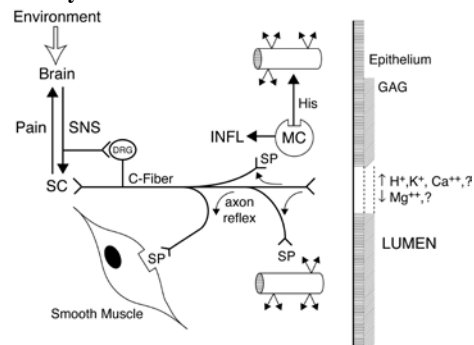
Damage or malfunction of either or both of these layers may permit constituents of the urine, such as protons, potassium ions, or hyperosmolar (>2,000 mOsm/L) fluid to activate the sensory fibers. The effects of stress on sensory fibers may be related to descending efferent sympathetic (SNS) signals 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.

Since GAG excretion is decreased in active and quiescent phases of FIC, is glycosaminoglycan (GAG) treatment helpful in the treatment of FIC ?

Three studies have employed glycosaminoglycan (GAG) as treatment for FIC, none of which were able to show a benefit over control. In the first study, 40 cats with recurrent idiopathic cystitis were treated with either 125 mg N-acetyl glucosamine or a placebo by mouth daily for six months. No significant differences were observed using the owner assessment of the mean health score, the average monthly clinical score, or the average number of days with clinical signs. Both groups improved over the course of the study, possibly due to salutary effects from dietary change initiated at the start of the study¹⁰. In a second study of 18 cats, injectable pentosan polysulphate (PPS) was compared to control injections in cats with non-obstructive idiopathic cystitis. Subcutaneous injections of PPS were given at 3mg/kg on days 1,2,5, and 10. Clinical signs were not different between treatment groups when evaluated on day 5, 10, 14, and then 2, 6, and 12 months¹¹. A multicenter study involved 4 universities comparing BID oral PPS to placebo as treatment in 107 cats with interstitial cystitis. Enrolled cats had at least two episodes of LUTS within the past six months, cystoscopic findings of glomerulations, and absence of an alternative diagnosis. Cats were randomly assigned to 0.0 (vehicle placebo), 2.0, 8.0 or 16.0 mg/kg PPS orally twice daily for 26 weeks. No statistically significant differences were observed between any of the groups based on the owner's evaluation of clinical signs or overall improvement in cystoscopic score. A statistically significant decrease in friability score on cystoscopy was observed at the 16.0 mg/kg dose. Clinical improvement occurred in most cats (owner reported scores decreased by 75% in all groups), regardless of the dose of PPS administration or changes in cystoscopic appearance of the bladder. It is likely that accidental environmental enrichment occurred during this study which could account for the improvement scores in all cats overall^{12,13}. In a 4th study, N-acetyl-d-glucosamine (NAG) at 250 mg PO once daily significantly increased plasma GAG concentrations in cats with IC after 21 days of treatment. Subjective improvements in LUT signs were suggested to occur in those treated with NAG but not those treated with placebo¹⁴.

Is there a role for pheromontherapy in treatment of FIC ?

Feline facial pheromones (FFP) are commercially available (Feliway®) with the listed indication to decrease urinary spraying and marking. Activation of the sympathetic nervous system is part of the vigilance system that results in urinary spraying and marking and it is thought that these products lower the intensity of sympathetic nervous system output. Since unrestrained output of sympathetic nervous system activity is a central component in neurogenic inflammation that occurs in FIC, it seems reasonable that use of FFP could also be useful for treatment of FIC. In one study of hospitalized healthy and sick cats videography was used to score behavior and food intake of cats in which the cage was pre-treated with vehicle placebo or feline facial pheromones¹⁵. Increased grooming, facial rubbing, interest in food, and walking were found in cats exposed to FFP compared to vehicle. Results of this study suggested that hospitalized cats exposed to FFP were calmer and more comfortable in their cages than cats exposed to vehicle. It has been our observation that some cats are very affected by FFP while in others the effect is minimal to nil. A randomized, double-blinded, placebo-controlled, crossover study was performed in 12 cats (9 of 12 completed the full study) with recurrent FIC, comparing once daily environmental treatment with FFP (Feliway®) or placebo; treatment was for 2 months and then switched to the other treatment for the next 2 months¹⁶. This small number of cats exposed to FFP had fewer mean days displaying signs of cystitis, a reduced number of episodes of cystitis, and fewer negative behavioral traits, but this data did not achieve statistical significance for a difference over placebo treatment of the environment.



Is there a role for amitriptyline or other tricyclic anti-depressant (or analgesic) TCA for the treatment of FIC ?

In some cases YES. The need for this kind of therapy has dramatically lessened since we as a profession have become much more successful at implementing environmental modification, which usually works well without need for chronic drug therapy. We do prescribe amitriptyline for its beneficial effects for cats with FIC that have frequent recurrences or persistent LUT signs AFTER the client's best efforts to implement environmental enrichment have failed to improve the cat's clinical signs. This type of therapy should NOT be undertaken for an initial episode of FIC or a "flare" of signs that occur infrequently. We sometimes prescribe amitriptyline for cats owned by clients that are considering euthanasia for their cat with FIC – this can sometimes allow the client to see early benefits while implementing environmental enrichment. Maximal beneficial effects of TCA, if any, often require weeks to months to be observed and in general should not be abruptly discontinued (so called "abrupt withdrawal syndrome"). Treatment series of FIC with amitriptyline has been reported 3 times, 1 study of chronic FIC (frequently recurrent or persistent signs) and 2 of acute bouts of FIC. In the chronic study, 15 cats were enrolled with FIC that failed to respond to other treatments; no placebo group was treated. Amitriptyline treatment (10 mg PO every 24 hours in the evening) successfully decreased clinical signs of severe recurrent FIC in 9 of 15 cats treated for 12 months (11 of 15 cats for the first 6 months). Somnolence, weight gain, decreased grooming, and transient cystic calculi were observed during treatment in some cats. Despite clinical improvement, cystoscopic abnormalities persisted in all cats at the 6- and 12-month evaluations¹⁷. In one short term study, 31 untreated male and female cats with acute (<14 days signs), nonobstructive, idiopathic lower urinary tract disease were enrolled in a placebo controlled study. Cats were hospitalized and treated with 5mg amitriptyline or a placebo daily for 7 days and then treatment discontinued. Clinical signs and hematuria resolved similarly in both groups of treated cats by day 8. Cats were evaluated in the clinic 1 month later and by questions over the telephone 6, 12, and 24 months after treatment. Clinical signs recurred faster and more frequently (10.5 vs. 2.4 events/1,000 days) in the amitriptyline treated cats, a finding likely attributable to the abrupt withdrawal of amitriptyline treatments after 7 days- there was no difference in recurrence when the first 21 days were excluded from the analysis¹⁸. In another short-term study of FIC, amitriptyline at 10 mg once daily per os (11) or placebo (13) was given for 7 days by owners at home. All cats were also treated with amoxicillin BID for 7 days. The severity of clinical signs was assessed at days 0, 7, and 14 – no significant difference was found between amitriptyline and placebo treated cats of this study¹⁹.

How do we treat an acute episode of LUT signs for either its first time, or an infrequently recurrent event ?

We treat nearly all FIC cats of this type with a combination of buprenorphine and acepromazine PO for 5 to 7 days. The combination of an analgesic and a tranquilizer with properties that also decrease urethral tone seem like a compassionate and appropriate choice of treatment. It is likely that the tranquilizer reduces the activity of the autonomic nervous system which is useful in the initial treatment of FIC. We believe that this helps to acutely decrease clinical signs in cats with acute episodes of FIC or flares of chronic FIC, though this has not been specifically studied. Whether this regimen reduces future episodes of FIC has also not been tested. We take the opportunity at the first visit to discuss with the owners that even a first event of FIC may be associated with recurrence and that there may be steps that can be taken to reduce this likelihood (not yet studied in a prospective way) when environmental enrichment and modification are successfully implemented.

What analgesic treatments should I consider?

The best approach to analgesia for bladder pain (visceral) has yet to be determined. Butorphanol has been used, but its effects are less long-lived or potent than those of buprenorphine^{20,21}. Sustained release formulations of buprenorphine have recently become available that can provide up to 72 hours of therapeutic drug levels for pain relief following a single injection. Fentanyl patches have been used in rare cases in which bladder pain was assessed as severe.

Should I consider NSAID treatment to provide anti-inflammatory and analgesic effects?

Anecdotal reports of the usefulness of non-steroidal anti-inflammatory drugs (NSAID)s, especially meloxicam and ketoprofen, abound, but no studies of safety or effectiveness are available for review. Some specialists have prescribed piroxicam for use on alternate days, but there are no controlled clinical trials of its effectiveness or safety. NSAIDs are not commonly used for treatment of interstitial cystitis in humans. NSAIDs that are licensed for use in cats list indications for pre-emptive pain management, usually as a single treatment before anesthesia and surgery. Chronic use of NSAIDs in cats can be dangerous due to the possibility for development of acute intrinsic renal failure; especially should the cat become dehydrated for any reason at the time of NSAID administration. The FDA recently required the following statement to be added to the label for meloxicam use in cats, "Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information." Robenacoxib, a long acting NSAID recently has become available for use in cats; its effectiveness and safety for use in cats with FIC has yet to be reported to our knowledge.

What is the most-important therapy to recommend to owners of cats with frequently recurrent or persistent signs of FIC?

There is no simple answer to this question but a key component to a successful outcome is empowering the owner with skills that allow the cat's husbandry to be improved and the environment enriched to a point that decreases the cat's stress response system. We refer you to the Indoor Cat Initiative site that is maintained by Dr. Buffington- this site provides a great number of details and resources that can be considered to implement that will reduce the cat's perception of stress and improve its general sense of well being while living largely in confined spaces with people (and often with dogs too). Environmental enrichment involves effective

resource management, including; litter box (es) (type, location, number, substrate, cleaning regimen,), food and water (type, location, number), resting areas, opportunities to climb and scratch, interactions with people that are positive, and methods to reduce conflict in the living space with other cats, dogs, and humans²²⁻²⁴. Outcome of environmental enrichment and modification was proven beneficial to most FIC cats of a study in which they had failed multiple other treatments²⁵. In addition to a dramatic increase in the use of the litterbox, there were benefits in behavior and some gastrointestinal signs.

Is there anything new regarding dietary treatment of FIC ?

