

**Lab Locations**

Atlanta  
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Fort Worth  
Texas

Denver  
Colorado

Honolulu  
Hawaii

Houston  
Texas

Los Angeles  
California

Memphis  
Tennessee

New York  
New York

Phoenix  
Arizona

Portland  
Oregon

San Francisco  
California

Tampa  
Florida

## FELINE HYPERCALCEMIA

Hypercalcemia is a significant pathologic entity in the cat. The following summarizes an Antech Medicine Consultants' meeting with Dr. Dennis Chew of the Ohio State University.

### **DIFFERENTIAL DIAGNOSIS**

Causes of feline hypercalcemia include:

- Chronic renal failure
- Idiopathic hypercalcemia
- Neoplasia – lymphosarcoma, squamous cell carcinoma, myeloma and others
- Vitamin D toxicosis
- Primary hyperparathyroidism
- Granulomatous disease

Renal failure constituted 27 of 71 cases (38%) in a recent retrospective study, with 21 (30%) having neoplasia, and 4 (6%) with primary hyperparathyroidism. In another 20 cats, the underlying pathophysiologic cause of hypercalcemia was not identified, and so could be presumed to be idiopathic.

Chronic renal failure, the most common cause of feline hypercalcemia, produces mild elevations in calcium concentration. Of the 27 cats with chronic renal failure (9 of them had urolithiasis), serum calcium concentration was  $11.5 \pm 0.5$  mg/dL (reference range 9.2-10.2 mg/dL). Ionized calcium concentrations ( $Ca^{++}$ ) are usually normal or decreased. A small % of cats with renal failure and tertiary hyperparathyroidism can have mild elevations of  $Ca^{++}$ .

Idiopathic hypercalcemia produces hypercalcemia of uncertain magnitude, and with uncertain pathophysiology. Some experts believe that acidifying, magnesium-restricted diets lead to idiopathic hypercalcemia in genetically predisposed cats, perhaps due to calcium resorption from bones. Other experts claim that cats with idiopathic hypercalcemia respond to fiber-supplemented diets, although results have not been uniformly beneficial.

The cause does not seem to be occult cancer, for cats with idiopathic hypercalcemia have been monitored for as long as 3 years without developing overt

neoplasia. Affected cats are usually asymptomatic, but chronic ionized hypercalcemia may lead to kidney damage and renal failure due to vasospasm, renal ischemia and necrosis, and nephrocalcinosis.

- Diagnosis – diagnosis of idiopathic hypercalcemia is made by excluding other causes. Radiographs, routine bloodwork, urinalysis, parathyroid hormone (PTH) and PTH-related protein (PTHrp) assays, and measurement of vitamin D concentrations may be necessary.
- Treatment – optimum treatment for idiopathic hypercalcemia is uncertain, although elevated  $Ca^{++}$  concentrations should be controlled to avoid long-term renal damage. Fiber-supplemented diets may be effective in some cases. Non-acidifying, magnesium-restricted diets (e.g. renal failure diet) may also be effective. Dietary trials are typically given 2-3 months before assessing efficacy. If dietary changes fail to resolve hypercalcemia, prednisone (5mg q 12 hrs) is initiated, as this form of hypercalcemia is typically very steroid responsive with resolution within 2 weeks. Treatment is likely to be needed life-long.

Hypercalcemia of malignancy. Lymphoma, squamous cell carcinoma, and other carcinomas are the most common malignancies that can cause hypercalcemia in cats. While measurement of PTHrp concentrations may be helpful in establishing this diagnosis, the usefulness of PTH measurements in diagnosing hypercalcemia of malignancy in cats is uncertain.

Granulomatous inflammatory disease as a cause of hypercalcemia in cats is uncommon. Three of 71 hypercalcemic cats in the study mentioned above had granulomatous disease (1 with feline infectious peritonitis, 1 with cryptococcosis, and 1 with chronic nasal actinomyces rhinitis). Granulomatous injection-site vaccine reactions can also cause hypercalcemia.

Primary hyperparathyroidism is an uncommon cause of hypercalcemia in cats. Affected cats are middle aged and older, and Siamese cats may be predisposed. A cervical mass may be palpable. PTH concentrations are elevated in about 50% of cases.

# CANINE NAIL DISEASES

Diseases restricted to the nail and/or nail fold are occasionally encountered in clinical practice. When disease involves only one or two nails, the most likely etiologies include trauma, bacterial or fungal infections, and neoplasia. When multiple nails are involved on all four feet, autoimmune or immune-mediated, genetic, endocrine, nutritional or immunosuppressive diseases should be considered.

## **ONYCHOMYCOSIS (DERMATOPHYTE INFECTION)**

This is a rare cause of nail disease. *Trichophyton mentagrophytes* is the most commonly isolated dermatophyte. Samples for fungal culture should be taken from the most proximal part of the nail plate, and multiple samples should be obtained. Nails can be washed with alcohol prior to placement on the culture media to reduce contaminants.

