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The Greatest Story Ever Told: The Story of Jeremiah; A Case-Based Approach to the Feline with Ventroflexion of the Neck

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The Problem-oriented Approach

Problem solving within veterinary practice can at times appear like magic to the casual observer. How the veterinary professional decides what is wrong with a pet and what course of action to take can appear to be somewhat of a black box process. In truth the process is fairly standardized and can be taught and practiced. Veterinarians use what has been termed the problem-oriented approach to veterinary medicine. The approach is defined but is flexible enough to be tailored to any practice environment. Some veterinarians even incorporate the approach into their record keeping by using the acronym SOAP. In the problem-oriented approach, the veterinary professional repeatedly defines and redefines problems and then uses the problem list and data about the case generated to assess each problem and to define a diagnostic, therapeutic, and client education plan necessary to solve each problem.

The problem-oriented approach begins by gathering a standard set of data. The data typically gathered initially includes; 1) the primary complaint of the owner, 2) the signalment (type of animal, breed, sex, and age) of the animal, 3) the past medical history, 4) the present medical history, and 5) the physical examination. The trained veterinary technician can be invaluable in these data gathering steps. Once the data is gathered a problem list is generated. The problem list becomes the back-bone around which the case is worked up and treatment decisions are made. Keeping in mind the defined problems the veterinary professional uses the data to make an assessment. The assessment might be a diagnosis, a list of potential diagnoses (differential diagnosis list or rule-out list), or might be an acknowledgment of the need for additional information. The assessment is used then to redefine the problem, in which case the process is repeated, or it is used to create a plan. The plan is always subdivided into diagnostic (gathering more data), therapeutic, and client education components.

Problem-oriented approach is often defined by the use of the term, SOAP. The S and O are the data arm, the A is the assessing arm, and the P is the plan:

- **S** **Subjective data** (that data usually the observations of the owner that is subjective in nature)
- **O** **Objective data** (that data, usually able to be quantified, that is generated by the observations of the veterinary professional)
- **A** **Assessment**

P **Plan** (subdivided in a diagnostic, a therapeutic, and a client education plan)

In this presentation the audience will be presented with a cat that is brought into a referral setting with a primary complaint of ventroflexion of the neck. The case will be followed as an example of the problem-oriented approach. Even though this is a fairly standardized process the ambiguity of practice is still significant and the results are often unexpected. This becomes obvious in this case. Not knowing precisely what each day may bring is one of the challenging aspects of veterinary medicine that makes the profession rewarding and fun. The following base of information will be used in the assessment of the cat's problems and the development of a rational plan.

Thiamine Responsive Neck Ventroflexion (common)

Thiamine deficiency has been uncommonly diagnosed since the advent of readily available, nutritionally complete cat foods. Yet diseases that are thiamine responsive are still occasionally encountered. Thiamine deficiencies have been reported to cause weakness secondary to polyneuropathy and polymyopathy in man. While this has not been experimentally confirmed in the cat, clinical observations of thiamine responsive neck ventroflexion might suggest the existence of a similar disease process. Classical descriptions of thiamine deficiency in the cat have included dilated, slowly responsive pupils and rigid flexion of the neck with extensor rigidity of the forelimbs. Signs of vestibular involvement are also reportedly common. In my experience most cats that presented with ventroflexion of the neck and were responsive to thiamine therapy have not shown significant evidence of vestibular disease, nor have they been in extensor rigidity. Dilated, poorly responsive pupils have been a common but not consistent finding. Most of the cats were fed an adequate diet, implying that some cats may require higher levels of thiamine than are currently available in most commercial cat foods.

Since there is no readily available diagnostic test to rule out thiamine responsive disease, a therapeutic trial of thiamine is recommended in all cats that present with ventroflexion of the neck. Thiamine should be administered at a dosage of 25-50 mg IM once a day for the first two to three days. Improved or normal head carriage is usually noted within 24 to 48 hours. It is important that blood be drawn for CPK evaluation before the administration of thiamine, as the IM injections may increase CPK activity. The therapeutic trial can be attempted while waiting for serum chemistry and cholinesterase results.