A non-blinded and non-randomized study of feeding canned vs. dry diets of similar formulation (Waltham pH Control®) in the treatment of 54 FIC showed a beneficial effect of the canned over the dry product²⁶. 52 of 54 cats exhibited more than one episode of LUT signs in the prior 12 months. The study lasted for 12 months, or until signs of recurrence occurred. Signs of LUTD did not recur in 16 of 18 cats fed the canned diet, and 17 of 28 cats fed the dry diet (P < 0.05). The recurrence rate in cats being fed the dry food was also reduced compared to the rate encountered in the previous year, but not to the degree of benefit observed in cats consuming the wet formulation. The mean urinary specific gravity was lower in urine from cats fed the canned formulation but the basis for the salutary effect of this particular canned product over the dry formulation was not determined²⁶. Other factors that could have influenced results of this study include hedonics (the mouth feel of the food) or the ritual associated with the feeding of canned foods and this effect on cat behaviors. The consumption of dry foods is known as a risk factor for the development of LUT disease in cats on a dose-related basis²⁷. The results of a test food vs control food as treatment of FIC was recently reported as an abstract in 31 cats over 12 months. The test food contained more anti-oxidants and omega-3 dietary oil than the control food as the main difference. The feeding of the wet or dry formulation was determined by owner preference. The number of episodes for LUT signs and days exhibiting LUT signs (1.3 vs. 10.3 events/1000 days) were fewer in cats fed the test food of this study. Outcome was the same during the feeding of either the wet or dry formulations of the test food²⁸. The event rate for the test diet was not significantly different from the same author’s previously reported event rate in untreated cats¹⁸; the basis for the effect of the control or test formulations in this study was not determined. The test diet is not available commercially, as the original diet was altered to include stress-reducing compounds for the commercial diet that was launched but this specific formulation was not studied.

How important are non-specific therapeutic responses in treatment of FIC?

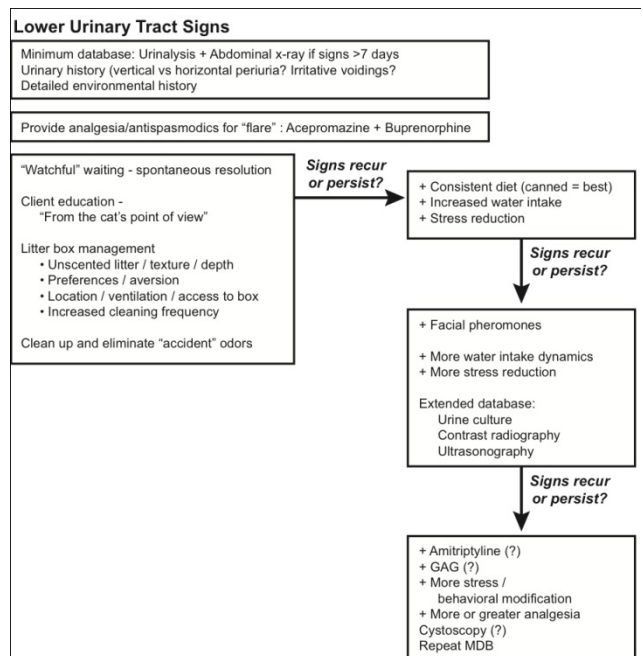
Nonspecific therapeutic responses might occur during treatment of cats with FIC, possibly by altering their perception of their surroundings as part of a placebo-response. The effectiveness of environmental enrichment suggests that pharmacological or other therapeutic interventions face an important barrier to demonstrate efficacy in the presence of the large therapeutic response to this approach in cats with the syndrome.

Figure 5.

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.

“Pearls” Pandora syndrome – aka feline interstitial/idiopathic cystitis (FIC)

1. Signs of urinary urgency during FIC may be expressions of a systemic disease created by a highly active outflow (unrestrained) from the sympathetic nervous system in response to stressors (provocateurs) .
2. When multi-modal environmental modification (including environmental enrichment) is effectively implemented, treatment with drugs is RARELY NEEDED.
3. Stress up-regulates the inflammatory potential of several organs, including the bladder.
4. Bacterial urinary infections (UTI) are rarely identified in cats with signs of lower urinary tract disease, unless they have specific risk factors (U-cath within last 6 months, perineal urethrostomy, dilute urine – CKD, diabetes mellitus, hyperthyroidism)
5. The term “Pandora Syndrome” should help to remind the clinician that LUT signs may be part of a bigger picture that involves other organ systems.
6. We advocate the use of analgesia (buprenorphine) during acute episodes of FIC.



7. We use tranquilization with acepromazine in combination with buprenorphine in most of our cases of non-obstructive episodes.
8. On occasion, the use of amitriptyline can be useful in the treatment of FIC.
9. The use of GAG (glycosaminoglycan) supplementation has failed to show an effect superior to placebo in several studies of FIC treatment.
10. The use of feline facial pheromones has not been shown to be superior to placebo in the treatment of FIC.
11. The feeding of as much wet food as possible in the diet is advocated by some for its protective effect on the recurrence of the signs of FIC, and may be helpful as long as it does not result in additional threat to the cat.
12. There is no indication for surgery in non-obstructive FIC.
13. When surgery is performed in patients with FIC, obtain a full thickness bladder biopsy to allow evaluation of mast cells with special stains (toluidine blue).
14. Sometimes a so-called “placebo” treatment actually can have a positive effect between the cat, the owner, and the environment such that a positive outcome is achieved.
15. In most cases, antibiotic treatment does not have a role in the treatment of FIC.
16. Treatment of FIC with glucocorticosteroids has not shown an effect greater than that of placebo in limited study.
17. Chronic treatment of FIC with NSAIDs is NOT ADVOCATED due to the high sensitivity of the cat to sustain renal injury with this class of drugs, especially if there is any tendency toward dehydration.

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Special Aspects of Diagnosing and Managing Chronic Kidney Disease in Cats

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The incidence of the diagnosis of CKD in cats is made 2 to 3 times as frequently compared to dogs and is especially common in geriatric cats.¹ CKD is clinically characterized by the development of variably progressive irreversible intrarenal lesions and loss of renal functions. Compensatory increases (so called adaptations) in glomerular hemodynamics and glomerular volume may actually be maladaptive in the long term as they cause increased protein trafficking across the glomerulus.

The initial diagnosis of CKD is made on some combination of findings from clinical signs, physical examination (especially large or small kidneys, irregular kidneys), renal imaging, urinalysis, and serum biochemistry. A surprising number of cats with CKD have upper urinary tract uroliths at the time of initial diagnosis.²⁻⁴ Abdominal radiographs should be routinely obtained to determine the presence or absence of radiopaque stones. Renal and ureteral ultrasonography should be performed in all cats in which renal or ureteral stones were found on radiography in order to tell whether or not there is an obstructive component to the CKD. T4 should be measured in all cats with suspected CKD since hyperthyroidism can mask the detection of azotemia by its effects that increase GFR and RBF; hyperthyroidism may also contribute to progression of CKD through a variety of mechanisms including intraglomerular and systemic hypertension. ⁵ Conventional wisdom and experience suggests that client owned cats with healthy kidneys elaborate urine with a specific gravity of >1.035. This concept was recently validated in a study of cats evaluated at first opinion clinics.⁶ Cats with USG < 1.035 should undergo further diagnostic investigation to determine if they have an endocrine or renal disorder with or without associated clinical signs. A surprising number of experimental ⁷ and clinical cats with CKD continue to be able to elaborate urine with a USG > 1.035, so the presence of “concentrated” urine and mild to moderate azotemia does NOT exclude the presence of primary kidney disease in cats as it often does in dogs. Cats that have thin body condition, prior periodontal disease or cystitis, anesthesia or documented dehydration in the preceding year, or being a neutered male (vs spayed female) were reported to be at increased risk for the diagnosis of CKD.⁸

A staging system initially based on the level of serum creatinine concentration has been developed by IRIS (International Renal Interest Society) for use in cats that are hydrated and stable. Serum creatinine is measured again on at least 2 occasions 2 weeks apart by the same lab. Sub-staging is then based on the degree of proteinuria as measured by UPC and also the magnitude of blood pressure. Staging using this system is designed to detect CKD much earlier than with traditional methods and also to potentially match treatments by stage. Normal and stage 1 CKD cats have serum creatinine concentrations < 1.6 mg/dl (< 140 μmol/L). Normal cats usually have a UPC < 0.2, with 0.2-0.4 considered borderline increased, and > 0.4 overtly proteinuric. Details of this staging system can be found online at <http://www.iris-kidney.com>. This staging system does not indicate the underlying cause for the CKD which requires other diagnostic workup to determine. It is important to remember that nearly all studies on the effect of diet or drugs have studied overtly azotemic cats (serum creatinine > 2.0 mg/dl). It has not been determined whether or not the salutary effects of treatment in azotemic cats confer the same benefits to CKD cats at earlier stages.

Tubulo-interstitial nephritis of unknown origin is the most common cause of azotemic CKD in the cat, as in the dog. However, cats have several renal diseases that deserve additional consideration as compared to dogs including breed related predilection for renal amyloidosis (Abyssinian, Oriental Short Hair) and polycystic kidney disease (Persian, Himalayan). Cats have greater frequency of CKD associated with renal LSA than dogs. Peri-nephric pseudocyst can be associated with CKD in cats and should be considered as a differential diagnosis for apparent renal enlargement in addition to renal LSA and hydronephrosis.

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. Dennis-I just moved this here as it opens your discussion re treatment.

Dietary interventions for CKD

Dietary therapy remains the cornerstone of management of CKD. Diet modifications include phosphorus restriction (most important), providing reduced quantity but high quality protein, adequate non protein calories from fat and CHOs, modifying sodium content (not the degree of restriction once recommended by some), supplementing potassium, B vitamins, alkali as needed and providing omega three fatty acids. In one 2-year study, cats with a serum creatinine > 2 mg/dl fed a renal diet had a median survival time that was 2.4 times longer than cats fed a maintenance diet (633 days vs 264 days).⁹ In another study, IRIS stage 2 & 3 cats were followed for 24 months. Cats fed the maintenance diet had more uremic episodes and more renal-related deaths compared with cats fed the renal diet.³ In a study of 175 CKD cats fed 1 of 7 different renal diets, the median survival time was 16 months (12 to 23 months) compared to a median survival time of 7 months for cats eating their maintenance diet. Interestingly, the longest survival period was found in cats eating a renal diet with the highest eicosapentaenoic acid (diet not available in North America), otherwise the renal diets were similar

in composition.¹⁰ Patients are more likely to accept a new renal diet if offered before uremia develops and a gradual transition may be needed.

The number one reason to restrict dietary protein is to provide an adequate degree of restricted intake of phosphorus, especially those associated with animal tissues in the diet. Decreased production of nitrogenous wastes can occur in those with large increases in BUN, and consequently improve the clinical well-being of the pet even though renal function remains unchanged. If proteinuria is present, dietary protein restriction may lower the magnitude of proteinuria through obscure mechanisms. Reduced dietary protein intake may also lessen inflammatory, fibrogenic and oxidative stress pathway.¹¹ The amount to restrict dietary protein is not known, so it is currently recommended to provide at least maintenance levels. For cats with CKD, the minimum dietary protein requirement suggested is 20% of calories, which equates to 24% protein on a dry-matter basis.¹¹⁻¹⁴ Others suggest 28–35% (DMB).¹⁵ It is emphasized that less total dietary protein can be fed if high biologic value proteins, such as egg, are fed.¹³ Lowering animal-derived protein (source of phosphates) in the diet may be essential to lower dietary phosphorus intake needed to achieve target levels of serum phosphorus.¹⁶ Too much dietary protein restriction can and often does result in protein: calorie malnutrition. Protein malnutrition from any cause is strongly correlated with morbidity and mortality. If protein malnutrition becomes evident in a patient (hypoalbuminemia, anemia, weight loss or loss of lean muscle mass), then the amount of protein should be increased until signs are no longer evident. Cats with sarcopenia, regardless of the stage of renal disease, may require more protein than a renal diet can provide—careful monitoring and adjustment will be needed in these cats.

