IDENTIFY AND ACT
Early detection of gingivostomatitis in cats can aid the veterinary team in starting therapy and working toward remission.

Abstract
Feline chronic gingivostomatitis (FCGS) affects around 0.7% to 12% of the feline population and is a source of frustration for the affected pet, pet owner, and veterinary team. The exact etiology of the disease continues to evade the veterinary community, making it difficult to explain to pet owners. Past and present studies are making progress toward identifying a link to the exact causality of this disease and have opened the door to multiple therapeutic modalities. Although surgical intervention in conjunction with medical management is still the gold standard, other options are now available to veterinary professionals. New modalities are discussed alongside current research detailing the long history of FCGS in cats today.
Feline Chronic Gingivostomatitis: An Update

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Feline chronic gingivostomatitis (FCGS) is a debilitating inflammatory disease affecting the oral cavity of cats. This disease is marked by severe to chronic inflammation of the gingiva, mucosa, and surrounding tissues that line the oral cavity.¹ Chronic gingivostomatitis affects approximately 0.7% to 12% of the general cat population.²⁻⁴

There is a great deal of frustration regarding the diagnosis and treatment of this oral inflammatory disease. The frustration is due in part to the high frequency of inflammatory diseases in the oral cavity of cats and veterinary professionals’ limited understanding of their etiology.³

Many studies are dedicated to the discovery of the true etiology of FCGS. Unfortunately, the exact cause of FCGS is currently unknown, but thankfully a decade’s worth of investigation has advanced the knowledge and treatment of this debilitating disease.

ETIOLOGY

This complex multifactorial condition does not have a simple etiologic agent. Several studies have found that FCGS is caused by an exaggerated immunologic response to antigenic stimulation.⁶ The causes of this stimulation can be exaggerated by viral diseases such as feline leukemia virus (FeLV) infection, feline immunodeficiency virus (FIV) infection, calicivirus infection, feline

Take-Home Points

- The etiology of feline chronic gingivostomatitis (FCGS) is unknown and most likely multifactorial.
- FCGS can affect any breed of cat, regardless of age or sex.
- FCGS is an exaggerated immune response to antigenic stimulation.
- Environmental stressors (especially in multicat households) can play a role in FCGS.
- Current treatment options involve partial- to full-mouth extractions, with or without medical management.
- Medical management alone is not acceptable.
- Regenerative therapy (currently in development) shows promise for management of FCGS.
- Nutritional support (via a feeding tube) may be indicated in severe cases.
infectious peritonitis, herpesvirus infection, and panleukopenia virus infection as well as bacterial organisms such as *Bartonella henselae*.6

The systemic and local consequences of FCGS are suggested by the presence of lymphocytes and plasma cells in affected oral tissues, with fewer neutrophils, Mott cells, and mast cells.7,8 In humans, a known ratio of low CD4+ to CD8+ T-cell count is a marker for immune dysfunction and chronic inflammation. Through this, we can infer a similar pathologic reaction in cats with FCGS that have an increased CD8+ (cytotoxic) T-cell count compared with CD4+ (helper) T-cell count. These cells have been detected locally as well as systemically, supporting the theory of an inflammatory response, likely a cell-mediated immune response, to antigenic stimulation probably caused by pathogens such as viruses.9-11 Recent studies focused on the shedding of calicivirus as an active virus in clinical cases of FCGS and found no association of viral shedding with FeLV, FIV, herpesvirus, and *Bartonella*.12

A 2021 study examined the oral microbiome of cats to determine whether an imbalance of the oral flora played a potential role in FCGS. In this small pilot study, 14 clinically healthy cats and 14 cats affected by FCGS were tested.13 A sterile swab was used to obtain a sample and tested using next-generation DNA sequencing. A high number of fungal species, such as *Malassezia restricta*, *Malassezia arunalokei*, *Cladosporium panidielloides*, *Cladosporium salinae*, and *Aspergillus* species, were found and detected in the FCGS group; the fungi *Saccharomyces cerevisiae* was found solely in the clinically healthy cat group.