Hypokalemic polymyopathy (Common; but less common since increased potassium has been added to feline diets)

A study by Schunk at Angell Memorial in Boston demonstrated that a high percentage of cats with neck ventroflexion and generalized muscle weakness were hypokalemic. Dow and coworkers from Colorado State University showed that renal potassium wasting associated with chronic renal disease appears to be the primary underlying etiology. Decreased dietary intake of

potassium and metabolic acidosis is also important for most of the predisposed cats to become severely clinically affected. Diagnosis is dependent on demonstration of a low serum potassium (less than 3.5 mEq/L) and a high CPK in a cat with consistent clinical signs. Most of the cats will have generalized muscle weakness and ventroflexion of the neck without pain. About 25 percent of the cats will have muscle pain and a stiff or stilted gait. Electromyography will demonstrate abnormalities in multiple muscle groups but muscle biopsy fails to reveal histopathologic evidence of myositis. Azotemia and mild to moderate metabolic acidosis are also common findings. The pathophysiology of the disease is not completely understood but it is speculated that sarcolemmal hypopolarization and attenuation of muscle blood flow associated with hypokalemia produces the profound weakness.

Potassium administration should be initiated as soon as the diagnosis of hypokalemia is confirmed. Oral administration is recommended for all except the most severely affected cats. Parenteral administration of fluids, even those containing high concentrations of potassium may transiently decrease the serum potassium and worsen the clinical signs. Complete paralysis necessitating intubation and ventilatory support has been reported. Despite the potential dangers of parenteral potassium administration, parenteral therapy may be required in cats that are extremely weak, especially those in which respiratory paralysis appears imminent. Potassium gluconate tablets, gel, or powder (Tumil-K, Virbac Animal Health) is recommended as the most palatable available potassium salts. KCl can be used but is considerably less palatable and may worsen pre-existing metabolic acidosis.

The dose of oral potassium has been empirically determined to be 5 to 8 mEq divided twice a day in cats with serum potassium less than 3.0 meq/l. Improvement is usually seen in 24 hours with most affected cats being markedly stronger in 2 to 3 days. A maintenance dose of 2 to 4 mEq of potassium per day should be continued after the serum potassium levels have normalized. Feeding a diet containing greater than 0.6 percent potassium is recommended and may be sufficient as the sole potassium supplement in cats without severe renal disfunction.

Hypernatremic Polymyopathy (real zebra)

A cat with hypodipsic hypernatremia developed a polymyopathy that resulted in ventroflexion of the neck. The neck posture became normal with correction of the hypernatremia and returned to the ventroflexed position when the hypernatremia returned. High extracellular sodium concentrations have been shown to accelerate sodium-potassium exchange across the myocyte membrane causing high intracellular sodium concentrations and low intracellular potassium concentrations. These alterations are thought to alter myocyte membrane potentials and induce a transient myopathy that resolves with correction of the hypernatremia. Marked increases in serum sodium and osmolality in a cat with neck ventroflexion should suggest a diagnosis of hypernatremia induced polymyopathy. Creatine kinase (CPK) activity will also be increased.

Idiopathic polymyositis (uncommon)

Idiopathic polymyositis may present with generalized muscle weakness and ventroflexion of the neck. Fever is occasionally observed. The initial diagnosis is dependent on increased CPK activity, normal serum potassium, histologic evidence of myofiber necrosis and lymphocytic inflammation, and improvement following corticosteroid therapy. Electrophysiologic findings during electromyography (EMG) are generalized and identical to those seen in cats with hypokalemic polymyopathy. The underlying etiology is unknown but is presumed to be immune mediated. Polymyositis is an uncommon cause of neck ventroflexion. Treatment consists of immunosuppressive therapy. Prednisone (1 to 2 mg/lb BID-TID then tapered) is the treatment of choice. Other immunosuppressive agents such as azathioprine or chlorambucil can be used with care.