Pets with CKD often suffer from poor appetite that can contribute to poor body condition. This is often associated with decreased prognosis as the owner's often euthanize when quality of life is perceived as unacceptable. *Mirtazapine (Remeron)* helps not only with appetite but with uremic-associated nausea. Recent work in cats indicates mirtazapine can be administered at a low dose (1.88 mg) every 48 hours to cats with CKD, but was only studied for its effects for 3 weeks.^{17,18} Remember that mirtazapine and cyproheptadine cannot be administered concurrently. Cyproheptadine is in fact used as an antidote for serotonin effects of mirtazapine overdose. *Maropitant (Cerenia)*: NK-1 receptors are in the chemoreceptor trigger zone, in the emetic center itself, as well as peripherally. Consequently, Cerenia is a great choice to treat vomiting/nausea in renal cats. Despite the label recommendation, many specialists are recommending Cerenia for longer than 5 days (personal communication with specialists and with Zoetis scientists). Dose: 1 mg/kg PO once daily. Refrigerate to help alleviate the sting associated with injectable cerenia.¹⁹ *Omeprazole (Losec)*: Studies in cats have also shown Omeprazole to be more effective than H2 blockers such as famotidine and ranitidine in decreasing gastric acidity.²⁰ Dosage: 0.5-1 mg/kg once a day. If H2 blockers are used, dosages recommended are *Famotidine* (Pepcid®) 0.5 mg/kg IM, SQ, PO q 12 hours or *Ranitidine* (Zantac®) 1-2 mg/kg q 12 hours (cat). Studies have shown most cats with uremia do have elevated gastrin levels (and likely corresponding hyperacidity) but no GI ulcers.^{20,21} Consequently, *sucralfate* is not usually indicated. The GI bleed with uremia could be from dysregulation of the vasculature and platelet dysfunction associated with uremia.^{20,21} If used, a dose of 0.25-0.5 g/cat q 12 hours is recommended. In some countries *sucralfate* is used as an intestinal phosphate binder due to its aluminum content. *Ondansetron* at the time of this writing is not highly recommended. The bioavailability is not high (maybe 30% at best in cats) and the half-life is very short (it would be best to give this drug 4 times/day).²²

Phosphorus

Higher concentrations of serum phosphorus predicted an increase in serum creatinine > 25% above baseline over 12 months in 47% of CKD cats.²³ Serum phosphorus was the only clinicopathologic variable predictive of survival in one study of CKD cats. There was an increase in risk of death of nearly 12% for each mg/dl increase in phosphorus in the same study.²⁴ Higher phosphorus concentration was associated with a higher risk of death within 1 month in another study.²⁵ Even when serum phosphorus was within the reference range, cats with CKD of one study that had phosphorus concentration > 4.7 to ≤ 6.8 mg/dl serum phosphorus had a higher risk of death compared to CKD cats in which circulating phosphorus concentration was ≤ 4.7 mg/dl.²⁶

Dietary phosphorus restriction is critical at least from Stage 2 onwards; there is no data to evaluate any potential benefit of Pi restriction in Stage 1. Compared to the average grocery or pet store foods, the renal friendly veterinary diets are restricted in phosphorus by 70 to 80%. Serum phosphorus concentration may increase in CKD pets that increase their food intake following other supportive CKD treatments. Renal diets may provide sufficient dietary phosphate restriction during early stages of CKD but often the addition of dietary phosphate binders will be needed to reach targeted control of serum phosphorus. Early phosphorus restriction in CRF has been shown in dogs and cats to blunt or reverse renal secondary hyperparathyroidism.²⁷

Intestinal phosphate binders

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. 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. 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. Animals should be monitored for development of hypercalcemia whenever calcium-containing phosphorus binders are used. Sevelamer hydrochloride (Renagel[®], Genzyme Corporation) and the more recently FDA approved Sevelamer carbonate (Renvela[®], Genzyme Corporation) are organic polymers that do not contain aluminum or calcium and are not absorbed from the gastrointestinal tract (excreted entirely in feces). Their effects on dogs and cats with clinical CRF have not been reported. Epakitin[®] (Vetoquinol 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. The results of two studies^{28,29} 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 carbonate (Fosrenol[®], Shire Pharmaceuticals) is a 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. A recent abstract in a small number of CKD cats administered lanthanum carbonate in food at 95 mg/kg/day to achieve very modest serum phosphate control.³⁰ Several reports of the efficacy and safety of lanthanum carbonate treatment in cats have been published.³¹ Lanthanum carbonate octahydrate (Lantharenol[®] Bayer HealthCare AG) is marketed as a feed additive for adult cats in order to decrease intestinal phosphate absorption. Renalzin[®] (Bayer HealthCare AG) is the proprietary name for the delivery system of Lantharenol[®] and comes as a pump system that delivers lanthanum carbonate along with kaolin and vitamin E at appropriate doses to food for cats. This system is widely available in the UK and Europe, but not in the USA or Canada. The proprietary formulation of human lanthanum carbonate is soon to become available as a generic product.

Pronefra[®] recently has been launched (Virbac, France) as a dietary supplement for cats with CKD. This product provides a combination of calcium and magnesium carbonate as the intestinal phosphate binders, chitosan for “uremic toxin” binding, vasoactive peptides (designed to maintain normal blood pressure) and an extract of *Astragalus membranaceus* (Chinese herb for anti-inflammatory and anti-fibrotic effects). Safety of this product was reported in 10 normal cats in which Pronefra was added to the food once daily for 12 weeks^{32,33} No changes in circulating calcium or magnesium were noted at during this study. Presently there are no reported studies of safety or efficacy in clinical cats with CKD treated with this supplement.

Novartis has developed a new oral phosphate binder for cats called Lenziaren[®] (SBR759). Iron oxide with starch and sucrose exist in this preparation as an insoluble complex. A dose of 0.5 to 1.0 Gm/cat/day is recommended when added to standard diets.³⁴ A dose of 0.25 Gm/cat/day to 1.0 Gm/cat/day is recommended when adding this phosphate binder to a renal diet.³⁵ Safety and efficacy of Lenziaren[®] in cats with CKD are not yet reported. Lenziaren is touted by the authors as a phosphate binder that does not contain aluminum, calcium, or lanthanum that could be problematic in cats with CKD. That is true for the aluminum and calcium as a factor in favor of its use, but there is no known toxicity of lanthanum yet reported.

Control of proteinuria

Cats with azotemic CKD 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 >0.4.³⁶ The prognosis for survival is influenced by the UPC despite what has traditionally been thought to be low-level proteinuria. The effect of treatments that lower proteinuria on survival have not been specifically studied. Since even low-level proteinuria is a risk factor for cats to not survive, it is prudent to consider treatments that lower the amount of proteinuria in those with CKD. See discussions about the potential benefits of dietary protein restriction (above) and RAAS inactivation (below) to reduce the magnitude of proteinuria.

RAAS inactivation

RAAS inactivation results in decreased generation of angiotensin-2 and aldosterone that can exert benefits to reduce progression of CKD. These beneficial effects can occur through variable combinations of reduction in systolic blood pressure, decreased intra-glomerular hypertension, decreased glomerular proteinuria, and less generation of pro-inflammatory and pro-fibrotic cytokines in patients with CKD.

Benazepril is labeled for treatment of azotemic CKD in cats in the UK, Europe, and Canada (Fortekor[®]), but not in the USA. The ACE-inhibitor benazepril consistently reduces proteinuria in various stages of CKD in cats even when the base line level of proteinuria is seemingly trivial. Benazepril has been shown in two clinical studies to reduce the UPC in cats with azotemic CKD.^{37,38} Despite reduction in proteinuria in CKD cats with initial UPC > 1.0 that were treated with benazepril in one study, increased survival

time was not found over placebo.³⁷ The average survival time of all benazepril treated cats in this study was 501 days vs. 391 days for placebo treated cats but this effect did achieve statistical significance.³⁷ In another study of 61 cats with CKD, benazepril treatment for 189 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).³⁸

The angiotensin receptor blocker (ARB) telmisartan (Semintra® Boehringer Ingelheim) was approved by the European Commission in 2013 for use in the European Union as a drug for use in cats with CKD and is available for use in Canada but not yet in the USA. Semintra was found to be at least as effective as benazepril in reducing proteinuria in cats with CKD and was well tolerated.^{39,40} A US Patent application was filed in July 2013 by Boehringer Ingelheim. It is not clear when or if an ARB should be chosen to reduce RAAS activity instead of an ACE-Inhibitor for treatment of CKD in veterinary patients to reduce proteinuria, systemic blood pressure, or intra-renal inflammation. A veterinary review of the RAAS system, ACE-Inhibitors and ARB's provides more detail for the interested reader.⁴¹

Activated vitamin-D metabolites: calcitriol

Calcitriol treatments help to decrease PTH or prevent its increase in those with renal secondary hyperparathyroidism. This occurs largely through genomic effects to block PTH synthesis in addition to a mild calcemic effect, and anti-proliferative effect that prevents parathyroid gland hyperplasia. It has become increasingly apparent that calcitriol has major beneficial anti-inflammatory and anti-fibrotic intrarenal effects that are independent of effects on PTH.²⁷ 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.

In a recent study of dogs with azotemic CKD that were treated with calcitriol a median of 365 days survival was observed compared to 250 days in dogs treated with placebo (renal diet in both groups).⁴² Similar studies were performed 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 CKD 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. The authors believe that beneficial effects of calcitriol treatment are likely to occur in cats with CKD.

A compounding pharmacy will be needed to reformulate calcitriol from the human parent drug to a concentration suitable for the dosing of cats. We recommend intermittent rather than daily dosing treatment protocols as the standard of care since less hypercalcemia occurs using 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/kg). 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.

Systemic hypertension

Systemic hypertension is common in cats with CKD with 13-28% of cats presenting with hypertension when CKD is first diagnosed and up to 65% of cats developing hypertension at some point during the progression of their renal disease.⁴³⁻⁵¹ Cats that have systemic hypertension from a variety of causes have been shown to survive longest when their blood pressure is well controlled.

Enalapril or benazepril as monotherapy has not been very effective for treatment of hypertensive cats or dogs. 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.^{43,46,47}

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Feline Acute Kidney Disease: Diagnosis, Management, and Prevention

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Acute kidney injury (AKI) is the term used to describe a spectrum of acute alterations in kidney function and structure that range from mild (clinically inapparent) to overt acute renal failure (varying degrees of azotemia). Portions of the nephron may be temporarily injured or they may sustain lethal injury resulting in permanent loss of nephron mass depending on the severity of the insult. Recovery of full renal function and histopathological structure is possible in some cases. Partial recovery with substantial nephron loss will result in recovery as a CKD patient in some. In other patients, severe injury results in substantial loss of nephron mass and renal function that will not allow a reasonable quality of life without dialysis. Severely azotemic AKI patients often require dialysis to be managed adequately.