This pilot study was able to identify the distinct differences between the oral microbiome of cats that were clinically healthy versus those affected by FCGS, with a potential biomarker identified as *Bergeyella zoohelcum*.13 Additional studies are needed to improve our understanding of the oral microbiome of cats, but this study supports the idea of a potential imbalance between the flora of the oral cavity of cats and its potential role in FCGS.

Additional studies point to a potential link to nutritional disorders and a breed predilection.14 A pilot study examined the oral microbiome of cats and the changes of the microbiome based on provided diets.15 The cats in this pilot study were divided into 2 groups; 1 was offered a dry diet and the other a wet-food diet. This study discovered that diet indeed had a significant influence on the overall diversity and abundance of specific bacteria in the oral microbiome of cats. The cats fed an exclusively dry diet had higher bacterial diversity than the cats fed a wet-food diet. While differences between the oral microbiome of the cats fed these exclusive diets were noted, the relationship between these differences and gingival health remains unclear. Further studies are needed to determine the full extent of the “diet factor” and FCGS.

As for breed predilection, unfortunately this disease can affect any breed, regardless of age or sex.16 Until 2007, it was believed that breeds such as Abyssinian, Burmese, Himalayan, Persian, and Siamese were mostly affected.16 In a survey of almost 5000 cats in 12 practices over a 12-week period, 34 cases of FCGS were noted, with no breed bias identified.2

A 2019 study noted a possible link between environmental stressors and FCGS, revealing a higher incidence in multicat households versus single-cat households; every additional household cat increased the odds of FCGS by more than 70%.17 Cats within this study were indoor-only; therefore, evidence was missing regarding indoor–outdoor cats within a multicat home. Further studies focusing on the interaction between cats in a multicat household, with access to the outdoors and possible circulation (reinfection) of infectious agents between housemates, must be conducted.

**CLINICAL SIGNS**

“Feline chronic gingivostomatitis” is an umbrella term used to describe the chronic stomatitis and gingivitis syndrome of cats. This disease can be further classified into types 1 and 2:18

- **Type 1 FCGS** has a better prognosis and is classified by its clinical characteristic alveolar, labial/buccal mucositis/stomatitis.
- **Type 2 FCGS** is classified by its characteristic location along the caudal aspect of the oral cavity, with or without alveolar and labial/buccal mucositis/stomatitis.

Cats affected by FCGS can show various clinical signs, but the most common are halitosis, dysphagia (difficulty swallowing), pawing at the mouth, reluctance to eat, anorexia, weight loss, growling/crying, drooling, blood-tinged saliva, change in temperament, enlarged lymph nodes, and a lack of grooming.19,20
It is important to note the difference between gingivitis and FCGS in cats affected by this disease. Gingivitis is inflammation of the gingiva and does not extend beyond the mucogingival line, whereas true stomatitis will extend into the alveolar, labial/buccal, lingual, and caudal aspects of the mouth as well as the palatoglossal folds. Caudal stomatitis is present in 85% of cats affected by FCGS.

**SIGNALMENT**
The average age of cats that are presented with FCGS is approximately 7 years. A juvenile form of this disease known as feline juvenile gingivitis/periodontitis typically presents in cats after the eruption of the adult teeth, from 3 to 6 months of age. As the patient matures and eruption is complete, this form of stomatitis typically resolves around 2 years of age.

**DIAGNOSTIC WORKUP**
To determine if a feline patient has FCGS, the veterinary team must obtain a thorough history (including nutritional history), perform a physical exam, and perform diagnostic testing. Any patient that has suspected FCGS should have a complete blood count, serum biochemical profile, bleeding time test, serology (FIV/FeLV), T₄ (thyroxine) test, and urinalysis test performed.

The purpose of these tests is to rule out underlying conditions that can affect anesthesia rather than diagnosing the disease. Testing for calicivirus and *Bartonella* is not recommended because results do not change the therapy. Although some cats with FCGS are positive for *Bartonella* species, a cause-and-effect relationship has not yet been established, as there is a high rate of antibody-positive cats within a healthy population due to flea exposure.