Polyneuropathy (rare)

Polyneuropathies are poorly documented in the cat. The best characterized example is diabetic neuropathy, which presents as a distal neuropathy with clinical signs including plantigrade stance, depressed reflexes, and poor postural reactions rather than neck ventroflexion. However, polyneuropathy as a cause of ventroflexion of the neck has been observed. It is probable that other polyneuropathies will be reported with neck ventroflexion being a potential presenting complaint.

Hyperthyroidism (uncommon manifestation of a common disease)

Hyperthyroidism should be considered as a possible cause of neck ventroflexion is any adult cat, especially those over eight years old. Hyperthyroidism is the most common endocrinopathy affecting cats. Common clinical signs include weight loss, polyphagia, polydipsia, diarrhea, and nervousness. A small percentage (less than 20%) of hyperthyroid cats will be presented with primary signs of weakness and inappetence. A few of these cats will have marked ventroflexion of the neck. Three percent of the hyperthyroid cats in one large study presented with neck ventroflexion as one of the clinical signs. The ventroflexion is rarely of significant owner concern but is a striking finding on physical examination. The reason for the neck ventroflexion is not completely understood. One potential explanation is a concurrent thiamine deficiency due to anorexia, malabsorption, and/or polyuria. Because of this possibility, treatment with thiamine is warranted. Weakness and fatigue are frequent complaints of human patients with thyrotoxicosis. Often the weakness is most prominent in the proximal muscles. Thyrotoxic myopathy probably also occurs in some hyperthyroid cats and may contribute to ventroflexion of the neck when present. Diagnosis of hyperthyroidism can be made by demonstrating elevated resting T4 values. Treatment of hyperthyroid related neck ventroflexion should be geared toward treatment of the thyrotoxic state. Thiamine should also be given because of the possibility of concurrent thiamine deficiency. Response to thiamine does not rule out hyperthyroidism so a T_4 should be checked on all adult cats that present for neck ventroflexion.

Hereditary Neck Ventroflexion in Burmese and Devon Rex Cats (rare in U.S.)

A heritable disease of Burmese cats manifested by episodic weakness and ventroflexion of the neck has been described in Australia. The signs were episodic and were apparently induced by stress. Less frequent signs included poor condition, muscle tremors, and limb stiffness. The age of onset varied from 4 to 10 months. Thiamine deficiency was thought to play a role in the observed clinical signs, but only equivocal improvement was reported following administration of thiamine. Since the report, there has been speculation that hypokalemia may have played a role in the pathogenesis of the disease syndrome. Serum and urinary electrolyte concentrations were not reported in any of the cats with congenital neck ventroflexion. However, one Burmese cat with hypokalemic myopathy has been reported. The diagnosis of hereditary neck ventroflexion is dependent on recognizing the typical clinical signs in a young Burmese cat and establishing a family history of the syndrome. There is no well accepted therapy, but thiamine and potassium supplementation should be considered. Breeding Burmese cats with this syndrome is not recommended.

A syndrome of muscle weakness manifesting as ventroflexion of the neck has been recognized in young Devon Rex cats in the UK and United States. It is an autosomal recessively inherited muscular dystrophy of congenital in origin. Typically the affected cats show marked cervical ventroflexion, a stiff gait, and dysphagia. Megaesophagus is often part of the syndrome. Only the most severely affected cats show generalized muscle weakness. Serum chemistries are reportedly normal and effective treatment has not been demonstrated.

Organophosphate Toxicity (uncommon, usually due to exposure to yard insecticides)

A myasthenia-like syndrome can occur in cats exposed to acetylcholinesterase (AChE) inhibitors such as organophosphate (OP) compounds. Clinical manifestations may include generalized muscle weakness, tremors, and/or ventroflexion of the neck. Acetylcholine is the neurotransmitter at cholinergic nerve synapses and neuromuscular junctions. The neurotransmitter is normally inactivated by AChE within 5 msec after its release from presynaptic nerve terminals. OP insecticides act by binding to AChE, inactivating the enzyme and allowing the uninhibited buildup of acetylcholine. Continual stimulation of postsynaptic neuromuscular junctions leads to fatigue of the muscles and myasthenia-like signs.