The details of a new grading system for categorization of acute kidney injury (AKI) developed by IRIS (International Renal Interest Society) are available for further review at <http://www.iris-kidney.com/guidelines/grading.shtml>. Much like the IRIS staging system for CKD, this grading system is designed to detect AKI at early stages when it is more likely that therapeutic interventions can avert further injury and allow recovery of renal function and tissue repair. The clinical prognosis is likely to align with the AKI grade that develops. Historically, attention was mostly directed to patients with serum creatinine that exceeded the reference range. In the IRIS AKI scheme, even a small increase in serum creatinine within the reference range is considered an important marker for potential acute renal injury. The IRIS AKI grading system involves evaluation of fasting serum creatinine concentration as the first step and then the staging is refined based on urine output if it is known (see Table 1). The same cutoffs for creatinine and urine output have been chosen for use in the dog and the cat. Oliguria, normal urine production, or polyuria can all occur depending on the specific cause and severity of renal injury sustained during AKI. History and physical examination parameters also enter into assignment of the grade. AKI typically focuses on those with acute injury to kidneys that were intrinsically normal prior to the acute injury. Pre-renal and post-renal disorders can occur in the absence of primary renal injury but they can also occur on top of a primary renal injury. Patients with CKD often have an “acute-on-chronic” presentation with changes in level of azotemia that falls into the AKI grading scheme. An inability to regulate solute and water balance is often present and renal synthetic and degradatory functions are impaired to varying degrees during AKI. It should be noted that this AKI staging scheme is dynamic in that the grade may increase or decrease in severity over time and treatment. Extensive diagnostic evaluation may be needed to determine the specific cause(s)/diagnosis underlying the AKI; specific diagnosis is not specified by the AKI grading status.

Differential diagnosis and frequency of AKI – See Table 2. Causes of AKI in cats

The frequency of underlying conditions associated with AKI varies with the nature of the veterinary practice. Nephrotoxicity is the leading cause for AKI at The Ohio State University Veterinary Hospital, followed by ischemia. The aggressive use of potentially nephrotoxic antibiotics, particularly the aminoglycosides, can contribute to nephrotoxic AKI. The exposure to cholecalciferol rodenticides, use of non-steroidal anti-inflammatory drugs (NSAID), and exposure of veterinary patients to extensive surgical procedures and aggressive post-traumatic resuscitative maneuvers as emergency patients can result in AKI. Ischemic and nephrotoxic AKI occur more readily in patients that have underlying chronic renal disease or renal failure.

Diagnosis of AKI

Rapid increases of BUN, serum creatinine, and serum phosphorus may be observed during severe AKI. This is particularly helpful to document AKI in the absence of recent serum biochemistry values for comparison. For example, a patient’s serum creatinine of 4.3 mg/dl, 6.0 mg/dl, and 7.5 mg/dl sequentially over three consecutive days supports a diagnosis of azotemic AKI. Serum creatinine and BUN do not increase over this short a time period in hydrated patients with CKD. Hyperphosphatemia may be out of proportion to the degree of increase in BUN or serum creatinine in those with AKI compared to CKD. The magnitude of elevation in BUN or serum creatinine concentrations is not helpful in the diagnosis of azotemic AKI vs CKD or in the differentiation of pre-renal, intrinsic renal, or post-renal azotemia. See Table 1 AKI grading for how to detect AKI at earlier levels of increasing serum creatinine. Urinalysis reveals a low specific gravity (USG) during the maintenance phase of azotemic AKI (SG less than 1.030, but most-often in the 1.007 to 1.015 range). Decreased maximal USG may be detected before an increase in serum creatinine is detected. Dipstrips may show proteinuria, hematuria or glucosuria on occasion. UPC can be increased due to increase in protein excretion normally handled by renal tubules. Urinary sediment is typically “active” at early stages of the maintenance phase of severe AKI exhibiting increased numbers of casts (particularly cellular casts) and small epithelial cells compatible with renal tubular epithelium. Animals with AKI as the sole problem should have smooth kidneys with normal or increased kidney size whereas those with chronic renal failure may show small and or irregular kidneys both on palpation and abdominal radiographs. Renal ultrasonography can provide additional anatomic information to confirm intrarenal lesions, but cannot be relied on to distinguish acute from chronic renal failure or to suggest a specific

microscopic lesion. Failure to document ultrasonographic renal changes does not exclude a diagnosis of AKI. Kidneys may enlarge during AKI but this may not be detected if they are still within the normal range for kidney size; kidneys tend to become “plump” before they measure elongated. Peri-renal effusion was described in 6 cats with azotemic AKI.¹ Renal biopsy may be helpful to determine that an azotemia is due to primary renal lesions and to characterize the changes as acute or chronic. A positive urine culture in the face of AKI is of concern for upper urinary tract infection, but this finding alone is not definitive to establish a diagnosis of pyelonephritis.

It is imperative to exclude acute post-renal azotemia due to ureteral stones or stricture in cats presenting with azotemia that appears to have developed suddenly. In some cats ureteral stones cause complete obstruction of one or both ureters resulting in varying degree of oliguria or anuria and rapidly escalating magnitude of azotemia. Due to the frequency of this syndrome associated with calcium oxalate urolithiasis, survey radiographs need to be evaluated in all cats suspected to have AKI. If renal or ureteral stones are noted, ultrasonography to determine the degree of any hydronephrosis and or hydroureter is the next step. Many of these cats have pre-existing chronic kidney disease that makes it relatively easy for azotemia to develop even when only one ureter is obstructed. In many instances, there is the presence of “big-kidney little-kidney” syndrome likely reflecting previous chronic kidney injury reducing the size of one kidney and hydronephrosis increasing the size of the second kidney.² Though the azotemia can be quite striking and rapid in development, these cases represent acute post-renal azotemia on top of chronic primary kidney disease. Medical therapy is not often successful in management of these cats and relief of the ureteral obstruction by minimally invasive stenting or traditional surgery will be needed in order to sustain life without dialysis. The prognosis following relief of the obstruction is often guarded due to the underlying chronic kidney disease.

Prognosis of AKI

The attending veterinarian and client often have greater expectations for immediate improvement following treatment than is realistic, remembering that the maintenance phase of azotemic AKI can last weeks in some cases before adequate renal repair and function can occur. The most likely causes for death during the initial management of the azotemic AKI patient in the maintenance phase are from the effects of hyperkalemia, metabolic acidosis, and severe azotemia. Overhydration and resulting pulmonary edema are the next major causes of death during vigorous fluid therapy.

There is no magnitude of increased serum creatinine concentration measured at one time point that determines prognosis. Serial serum creatinine measurements over time are much more informative. Acute changes in the concentration of serum creatinine were associated with prognosis in one study of 209 cats with an initial serum creatinine of < 1.6 mg/dl and at least 2 serum creatinine measurements within 7 days. A poorer prognosis was found in cats that increased their highest serum creatinine to > 1.6 mg/dl with at least an increase of 0.3 mg/dl. If this increase in serum creatinine were achieved within 3 or 7 days, cats were about 3 times more likely to die at 30 days and 4 times more likely to die within 7 days. When this increase in serum creatinine occurred within 2 or 3 days, death within 90 days was 3 times more likely.³ Azotemic AKI was diagnosed in 32 cats of an earlier study (serum creatinine >2.5 mg/dl); 18 cats were oliguric at the time of diagnosis. About half of these AKI cats survived (53%) with complete resolution of azotemia in 25% and persistent azotemia (CKD recovery) in 28%. The initial BUN or serum creatinine concentration did not predict survival nor did oliguria. Serum potassium increases seemed to be the most important predictor of survival; a 57% decreased chance in survival occurred for each mEq/L increase over the initial serum potassium concentration. Low initial serum albumin and bicarbonate were also associated with less survival.⁴

A grave prognosis is warranted for cats that develop anuric AKI after IV fluid treatment, a situation most-likely to develop in ethylene glycol intoxication but may also be encountered in cats following ingestion of Easter or day lilies. It should be noted that dogs and cats with severe oliguric AKI have recently been shown to survive with return of renal function and urine production following several months of hemodialysis. The presence of non-oliguria does not guarantee survival either. Due to the poor to grave prognosis for many cases with severely azotemic AKI, prevention is far preferred to treatment.

General goals for treatment of azotemic AKI during the maintenance phase

Placement of an indwelling intravenous catheter is necessary to adequately administer fluids and drugs in the management of azotemic AKI. Rapid correction of dehydration is indicated and can be individually calculated (estimated % dehydration x body weight in kg = Liters of dehydration) or given as 2 to 3 times maintenance fluid needs (60 to 90 ml / pound per day). Further fluids are given to match sensible (urinary volume), insensible (respiratory losses at about 10 ml/lb/day), and contemporary (an estimated volume from vomiting and diarrhea) fluid losses. Since urine output is widely variable in AKI, it is advisable to place an indwelling urinary catheter to monitor urine output to facilitate fluid therapy decisions for the initial 24 to 48 hours. The recognition of oliguria is important initially as it dictates the volume of IV fluid therapy that can be safely given. Urine production less than 1.0 ml/kg/hour (24 ml/kg/day) qualifies for oliguria in our hospital prior to rehydration and volume expansion. Relative oliguria exists if urine production is from 1.0 to 2.0 ml/kg/hour while on IV fluids. Urine output should be from 2.0 to 5.0 ml/kg/hour during vigorous administration of IV fluids if the kidneys are healthy. It is essential to curtail the fluid prescription for volume to be further infused once hydration has

been established especially when urine output does not increase. It is the author's impression that it is easier for cats with AKI to develop overhydration compared to dogs with AKI even with careful monitoring.

Newer thinking about the dangers of IV fluid therapy in the critically ill

If insufficient fluids are given to the AKI patient, the kidneys are not optimally perfused and sustain further ischemic injury. If too much fluid is given, then overt overhydration with pulmonary edema, congestive heart failure, and death follow. A new paradigm suggests that too many fluids and subclinical development of overhydration also result in further renal injury from visceral overhydration and reductions in renal blood flow and GFR as renal interstitial edema develops.⁵⁻⁹ Renal edema can be an early development following some forms of renal injury. It appears that renal edema can also develop as a consequence of too aggressive fluid therapy. Conventional wisdom has been that it is better to have a little over-hydration than to have the damaged kidneys endure any chance for underperfusion and ischemic injury. It now appears that contrary to popular opinion, it is better to be a little on the "dry" side following rehydration and moderate resuscitation rather than to risk the development of over-hydration. It is possible that declining renal functions in the face of aggressive fluid therapy (reflected by rising BUN, creatinine, and phosphorus) may actually be caused by this treatment and resulting renal edema. Interstitial edema decreases renal blood flow by compression of renal vessels, and opposes GFR by compression of Bowman's capsule and compression of renal tubules. This concept needs to be further evaluated in both human and veterinary medicine. For now, caution is advised so that minimal fluids following correction of hypotension and rehydration are administered. The concept that "less is more" has been advocated in a veterinary review of AKI in cats.¹⁰