In a study of 60 cats with FCGS, 7% were positive for FeLV and 8% were positive for FIV. Often, hyperglobulinemia and increased total protein are noted on serum biochemical results in patients with FCGS. Conversely, neutrophilia is not a hematologic finding in cats with FCGS.

**Radiographs**
Intraoral radiographs are always warranted and should be obtained on any patient undergoing a dentistry procedure (FIGURE 1). The radiographs help determine the extent of any dental disease, such as periodontal disease, tooth resorption, retained roots, and missing teeth—conditions that are often present in conjunction with FCGS. These radiographs will also assist the veterinarian with extractions and treatment of FCGS.

**Histopathology**
Because of the proliferative and ulcerative presentation of FCGS, collecting a biopsy specimen of the mucosa and submucosa is advisable and will help the veterinarian diagnose FCGS. Similar oral lesions, such as eosinophilic granulomas, indolent ulcers, and squamous cell carcinoma, can grossly present as FCGS. The histopathologic results concurrent with FCGS reveal plasma cells and a diverse number of...
lymphocytes, mast cells, Mott cells, macrophages, and neutrophils. Often, neoplasia can be seen concurrently with FCGS and should always be ruled out.

**MEDICAL MANAGEMENT VERSUS SURGICAL INTERVENTION**

There are 2 main approaches to treating FCGS: medical management and surgical intervention. Although medical management is an option, it often yields limited and unfavorable outcomes, making surgical intervention the preferred treatment of choice. Depending on the severity of the disease, the option for partial-mouth extractions over full-mouth extractions is warranted on a case-by-case basis.

Studies have shown that partial-mouth (all premolar and molar teeth) or full-mouth extraction provides the best long-term results. Approximately 70% to 80% of cats will show substantial improvement or resolution of FCGS, with minimal or no improvement in approximately 20% to 30% of cats. Although surgical intervention yields the best therapeutic results, it is still important to provide medical management alongside surgical treatment.

For patients that have mild to moderate anorexia due to FCGS, the placement of a pharyngostomy or gastrostomy tube is indicated to provide nutritional support, both before and after surgical intervention, or until the patient can eat on its own.

**Antibiotics**

Antibiotics are recommended only when used in conjunction with surgery. An antibiotic will decrease the bacterial load and help the gingiva heal to some extent, so that at the time of surgery the veterinarian has less friable tissue to work with. The antibiotic of choice for the oral cavity is one that will target both the gram-positive and gram-negative organisms in the mouth.

The antibiotics that are approved by the U.S. Food and Drug Administration (FDA) for use in FCGS are clindamycin and amoxicillin/clavulanate potassium. Although not approved by the FDA for use in feline dental disease or infections, metronidazole is another antibiotic of choice. Use of antibiotics alone for treatment/management of FCGS is not recommended and will only increase the likelihood of bacterial resistance.
Anti-inflammatory Medication
Although not considered for long-term therapy and treatment, a corticosteroid injection will provide some clinical relief but can decrease a patient’s ability to resist the inflammatory process while increasing the chance for diabetes mellitus.18

Prednisolone is often the short-acting steroid of choice to control inflammation and provide relief for patients affected by FCGS. Prednisolone is often used on an as-needed basis for symptomatic treatment on a tapering dose in patients with refractory FCGS.12,25

NSAIDs (nonsteroidal anti-inflammatory drugs) such as meloxicam and robenacoxib are often used for postoperative care, although use in patients with contraindications such as hepatic or renal disease should be avoided. Meloxicam is a great short-term NSAID; however, repeated doses of meloxicam over time has been associated with acute renal failure in cats. Close monitoring and avoidance of long-term use are advised.12,18

Cyclosporine
Cyclosporine is an immunosuppressive drug that exerts its effect through inhibition of T-cell activation, reducing interleukin-2 expression, and increasing T-cell numbers within the body.26,27 Cyclosporine may have an inhibitory effect on B cells as well.28

This medication is most often used to decrease inflammation in refractory (nonresolving) cases of FCGS after full-mouth extraction. Due to its immunosuppressive effects, it should be used solely on indoor cats because cats that venture outside will be at a higher risk of infection. The positive effects of cyclosporine can be noted within 4 weeks of treatment.18 Vomiting and diarrhea are the most common side effects seen with patients taking this medication.