The diagnosis of OP induced myasthenia-like disease is dependent on historical evidence of exposure to an OP in a cat showing consistent clinical signs. OP insecticide poisoning can be confirmed by demonstration of reduced cholinesterase activity in whole blood (EDTA or heparinized). A decrease in cholinesterase activity of at least 50% is considered significant inhibition with most cases of toxicity resulting in less than 25% activity. Cats with neck ventroflexion caused by myasthenia-like syndrome fail to respond to edrophonium. The weakness may even be more severe following edrophonium administration. Repetitive nerve stimulation will result in a decremental response similar to myasthenia gravis but the

decremental response will not be abolished by administration of edrophonium (see discussion of myasthenia gravis).

Treatment with atropine will block the muscarinic and some central nervous system effects of OP but will not block the nicotinic receptor overstimulation that results in ventroflexion of the neck. Pralidoxime chloride (2-PAM) (20 mg/kg IM q 8-12 hr) also acts primarily at muscarinic sites but have been shown to be of benefit in treating cats with this form of toxicity. Diphenhydramine (Benadryl) (4 mg/kg of body weight PO every 8 hours) has been shown to block the nicotinic effects in man and dogs. Our clinical experience would suggest a similar efficacy in the cat. Diphenhydramine does not alter inhibition of cholinesterase but appears to act centrally to prevent the receptor paralysis.

Myasthenia gravis

Both congenital and acquired forms of myasthenia gravis have been reported in cats. In a review of eight cases, three presented with ventroflexion of the neck. Short strides, a choppy gait and weakness are other common signs. Palpebral reflexes are absent in most cats with myasthenia gravis. Voice change, regurgitation, and fine muscle tremors is less commonly seen. Megaesophagus, a common abnormality associated with myasthenia gravis in the dog is less commonly seen in cats. Episodic weakness that worsens with exercise or activity is the typical presentation for myasthenia gravis in the dog but in our experience, clinical signs appear to be less episodic in cats. Approximately 50% of the cats that I have diagnosed as having myasthenia gravis presented with ventroflexion of the neck as the primary or only complaint. The ventroflexion worsened with activity in only one of these cats.

Diagnosis is dependent on pharmacologic, immunologic, and electrodiagnostic tests. Serum chemistry values, including CPK and electrolytes are consistently normal. Pharmacologically, a positive edrophonium test is suggestive of the diagnosis. Edrophonium chloride (Tensilon®), an ultrashort acting acetylcholinesterase inhibitor, is administered at a dosage of 0.25 - 0.5 mg IV. Alleviation of the weakness is considered a positive test result. Care must be taken in the interpretation of equivocal improvement as the weakness associated with other diffuse neuromuscular diseases will occasionally improve after the administration of edrophonium. Muscarinic signs of overdosage include salivation, lacrimation, urination, defecation, and bradycardia. These signs can be countered by the administration of atropine. Nicotinic signs of toxicity can be more serious and include exacerbation of weakness and respiratory paralysis. Animals with organophosphate toxicity are most likely to show these signs when given edrophonium. An endotracheal tube should be available during an edrophonium test so that intubation and ventilatory support can be performed should nicotinic signs of toxicity occur. Unequivocal confirmation of acquired myasthenia gravis can be immunologically documented by detection of acetylcholine receptor (AChR) antibodies. Cats with congenital myasthenia gravis will not have AChR antibodies. Electrophysiologically, a decrement of the evoked muscle action potential during repetitive nerve stimulation with normalization of the

decremental response after administration of edrophonium is consistent with a diagnosis of myasthenia gravis.

Other potential causes
Hypocalcemia
Hepatoencephalopathy
Ammonium chloride toxicity
Chronic metabolic acidosis