Conversion from oliguria to non-oliguria

Mannitol, furosemide, dopamine, or combinations of these are the diuretics most often employed in attempts to convert oliguria to non-oliguria or to increase renal function (RBF, GFR) Rehydration prior to use of diuretics should occur first to allow greater delivery of the diuretic to its site of action. There are no reports that detail the response of cats or dogs with clinical AKI to these treatments. The so-called "renal-dose" of dopamine (below the vasopressor dose, often from 2 to 5 micrograms/kg/minute) has surprisingly little clinical documentation to support its use in either human or veterinary medicine.^{11,12} A combined infusion of dopamine and furosemide to awake normal cats increased urine output but did not increase GFR.¹³ Fenoldopam as a selective DA-1 receptor agonist has the potential to cause renal vasodilatation with increased RBF, GFR, and natriuresis without activation of alpha and beta adrenergic receptor effects that occur with dopamine at higher doses.¹⁴

Ethylene glycol nephrotoxicity

The gold standard to prove the presence of ethylene glycol or its toxic metabolites following bioconversion remains testing with HPLC on serum or plasma samples. This type of testing is not commonly available, though it can be performed at local human hospital laboratories. The EG Test Kit (Allelic Biosystems, Kearnesville WV) is supposed to be able to detect 50 mg/dl of ethylene glycol in a serum/plasma sample but this has not been studied in cats. Test strips designed to detect ethylene glycol (Kacey ethylene glycol test, Kacey Inc, Asheville, NC.) were found to have too many false positives and false negatives to be useful for clinical work in cats.¹⁵ The Catachem test kit (Catachem Inc., Oxford, Connecticut) detected the presence of EG when added to serum or plasma of dogs and cats but did have a positive bias in slightly overestimating actual EG concentrations.¹⁶ This company provides both a quantitative and qualitative test to detect EG. The utility of the osmole gap has been ignored by many in the critical care community. A large osmole gap is proportional to the amount of unmetabolized ethylene glycol in many cases. A large osmole gap is most commonly created by ethylene glycol ingestion in small animals, but a large osmole gap could also result in animals that have consumed propylene glycol as an alternate and less toxic formulation of antifreeze. The presence of calcium oxalate crystalluria is supportive for the diagnosis of ethylene glycol intoxication in the appropriate setting – cat that is sick, possible history or observation of ingestion, and sub-maximally concentrated urine. Calcium oxalate crystalluria is observed in fewer cats than in dogs with ethylene glycol intoxication.^{17,18} Calcium oxalate monohydrate crystalluria is more commonly detected than calcium oxalate dihydrate crystal following EG ingestion. Calcium oxalate monohydrate has several different morphologic appearances that can be difficult to identify whereas calcium oxalate dihydrate is more easily recognized.¹⁹ An extremely hyperechogenic renal cortex and medulla may be observed soon after ingestion of lethal quantities of EG in the cat as in the dog.^{20,21}

Fomepizole at high doses is the antidote of choice to treat cats following EG ingestion. Fomepizole is administered in higher doses than needed in dogs in order to effectively inhibit alcohol dehydrogenase²², which otherwise is the first step in the bioactivation of EG to its toxic intermediary metabolites. Fomepizole is given to cats with an initial dose of 125 mg/kg IV followed by 31.25 mg/kg at 12, 24, and 36 hours. Use of this treatment protocol was effective in prevention of azotemic AKI in experimental cats treated within 3 hours of exposure to an otherwise lethal dose of EG. Fomepizole was a more effective treatment than ethyl alcohol and provided less CNS depression (some sedation was observed).²³ This fomepizole protocol was successfully used to treat 3 cats with naturally occurring EG poisoning that were not azotemic at presentation.²⁴ If fomepizole is not available and it is within 3 hours of EG ingestion, 20% ethanol at 5mL/kg IV initially, followed by the same dose every 6 hours for 5 treatments and then every 8 hours for 4

treatments could be a life-saving alternative antidote. Ethyl alcohol should ALWAYS BE DILUTED prior to administration, otherwise IV administration can cause cardiac arrest.

Lily nephrotoxicity²⁵⁻³²

The cat is exquisitely and perhaps uniquely sensitive to the nephrotoxic effects following lily ingestion. The specific toxic principle is unknown but all parts of the lily are toxic to cats. Nephrotoxicity has been observed in cats that have chewed only a small portion of a single lily leaf. The *Lilium* genus contains nearly 100 species and hundreds of hybrids that are thought to be toxic too. Aqueous extracts of the flower and leaf from the Easter lily contain the toxic principle, with the flower being more potent. Calla lily and peace lily are not real lilies and are not associated with AKI in cats. Lily of the valley does not contain a nephrotoxin, but does contain a digitalis-like toxin. Pancreatic histopathology is observed in some cats.

A history that the cat was observed chewing on lily plants or the finding of fragments of the plant observed in the cat's vomitus provides pivotal clues to the diagnosis. Hypersalivation and vomiting may occur soon after ingestion of lilies due to local irritant effects on the GI tract. Vomiting and lethargy are commonly described 1 to 5 days after plant ingestion in those suffering AKI. Renomegaly and abdominal pain may be detected on physical examination. Varying degrees of azotemia may be documented in cats presenting days after lily ingestion. On urinalysis, isosthenuria, proteinuria, glucosuria, cylindruria, and occasionally ketonuria are present in those with severe AKI but crystalluria is notably absent. Oliguria or anuria may persist despite intravenous fluid therapy in those with severe AKI.

Decontamination combined with fluid diuresis for 48 hours prevents development of azotemic AKI for up to 6 hours after ingestion of lilies. Decontamination 18 hours or more after lily ingestion does not prevent development of azotemic AKI. Induction of vomiting followed by administration of activated charcoal and a cathartic is recommended by the Animal Poison Control Center. Vomiting should not be induced in cats that already are vomiting as a consequence of lily ingestion. No antidote is available to counteract effects of the absorbed nephrotoxin. Nearly all cats presented early with GI signs alone survive after decontamination and induction of diuresis.

As many as 33% to 50% of cats that ingest lilies will develop azotemic AKI if not treated within a few hours following lily ingestion. Anuric AKI can occur 18 to 24 hours after ingestion. Prognosis for recovery is poor after lily-induced development of severely azotemic AKI. The magnitude of azotemia that develops during AKI does not predict survival, but urine output does. Cats with azotemic AKI that are polyuric are more likely to survive. Cats with azotemic AKI and persistent oliguria or anuria are unlikely to survive. Cats that survive severe azotemic AKI after lily ingestion tend to have substantial permanent loss of renal mass and go on to develop various stages of CKD.

In a recent abstract, 30 cats were treated for lily ingestion associated AKI and 22 cats survived. Eighteen of the 30 cats were managed with aggressive medical treatment in which 89% survived. Twelve of the 30 cats were treated with intermittent hemodialysis with a 50% survival rate. Urine output and hydration status at time of diagnosis were not related to survival. Cats with a serum creatinine > 2.0 mg/dl at the time of diagnosis were more likely to die.³³

NSAID AKI

NSAIDs are not directly nephrotoxic, but rather work as nephrotoxicants that cause their damaging effect through intense vasoconstriction that develops under special circumstances. NSAID cause AKI only if systemic vasoconstrictor signals have been activated following hemodynamic insult (sodium depletion, volume contraction, hypotension, shock, anesthesia). Normal renal vascular resistance and renal blood flow are relatively well maintained during times of vasoconstriction if synthesis of renal vasodilator substances is normal. Renal vasoconstriction however proceeds unopposed if the synthesis of renal vasodilatory prostaglandins has been blocked by NSAID administration. In these instances, progression to acute azotemic AKI and papillary necrosis may occur. An increased frequency of azotemic AKI was reported in 16 young cats given NSAID at the time of routine desexing without IV fluid administration. Four of these cats were euthanized due to failure of severe azotemia to resolve, 4 cats survived with azotemic CKD, and 8 cats recovered with complete resolution of azotemia.³⁴ In 21 cats with NSAID AKI of another study, the mortality rate was 25% mostly in cats associated with papillary necrosis. Supportive therapy for up to 4 weeks was required for some survivors.³⁵ The FDA recently required the following statement to be added to the label for meloxicam use in cats, "Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats..." Robenacoxib, a long acting NSAID, recently has become available for use in cats in North America. Whether the incidence of NSAID-associated AKI is less during treatment with newer generation NSAIDs touted to have less GI side effects remains to be determined.

Table 1. IRIS AKI grading criteria – 2013 guidelines

Each grade is sub-graded as non-oliguric (NO) or oligoanuric(O) and if needing renal replacement therapy (RRT)

AKI Grade	Serum Creatinine	Clinical Description
Grade 1	< 1.6 mg/dL < 140 µmol/L	Non Azotemic AKI: a. Documented AKI: Historical, clinical, laboratory, or imaging evidence of acute kidney injury, clinical oliguria/anuria, volume responsiveness**, and/or b. Progressive non azotemic increase in blood creatinine; ≥ 0.3 mg/dl (≥ 26.4 µmol/L) within 48 hours c. Measured oliguria (< 1 ml/kg/hr) or anuria over 6 hours
Grade 2	1.7 – 2.5 mg/dl 141 – 220 µmol/L	Mild AKI: a. Documented AKI and static or progressive azotemia b. Progressive azotemic increase in blood creatinine; ≥ 0.3 mg/dl (≥ 26.4 µmol/L) within 48 hours, or volume responsiveness** c. Measured oliguria (< 1 ml/kg/hr) or anuria over 6 hours
Grade 3	2.6 – 5.0 mg/dl 221 – 439 µmol/L	Moderate to Severe AKI: a. Documented AKI and increasing severities of azotemia and functional renal failure
Grade 4	5.1 – 10.0 mg/dl 440-880 µmol/L	
Grade 5	> 10.0 mg/dl > 880 µmol/L	

** Volume responsive is an increase in urine production to > 1 ml/kg/hr over 6 hours; and/or decrease in serum creatinine to baseline over 48 hours

Table 2. Causes for AKI in cats**Renal ischemia (hypoperfusion)**

Dehydration	Shock
Trauma	Hemorrhage
Anesthesia	Surgery
Sepsis	Burns
Hyperthermia	Hypothermia
Hemolysis	Myoglobinuria
ACE Inhibitors	Non-Steroidal Anti-Inflammatory Drugs (NSAID)

**Note that renal ischemia can occur in the absence of systemic arterial hypotension.

Nephrotoxins

- More Common
 - Glycols (Ethylene Glycol)
 - Antimicrobials
 - Aminoglycosides
 - Amphotericin-B
 - Sulfonamides - dehydration
 - Tetracyclines – IV
 - Fosfomycin – not dogs³⁶
 - Easter Lilly – Cats
- Less Common
 - Hypercalcemia
 - Cholecalciferol Rodenticide
 - Cholecalciferol – Diet
 - Calcipotriene – antipsoriasis cream
 - Cancer Chemotherapeutics
 - Platinum compounds alone and more so when combined with piroxicam

- Radiocontrast Agents - IV
- Heavy Metals

Miscellaneous causes of AKI

- Renal thromboembolism – renal infarction
- Acute-on-chronic renal failure
- Renal amyloidosis with acute papillary necrosis
- Acute Hyperphosphatemia
- Tumor lysis syndrome
 - Phosphate enema
 - Phosphate acidifier
 - Massive soft tissue trauma
- Pancreatitis
- Food-associated renal failure – FARF
- (melamine with cyanuric acid tainting)

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Navigate Bumps in the Road: Steps to Create a Thriving Cat Friendly Practice

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The single biggest opportunity to grow small animal practices lies in the chronically underserved feline patient. With nearly 1500 participating practices there is emerging a body of knowledge that is critical for prospective practices to understand. Overcoming resistance on the part of unconvinced staff members and building a team to accomplish Cat Friendly designation are critical to accomplishing the establishment-wide changes that improve the experience that cats and their owners have. 83% of adopted cats are seen within the first year of adoption. Fewer than 50% of those return for regular veterinary care. Based upon HSUS adoption data, approximately 1.7 million cats are seen once and do not return. If 3000 practices became Cat Friendly Practices and the population was divided equally among them, there would be over 550 new patients per practice per year.