## **BACTERIAL INFECTION**

Bacterial infections of the nail are usually secondary to underlying local or systemic disease. Trauma (fracture, nails clipped very short) affecting only one or a few claws is most common. Bacterial cultures should be taken from the most proximal portion of freshly avulsed nails or nail fragments. Only the proximal portion should be placed in sterile transport media for submission to the laboratory; and alcohol should **not** be used to wash these samples. With chronic or severe cases, radiographs should be taken to evaluate for the presence of osteomyelitis.

## **ONYCHOMADESIS (NAIL LOOSENING/SLOUGHING SYNDROMES)**

When this involves multiple nails, a thorough clinical and laboratory work-up should be performed, including: CBC, chemistry profile; urinalysis; cytology, fungal and bacterial culture of affected nails; ANA, complete thyroid profile, radiographs, and a third phalanx biopsy. In the dog, pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, systemic lupus erythematosus, lupus-like syndrome, cold agglutinin disease, drug eruption, and vasculitis have all been reported to cause symmetric onychomadesis and onychodystrophy (abnormal nail formation).

Metabolic epidermal necrosis (hepatocutaneous syndrome) may also cause nail loss, but other skin changes are usually present and affected patients usually have concurrent liver disease. One of the most common causes of generalized onychomadesis in the dog has been referred to as an idiopathic lupus-like or "lupoid" syndrome. While it has been recognized in many breeds, Rottweilers and German shepherd dogs are predisposed. The age of onset is variable, but tends to occur in young adult dogs (1-6 years of age). The onset may be acute and widespread or chronic, in which case only one or two nails are

affected at a time. Paronychia (inflammation of nail fold) is usually not present, although affected nails may be painful and result in lameness. Left untreated, the tendency is to have partial regrowth of abnormal, friable nails that continue to be sloughed off. There is no apparent systemic involvement.

## **DIAGNOSIS**

The diagnosis is based on ruling out other causes of nail disease and histologic evaluation of a third phalanx biopsy. The nail, third phalanx, and a small amount of the nail fold, excluding the pad, are harvested in a standard "declaw" fashion. The dewclaw (if involved) may be the site most readily harvested. Following removal of the claw, the site should be sutured perpendicular to the long axis of the toe to minimize post-operative pain. The sample should be placed in formalin and submitted to a veterinary histopathologist.

Histologically, there is usually widespread hydropic degeneration of the basal cell layer of the epidermis, mononuclear interface dermatitis, and marked pigmentary incontinence.

## **TREATMENT**

Treatment should include removal of loosened nail plates. Systemic antibiotic therapy is recommended for secondary bacterial infection. In a recent prospective study of 24 dogs exhibiting only claw disease, four patients showed complete or near complete remission when an elimination diet was instituted. In two of these patients, adverse food reaction was conclusively identified as the cause for the claw disease, suggesting that interface onychitis may not always be due to immune-mediated disease. Other recommended therapies have included prednisone at 2-4 mg/kg/day for 2-4 week, then half this dose for 2-4 weeks, then gradual reduction to the lowest every-other-day dose for maintenance. After several months of successful therapy, one should attempt to discontinue the medication. An alternative therapy involves the combined use of tetracycline and niacinamide as described for discoid lupus erythematosus. Fatty acid therapy at routine dosages also may be of benefit in some cases.

## **NEOPLASIA**

Squamous cell carcinoma, melanoma, mast cell tumor, keratoacanthoma, inverted papilloma, lymphosarcoma, eccrine adenocarcinoma, hemangiopericytoma, and various other sarcomas have all been reported to involve the distal digit/nail in the dog. Of these, squamous cell carcinoma is the most common. Large breed dogs with black coats, particularly Labrador retrievers, and standard poodles, are predisposed. Multiple digits may be involved over a course of 2-4 years. In the dog, they appear to be slow growing and metastasis is rare. However, treatment requires amputation of the involved digit. Melanomas of the canine digit are highly malignant.

*References:* Rosychuk, RAW, *Current Vet Therapy* XII, Saunders, Phila, 1995, pp 641-647; Boord, MJ, et al, *JAAHA* 33: 131-138, 1997; Bergvall, K, *Vet Dermatol* 9: 263-268, 1998; Mueller, RS, Friend, S, et al, *Vet Dermatol* 11: 133-141, 2000.

## **LAB TIPS**

### **SUBMITTING NAILS OR TOES FOR HISTOPATHOLOGY**

When submitting nails or toes for histopathology, be sure to mark the proximal margin with a suture. This ensures correct orientation, especially if the toe is markedly distorted by infection or neoplasia. These tissues will need to be in fixative and decalcifying solutions for extended periods of time to allow proper processing. Turnaround time is often 7-10 days for toes and nails. **Be sure to use sufficient formalin (10 to 1 ratio) to permit proper fixation.**