The Bayer Veterinary Care Usage Study 3 – Feline Findings focused on the population of cats and their owners that do not seek regular veterinary care and the views veterinarians and practice owners have of this underserved population. More than half of these 401 practice owners reported less than 70% of appointment times were filled. This represents a significant opportunity to better utilize veterinarians, professional staff and improve the work flow of the practice. When asked what could impact growth, the top two choices were increasing cat and dog visits. However, more than 50% had no method in place to monitor or evaluate the efficacy of their reminder systems. They did not, then, know whether their existing clients were being effectively encouraged to return to the practice.

While increasing cat visits was the second most cited way to grow and practices did not believe they would need to make many changes in the practice to increase visits, less than 1 in 5 had actually taken any steps to do so. More than 1 in 3 practice owners had no intention of implementing changes that would reduce stress for cats. Almost as many had made no attempt to train staff to make feline visits less stressful.

As research has shown, there are more companion cats than dogs. This should mean that veterinary practices see more cats than dogs, but the opposite is true. Many cat owners avoid veterinary visits for a variety of reasons. One major reason is that they are convinced that their cat hates the experience. Another is a lack of understanding of the need for preventive health care for creatures who seem to be independent and healthy. Clients also dislike the experience of the 30+ minutes that precede the visit during which conflict arises around the carrier, the traumatic experiences in the automobile and the disruption of routine that is so important to cats.

Cats seem to experience forceful handling by their otherwise predictable and beloved human as a betrayal of their trust. The car, carrier and veterinary establishment are unfamiliar to a creature who values a sense of control and familiar routine. As a veterinary team, we may not understand cats, their behavior cues, or normal behaviors. We may feel as if cats are more of a nuisance, take too much time or will potentially cause injury. Our attitude is conveyed through approach, body language and other forms of communication apparent to both cats and their owners.

When a cat visit becomes disruptive we lose the fundamental opportunity to form the trusting relationship we need to have with our clients so that we can practice the best medicine. We lose the chance to calmly build rapport, establish trust and educate clients that is so crucial to our future with them and their cat.

The solution to declining cat visits, to resulting welfare issues, and to our ability to serve this patient population is to become cat friendly. We must create a practice culture in which the entire staff is committed to improving the experience of the feline patient and their owner. We must incorporate this into staff training and education, into the practice physical environment and into our plans for the future.

We must begin by educating our clients. By sharing with them our knowledge of the characteristics of the feline, we can teach them to have reasonable expectations, to understand the subtle signs of illness, and to prevent unacceptable behavior before it starts. By understanding the social groups in multiple cat households and how the social structure of cats has evolved, we can decrease the stress experienced by companion cats and their owners. We can teach breeders and “accidental” breeders to raise well-adjusted flexible, social kittens who will become wonderful cats for the people who adopt them. We can teach them how to lower the household stress by giving them a better understanding of their cats’ needs, sensory awareness, and perception of safety.

Our outreach has to be where our clients are, i.e., on the internet. We need lively web sites with important educational links. We need Facebook pages that are constantly updating and providing tips and entertaining topics that engage the clients before we meet them in the practice. Our educational efforts can result in happier households and healthier cats. Clients need to understand how cats prefer being alone when eating, why play is important and how cats interact with each other and humans.

The Bayer Brakke study showed that the recession did not cause the decline in visits but rather, unmasked a phenomenon that has been going on since the late 1990’s. This investigation made several recommendations regarding the goals that would improve cat visits including understanding the client household, addressing handling, communication, and safe transport.

Becoming cat friendly is not a construction project; it is seizing this opportunity to harness the talent and intellect of the staff to change behavior and attitudes. Cat friendly practices nurture relationships with clients by employing open communication and active listening. The staff becomes deeply committed to achieving skills in gentle handling, understanding behavior, and the unique medical and surgical needs of cat patients.

Change in the busy veterinary practice is difficult. One of the most important roles in affecting the practice culture is to assign a Cat Advocate to the project. That person is not responsible for doing all the work to become cat friendly but to make sure the work is done. Cat friendly is not a project, it is a cultural shift within the practice that must be continually monitored and assessed. Education plans, physical changes, communication training are ongoing. By evaluating the cat and client's experience from before the visit to the time they leave, we can establish a plan for improving that experience.

The first experience of the practice environment is often the first phone call. Using that contact to educate clients or potential clients about resources available to help make the pre-visit experience less stressful are key. Questions about carriers, automobile transport and other cats in the household can be satisfactorily answered. Resources can be sent in a variety of ways from web links, pdfs or written brochures.

The physical presence of other animals in the reception area is a key consideration for reduction of stress. Many strategies for reducing the negative effects can be implemented including, separate entrances, separate waiting areas, or "cat only" days. Voices should be kept low, sounds kept to a minimum, unnecessary odors like perfume or cologne avoided. Visual barriers can be employed to keep cats from seeing dogs or other cats. Staff members must be counseled not to look directly in the face/stare at cats.

In the exam room, the cat should be allowed to walk out of the carrier while the doctor is speaking calmly with the client. If the cat leaves the carrier, remove it from sight as it has become the most familiar thing in the room and the cat will be inclined to return to the carrier. If, after an appropriate time, the cat remains in the carrier unwilling to exit voluntarily, remove the lid of the carrier. This is far less stressful than other ways of removing the cat. Towels can be employed to help fearful cats remain calmer.

One of the most critical skills required for becoming cat friendly is to learn to read how cats communicate their emotional state through their body posture, facial expression and movement. Fear is the #1 cause of "bad behavior" in the veterinary environment. By learning to assess emotional states, we can avoid a fully aroused state that takes a cat 30-40 minutes to recover from. Cats leave behind a scent from their pads that indicates stress. Careful cleaning between appointments is not only important for disinfection but also to remove this form of communication between cats.

A cat examination room should contain all of the equipment and supplies needed to perform most outpatient services. By approaching in a calm manner, keeping the people in the room to a minimum, using quiet voices, towels for restraint if needed, and being flexible about the order the exam is performed in, there will be more successful experiences than usual. Scruffing or stretching should never be necessary and is counter-productive. In a calm environment the doctor can talk through the exam, making sure clients understand what is being done and the value and importance of the physical exam.

Many gentle techniques are described in the photos in the Cat Friendly Practice (CFP) program that offer ideas regarding restraint. The examination table may be the least necessary piece of equipment in the room. Cats may prefer the bottom of a carrier, a lap, a chair or the floor and should be accommodated. Moving cats by picking them up adds a level of stress to an already fearful cat. The reflex response to fear is to flee thus maintaining all four feet on the floor is very important to a sense of control and reassurance. Every effort should be made to avoid taking the cat to the "back" of the hospital. The exam room is now somewhat familiar. To move to a foreign space offers new stressors, different smells, bright lights, more animals, people, and noises.

Cats who must be admitted to the hospital have an increased need for a sense of familiar comforts. This can be provided by asking the client to bring known items from home; bedding, brushes, food, bowls or toys. Soft bedding, a place to hide and gentle nursing techniques are critical. For cats who enjoy social interaction, petting, brushing and other forms of interaction can be employed.

The cat ward should be separate from dogs and other animals, big enough so that cats cannot see one another. Cages should not face each other. Cats passing each other for treatment or discharge should be shielded from view. When removing a cat from a hospital enclosure, allow the cat to come forward or use bedding, towels or the bottom of the carrier to slide the patient forward. Do not loom about the cat or block the light.

The entire inventory of equipment, instrumentation, physical facility should be examined to make sure they are appropriately sized for the feline patient.

The Cat Friendly Practice program provides veterinary practices with ALL of the information, tools and techniques for becoming cat friendly. There are ten areas to evaluate with resources to achieve compliance with all of them. This program will continue to evolve and grow as new phases are implemented. The next of these will be Preventative Health Care. To participate the practice must have one AAFP member, identify the Cat Advocate for the practice and use the website, manual and checklist to achieve either gold or silver CFP status.

In recognition of this effort, the program provides you with a toolkit to market your practice as one that has made this significant effort and to distinguish yours from other practices that have not. A searchable website will allow clients to look for Cat Friendly

Practices in their region. Beginning in the fourth quarter of 2012, the AAFP began a national consumer awareness campaign to encourage cat owners to seek a Cat Friendly Practice. Refinements and additions to this campaign will continue.

As we discuss each aspect of the program, specific examples of creative and innovative methods CFP practices used to overcome barriers to certification, to market themselves and to significantly benefit by the effort made to implement the program will be discussed. Almost every CFP practice currently certified plans to renew their certification when the two -year membership period expires. Recertification is intended to reinforce the CFP concepts and to introduce new tools and resources made available since the program began.

The CFP task force and internal team are continually analyzing the feedback from member practices, both designated and working on becoming so. Based upon that feedback there are videos directed at both the veterinary team and clients to demonstrate techniques important to improving the experience. New tools are being developed through out the year to meet their needs for social media, staff meetings, owner education and staff development. In 2015, the task force and AAFP board will create a strategic plan for the future of Cat Friendly Practice. It is our intention to keep evolving the program to add value to participating practices, to create tools and resources for practices to attract cat owners and to drive cat owners to practices that participate.

Communications Boot Camp: See More Cats!

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In human medicine much research has occurred regarding the “Patient-centered Interview”, resulting in evidence based method used to train medical students, nurses, physicians and other health care workers who must have a successful interview with a patient in order to assure the best possible outcome. This evidence based approach to patient interviewing has valuable parallels in our desire to build trusting relationships with our clients.

With client-centered skills, we encourage them to express what is most important to them. This approach recognizes the importance of their personal concerns, feelings, and emotions. The patient is not isolated from its context. For example, a patient of mine recently presented for inappetence, lethargy and icterus, which the owner thought, had only developed in the last 2 days. This client is a very aware client and one who recognizes the subtlety of feline symptom exhibition. It was clear, however, from the physical exam that this patient had been ill for quite a bit longer than the owner thought. After we talked for awhile, she shared with me that her husband had an inoperable tumor and was about to start a new round of chemotherapy and radiation before referral to a tertiary hospital for very complex surgery. My patient’s condition was clearly a part of a complex emotional time for this owner. She said, too, that her cat was the one who gave her the love and affection she needed when she was upset by everything that was arising and that she could not bear to lose her. The emotional context and family circumstances are often part of the reason a cat is presented to us and we need to be able to elicit and understand them. The level of satisfaction a client will express is directly associated with feeling understood.

Clients usually have more than one concern. Indeed the first concern mentioned may not be the most important one to the client. Sometimes the last concern raised is the most important one but was saved for last because it is the more frightening or sad. By asking the right kind of questions, we can be sure that we understand the whole story. It is also therapeutic for the client to tell their story rather than be asked a series of questions. It can be cathartic. Most of us have experienced feeling unburdened and less alone after sharing a story of difficulty with a good listener. Our clients don’t expect us to “fix” everything. They understand that we cannot. Sharing the struggle a client is experiencing and responding empathetically is often enough.

Three broad types of skills need to be addressed in communication skills training:

1. Content skills – what we communicate. The substance of clients’ questions and our responses, the information we gather and give, the treatment plans we discuss
2. Process skills – how we do it. The ways we communicate with clients, how we discover history, provide information. The verbal and nonverbal skills we use, how we develop a relationship with the client, the way we organize and structure communication

Perceptual skills – what the clients and we are thinking and feeling. The internal decision-making, clinical reasoning and problem solving skills we bring to the encounter. Our attitudes, personal capacities for compassion, mindfulness, integrity, respect and flexibility are critical to understanding how to create a successful relationship and achieve the best outcomes. We need to be aware of our feelings and thoughts about the client, about the patient’s condition and other issues that may be concerning the client; awareness of our own self-concept and confidence, of our own biases and distractions.

It is important to emphasize that content, process, and perceptual skills are inextricably linked and cannot be considered in isolation.

In 1998, the Calgary-Cambridge guide was created to provide a structure for teaching and learning communication skills. It provided a comprehensive repertoire of skills validated by research and theoretical evidence. It provided guidance on skills that make a difference in medical communications. In 2003, enhancement to the guide were developed which visually and conceptually improved the way communications skills training took place. Three diagrams helped to place the skills in relationship and context. With this enhancement came a new content guide for skills training. Since then communication experts in veterinary medicine have utilized this evidence based approach to adapt the guide to client communications. Studies in JAVMA since 2001 have demonstrated strong evidence of the value of this approach over the paternalistic approach favored by physicians in the past. For example, a study published in JAVMA in 2012 demonstrated a clear relationship between client compliance and satisfaction with their relationship with the veterinarian

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Old Thin Cats: Is it Really Just Old Age?

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In both people and companion animals, cachexia and sarcopenia are 2 important syndromes that occur in a variety of chronic diseases and aging, respectively. Although cachexia has been recognized in people for over 2,000 years, only recently has it become acknowledged as a common and detrimental finding that is associated with increased morbidity and mortality, and with this observation has come rapidly expanding interest and research. Both of these syndromes are becoming increasingly important in human and veterinary medicine because of their high prevalence and adverse clinical effects, and a better understanding of the mechanisms underlying these syndromes is critical for optimal patient care, whether human or veterinary.

Cachexia is defined as loss of weight and muscle mass secondary to chronic inflammation or disease. Sarcopenia, “poverty of flesh”, is an age-related loss of lean body mass. Sarcopenia is not caused by disease, is a gradual process and progresses with age. Loss of muscle can occur without fat loss or a decrease in Body Condition Score (BCS). Individual cats, particularly those with long coats or a history of obesity may appear to have a high BCS and yet be under muscled.

One of the keys to the management of cachexia and sarcopenia in dogs and cats is recognizing it in its earliest stages. To achieve this, BCS and Muscle Condition Score (MCS) must be consistently assessed. The goal for BCS in a healthy cat is 4–5 on a 9-point BCS scale. However, in certain diseases (eg, CHF, CKD), a slightly higher BCS may be desirable (ie, a BCS of 6–7/9), although further research is required to make specific recommendations. Even in animals with these diseases, obesity (BCS > 7/9) should be avoided.

The MCS differs from the BCS in that it specifically evaluates muscle mass. Evaluation of muscle mass includes visual examination and palpation of the head, scapulae, epaxial muscles over the thoracic and lumbar vertebrae, and pelvic bones.

In people, the loss of LBM has direct and deleterious effects on strength, immune function, wound healing, and survival. In fact, cachexia is an independent predictor of survival in people. The specific deleterious effects of muscle loss have not been as well studied in dogs and cats although there are studies associating thin body condition with decreased survival.

The weight loss that occurs in cachexia is unlike that seen in a healthy animal that loses weight. In a healthy animal that is receiving insufficient calories to meet requirements, metabolic adaptations allow fat to be used as the primary fuel source, thus preserving LBM. Conversely, acute and chronic diseases alter concentrations of a variety of mediators (eg, inflammatory cytokines, catecholamines, cortisol, insulin, glucagon), which then decrease the ability to make metabolic adaptations required to switch to fat utilization, and amino acids continue to be used as a primary source of energy. Therefore, muscle and LBM quickly are catabolized.

Numerous other factors can contribute to muscle and weight loss. Maintenance energy requirements vary with age, genetics, health status and gender (intact or altered). In presence of some disease states, maintenance energy requirements increase significantly. Decreased nutrient absorption is another possible mechanism for muscle loss in cachexia and sarcopenia. Studies in cats have shown decreased digestive ability. One investigator showed a reduced ability to digest protein in 20% of geriatric cats with about 33% having a significant reduction in ability to digest dietary fat. Micronutrient absorption, potassium, phosphorus, sodium, choline, B vitamins and Vitamin E, is also decreased.

Cats derive most of their energy requirements from protein and are metabolically less able to handle decreased amounts of protein and increased amounts of carbohydrates to maintain their energy requirements. Omnivores adapt to lower dietary protein by down regulation of their protein metabolism (protein sparing) but cats have been proven to be unable to make this physiologic adaptation. This preferential use of protein for energy can have clinical effects when cats are ill or anorectic as protein malnourishment can occur.

An important problem in cardiac and other forms of cachexia is a decreased calorie intake. The anorexia may be secondary to fatigue, dyspnea, or may be because of medication toxicity or alterations in appetite that often accompany CHF, cancer, and CKD in cats. Absolute food intake may decrease in animals with these diseases, but there also may be altered food preferences, cyclical appetite, and other issues that negatively affect overall food intake. Anorexia, for example, is present in 34–84% of dogs and cats with heart disease.

Increased energy requirements, alterations in nutrient absorption, and decreased energy intake all likely play important roles in the pathogenesis of cachexia by causing a net calorie deficit. However, a healthy animal that has a calorie deficit, either as a consequence of decreased food intake or increased energy requirements, would primarily lose fat. Therefore, these factors are not sufficient to explain the muscle and LBM loss and relative sparing of fat that are the hallmarks of cachexia and sarcopenia. This discrepancy suggests that metabolic alterations also are present.

Because of the important implications of cachexia and sarcopenia on morbidity and mortality in people, there is now extensive research into the prevention, diagnosis, and treatment of these syndromes. There are exciting opportunities for new and effective

targets to decrease energy requirements, enhance energy intake, improve nutrient absorption, and modify metabolic alterations to prevent and even reverse the effects of both cachexia and sarcopenia.

A 2008 study on longevity in aging cats studied in a controlled environment for 5 years showed that all cats lost weight over time. However, cats supplemented with dietary antioxidants, prebiotic chicory root and a blend of Omega 3 and 6 fatty acids had a beneficial effect over a commercially fed diet alone or one supplemented only with antioxidants (Vitamin E and beta carotene). Cats in the fully supplemented group lost less weight, lived longer, had better LBM scores, improved fecal flora and fewer diseases.

In many cases, practical methods to help owners manage their animal's appetite are critical to success. This is particularly important because anorexia is one of the most common contributing causes to an owner's decision to euthanize his or her pet.

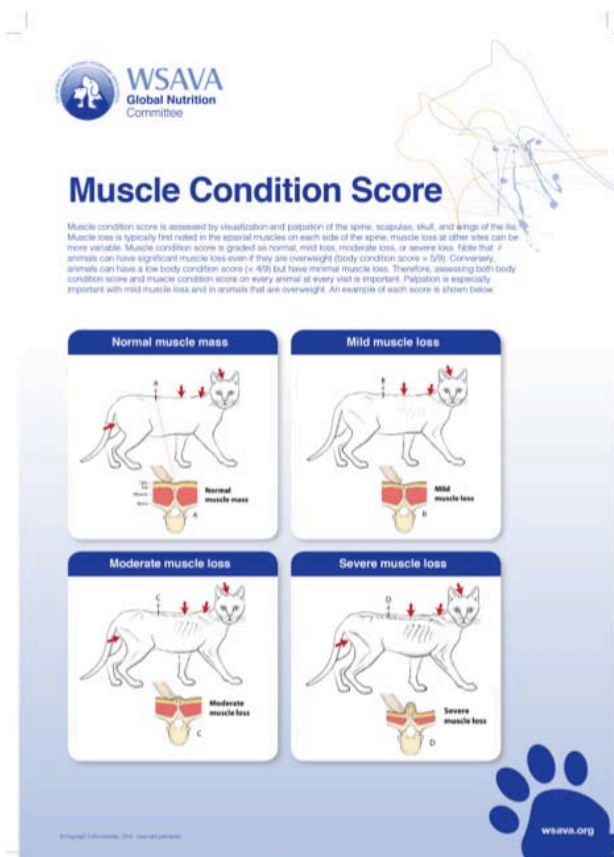
Any issues that potentially can affect food intake should be addressed, whether physical or environmental. Dental disease, for example, can substantially impair food intake in an otherwise healthy or sick animal. Pain (eg, back or joint) can decrease an animal's mobility and make it more difficult to secure adequate food intake. Environmental issues also can negatively impact food intake. Multipet households may impede the ability of an individual animal to gain access to food (eg, a more frail or timid animal may be crowded out from the food bowl). Stress often can increase for animals after diagnosis of any illness because of lifestyle changes (eg, medication administration, new foods), as well as increased stress on the part of the owner, which may be detected by the animal.

Once environmental issues are ruled out as a cause of weight loss, a nutritional screening is crucial. Older cats may need 5-6 g of protein/kg to prevent protein catabolism. Reduced digestive ability indicate that a high energy, highly digestible diet may be needed. Some kitten formulas may be more appropriate. Folate and cobalamin supplementation may be useful. Commercial cat foods vary quite widely in caloric density. Specific formulas should be investigated for adequacy.

Cachexia should be anticipated in animals with chronic diseases such as CHF, CKD, cancer, and others. Consistently evaluating MCS in all patients will help identify muscle loss at an early, mild stage in aging or ill animals, rather than waiting until muscle loss is moderate or severe, when it may be more difficult to successfully manage. Similarly, as animals age, muscle loss is likely to occur, even in healthy individuals. Therefore, muscle mass should be thoroughly evaluated in geriatric cats and dogs.

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Complicated Senior Cats: Managing Multiple Conditions in One Patient

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Old age is not a disease. Both veterinarians and owners must resist the temptation to ascribe signs of illness to aging. Some signs of illness such as chronic pain, dehydration or hypokalemia may lead to clinical signs that owners scribe to “slowing down” with old age. Many problems of senior cats are chronic and progressive so that early diagnosis and treatment is important for pain management and quality of life. It can also be tempting to find a “diagnosis” and treat for that without continually evaluating the “whole” cat. The focus on a single diagnosis and treatment plan can neglect common comorbid conditions that can dramatically affect quality of life. A hyperthyroid cat, for example, may suffer from other conditions more common in older cats; overgrown nails, decreased olfactory sensing, which can impact appetite, muscle atrophy and osteoarthritis or periodontal disease.

For these reasons and a host of others, comprehensive wellness examinations, history assessment and a minimum database are recommended every 6 months for seniors. Health status may change rapidly in this group and early detection and treatment is important to preserve quality of life. Signs of illness in cats are often quite subtle and easy for owners to overlook. The minimum database includes a complete blood count (CBC), a full serum chemistry panel with electrolytes, a full urinalysis and total T4. Early detection of a decline in renal function will be found in declining urine specific gravity before BUN and Creatinine are beyond the normal range, making the urinalysis a critical part of information gathering. Depending upon risk factors, fecal examination and retrovirus testing may also be indicated. Blood pressure measurement should also be included in any cat with known risk factors.

Because senior cats’ response to vaccination is largely unknown and immune function may be affected by both aging and the presence of chronic disease, vaccinations should be given according to the AAEP Feline Vaccine Advisory Panel for all cats.

The home environment is critical to wellness. Staff members should be trained to educate owners about enrichment, stress identification and modification for aging changes. Senior cats may benefit by an additional heat source such as a heated bed or one placed close to a heat source. Resting or hiding areas that are inaccessible to other pets, quiet and easily accessible for the senior may help with stress reduction. Litterboxes should be large and shallow with low sides and placed in quiet locations. If the home has multiple stories, boxes should be placed on each. Night-lights may be helpful with declining vision. Multiple fresh water sources can encourage moisture consumption in cats that may be prone to dehydration because of reduced urine concentrating ability.

In senior cats, cognitive dysfunction (CD) is now recognized as an important problem. Formal diagnostic criteria have yet to be established. It is a diagnosis of exclusion. The most common signs are disorientation in time and space, altered learning, house soiling, altered interactions (e.g. attention seeking, anxiety, irritability) changes in activity (wandering or pacing) changes in sleep patterns, decreased appetite, decreased grooming and increased vocalization. Medical problems such as hyperthyroidism, hypertension, pain of osteoarthritis, or chronic kidney disease can mimic many of these signs and so must be excluded before presuming CD.

Published studies are lacking on the efficacy of treatment. Therapies extrapolated from studies in humans and dogs include anti-oxidant enriched diets, supplements phosphatidylserine, omega-3 fatty acids, Vitamins E and C, L-carnitine. One ingredient found in supplements for dogs, alpha-lipoic acid, is toxic in cats. SAME improved activity and awareness in dogs and is commonly used in cats with hepatic disease. No trials with these supplements have been published for cats with CD. Therapies for cats with CD are anecdotal.

There is evidence of cholinergic decline in senior cats so drugs with anticholinergic activity (e.g. some SSRIs such as paroxetine and TCAs) should be avoided. Selegiline (Anipryl), which has been anecdotally reported to be useful in cats and proven beneficial in dogs for CD, should not be combined with SSRIs or TCAs. Environmental enrichment and Feliway have often been recommended but no studies in cats show benefit. In fact, in cats with CD modifications to the environment may be detrimental. Regular and predictable routines are most desirable. Any changes should take place slowly.

Hyperthyroidism and chronic kidney disease (CKD)

The presence of these occurring concurrently affects not only the diagnosis but also the treatment and prognosis. A more cautious approach to treatment is required. The relationship between the two is not known. Hyperthyroidism may damage the kidneys or the consequent hypertension may contribute to renal damage. Hyperthyroidism seems to mask a decline in renal function by increasing renal blood flow and hence glomerular filtration rate (GFR).

Diagnosis is complicated by the suppression of thyroid hormones by a concurrent illness or “sick euthyroid”. Cats with both an upper reference range normal Creatinine and TT4 are likely to have both hyperthyroidism and CKD. A TT4 can be repeated in a few weeks or a free T4 by equilibrium dialysis can be done though it carries a slightly higher risk of false-positive results. The presence of CKD can affect hematology results. Erythrocytosis occasionally seen in hyperthyroidism may be masked by anemia of CKD.

Presently the assessment of kidney function depends upon elevated BUN and Creatinine with a reduced urine specific gravity. However concentrations of BUN can be increased by the polyphagia of hyperthyroid, Creatinine reduced because these cats are thin and have lost lean body condition, while increased GFR can reduce both. Urine specific gravity can be low because of either disease; both increase the risk of urinary tract infection.

All treatments for hyperthyroidism can worsen kidney function. Hyperthyroidism increases renal blood flow and GFR. Treatment may lower GFR by up to 50%, which may unmask previously unrecognized kidney disease. Treatment may initiate a crisis. Affected cats become azotemic and may start to show significant decreases in renal function by 4 weeks of treatment. No significant differences in pretreatment parameters have been shown between cats that will become azotemic after treatment and cats that will not. GFR, iohexol clearance and other assessment tools are not readily available in practice yet.

For these reasons, treatment with medical management for all cats should precede any other form of therapy. Medical management is reversible, can be reduced, and induces euthyroid states more gradually. Radioiodine and surgery may result in acute destabilization. Medical management should continue for a period of time, months before considering curative, permanent treatments.

If a cat is known to have CKD at the time of diagnosis, treatment with a lower dose of medication should be given at the start. For methimazole, 1.25mg- 5 mg once daily with frequent checks of renal parameters, titrating the dose upward. Renal parameters should be monitored at 3 and 6 weeks following start of therapy.

Attaining a euthyroid state should be the goal unless this level of thyroid hormone worsens renal parameters. Ongoing management should aim for a balance between the two conditions. Individual response to therapy should guide treatment. For example, if euthyroidism causes significant renal dysfunction, suboptimal control of hyperthyroidism may yield a patient that maintains weight and body condition.

Heart failure and chronic kidney disease (cardiorenal syndrome or CRS)

In the cat, the incidence of chronic abnormalities in cardiac function (e.g. congestive heart failure) causing progressive and permanent chronic kidney disease is unknown. A study of 102 cats with hypertrophic cardiomyopathy reported 59% prevalence for azotemia as compared to 20% for age-matched controls.

CRS occurs when worsening renal function limits diuresis despite clinical volume overload associated with heart failure. In cats being treated for chronic heart failure, declining renal function should be anticipated. The diagnostic marker for CKD, isosthenuria, cannot be relied upon in cats being treated with diuretics. Monitoring of Creatinine especially should be used to discern trends in renal function. A progressive rise even within the normal range should alert the practitioner, along with clinical signs: PU/PD, hyporexia, anorexia, weight loss and vomiting.

A minimum database should include abdominal ultrasound to assess for typical changes in renal architecture and to identify underlying causes that may have specific treatments, such as neoplasia, pyelonephritis, and nephrolithiasis. Blood pressure monitoring should be included as well as hypotension from therapy can decrease renal perfusion. The usual diagnostic imaging; echocardiogram, thoracic radiographs are important for type of cardiac disease, risk assessment, and treatment planning.

Goals of treatment are to recognize CRS, reverse it as much as possible and deal with the renal consequences of heart failure and the complex relationship between heart failure and renal injury. The difficult balance is to "dry out" the heart failure and hydrate the kidneys. Different therapeutic strategies are based upon the degree of compromise of each organ.

Ace inhibitors are the mainstay of therapy for CRS especially in the presence of hypertension or proteinuria. Cats with CRS should be hydrated before starting therapy. Low dose benazepril or enalapril 0.25mg/kg Q 24 hours can be increased to provide better control for heart failure. Benazepril is metabolized in the liver, Enalapril in the kidneys. Therefore, cats with CRS may need a lower dose of enalapril than benazepril. Initiation of therapy may show a transient increase in BUN/Creatinine concentrations. If persistent, lowering the dose is usually sufficient.

If azotemia is becoming a concern, the first step is to lower the dose of diuretics. The goal is to find the lowest effective dose that controls heart failure. The dose must be continuously reassessed. The ideal dose for an individual patient achieves the threshold rate of drug excretion. An individual HF patient that is not responsive to 5mg of furosemide per 24 hours for example will need 10 mg per 24 hours, not 5mg every 12 hours. Adequate natriuresis can be grossly assessed by observation of increased urine volume and decreased specific gravity. Periodic drainage of pleural fluid or ascites can be used to avoid excessive diuretic use.

In the event that diuretic resistance occurs, several options are available to correct fluid balance. A CRI of furosemide (0.3-0.6mg/kg/hour IV) inhibits sodium resorption more effectively than oral or IV Boluses. Once the volume overload has resolved, most cats will again respond to oral therapy. Another loop diuretic, torsemide has superior diuretic action and long half-life. (0.3mg/kg PO Q 24 hours) It appears to be 10 times more potent than furosemide. Dual-diuretic therapy can be considered when furosemide dose needs to be decreased. Spironolactone (1-2 mg/kg Q 12 hours) may cause severe facial pruritus and must be used with caution. Aldosterone sometimes causes significant hyperkalemia. Each work at different sites within the nephron and if tolerated may be helpful.

Systemic hypertension is common in CKD and by increasing afterload increases the cardiac workload. Hypertension worsens both CKD and heart failure. If present, amlodipine (0.625 mg/cat PO Q 24 hours) should be added. Blood pressure monitoring is critical to avoid the effects of iatrogenic hypotension.

In advanced CRS, a positive inotrope (pimobendan) may improve azotemia, demeanor and appetite and allow reduction in diuretic dose.

Dietary modification should consider both conditions. Sodium restriction is sometimes needed and the extent to which it is required will vary. Distilled or low sodium water may be offered for drinking if more sodium restriction is needed than can be provided with diet. Clients should be cautioned not to feed high sodium treats. Lower phosphorus diets may be helpful in managing kidney disease but may result in the loss of lean body condition. High quality protein should be given to the level that it does not worsen azotemia. Omega-3 polyunsaturated fatty acids have been shown to be beneficial in both cardiac and renal conditions. Many renal diets are supplemented or if given separately EPA 40mg/kg/day, DHA 25mg/kg/day.

Fluid administration is a balance between improving renal blood flow without precipitating congestive heart failure. Fluids should be given slowly to correct azotemia, tailored to the individual's ability to tolerate. Abrupt changes in weight, a new gallop heart sound and/or heart rate may indicate impending congestive event and justify fluid rate reduction. Sometimes a low-dose CRI of furosemide will be indicated concurrently in cats with end-stage CRS. SQ fluids may be less likely to trigger a congestive event and can be given every 24-48 hours via a balanced electrolyte solution and adjusted to the individual patient's ability to tolerate. In fragile patients, a smaller volume of fluids, as little as 30mls every 48 hours may be necessary, titrating slowly upward if the expected effect on uremia is not evident. Electrolytes should be monitored closely, especially potassium, as hypokalemia can trigger arrhythmia. Correction can take place through fluid therapy or oral means.

Although renal function may remain stable for a period of time in cats with heart failure, when CRS occurs it leads to frequent hospitalization, difficulty maintaining good quality of life and eventually euthanasia. The therapy described here is directed at improving quality of life for cats with CRS. Whether they contribute to prolonged survival is unknown.