Interferon
A group of signaling proteins that can interfere with viral replication is known as interferons. Recombinant feline interferon omega (rFeIFN-ω) was the first interferon licensed for use in cats in veterinary medicine.29

rFeIFN-ω is available in the United States solely through the FDA Expanded Access/Compassionate Use Program.12 This medication is imported on a strict individual basis.12 It is used to treat retroviral infections, with studies reporting that interferon delivered via oral mucosal absorption was as effective as prednisolone in decreasing clinical signs in refractory cases of FCGS.12,25

Bovine Lactoferrin Therapy
Lactoferrin is an antimicrobial and anti-inflammatory that helps to decrease the proliferation of mononuclear cells and downregulating inflammation.18 In a study of 13 cats with caudal FCGS, 77% of the clinical signs were improved with treatment.30 The protocol used was a combination of piroxicam and bovine lactoferrin spray given once every other day for 4 weeks.

Mesenchymal Stem Cell Therapy
Mesenchymal stem cells (MSCs) are a promising therapy for immune-mediated/inflammatory disorders, due to their potent immunomodulatory properties.11 MSCs inhibit activated T-lymphocyte proliferation.18

In a study of 9 cats affected by refractory FCGS, patients were given 2 intravenous injections of 20 million autologous adipose-derived MSCs every other month. Seven of the 9 cats completed the study, with 5 cats achieving substantial or complete remission and 2 cats with no clinical response to the treatment.11

A follow-up study testing the effects of autologous or allogenic cell fusion given twice a month every other month resulted in the cure/remission in more than 60% of the cats affected by refractory FCGS.19

As promising as these results are, more testing is needed. Researchers at the University of California, Davis, are conducting ongoing trials with MSCs and cats affected by FCGS. The cost of MSC therapy typically ranges from $2000 to $4000, with many pet insurance companies not offering coverage for treatment.31

Carbon Dioxide Laser Therapy
The use of carbon dioxide (CO₂) laser therapy for FCGS has been met with favorable results when combined with quality home care. The energy from the laser decreases pain while enhancing healing through protein synthesis, cell proliferation, and migration. Some veterinarians opt to use CO₂ laser therapy at the time of initial surgical extraction; CO₂ therapy may be helpful in cases of refractory FCGS as well.18
Cannabinoids
A 2021 study explored the potential for cannabinoid use in cats by investigating potential cannabinoid receptors within the oral cavity of healthy cats and cats with FCGS. This study focused on the potential expression of cannabinoid receptors CB1 and CB2, GPR55 (G-protein–coupled receptor 55), TRPA1 (transient receptor potential ankyrin 1), and 5-HT1A (serotonin 1A) receptors. Samples were collected from 8 healthy feline patients and 8 feline patients with FCGS. Compared to their healthy counterparts, the cats affected by FCGS presented with markedly upregulated cannabinoid and cannabinoid-related receptors.

Based on the results of this study, there is evidence to support the endocannabinoid system as a potential therapeutic target for patients affected by FCGS. This study is the first of its kind, garnering the need for further investigation and the application of a cannabinoid-rich product to determine the efficacy of this potential adjunct therapy for cats with FCGS.

Opioids
Many of the patients affected by FCGS are in moderate to severe pain and are typically malnourished. Managing pain pre-, intra-, and postoperatively is a major component to providing quality care.

Using a pure opioid to treat moderate to severe pain in these patients is a must. Opioids such as morphine, methadone, hydromorphone, and fentanyl are great options for these patients in the perioperative phase. Constant rate infusions of an opioid are also warranted during the intraoperative portion of the procedure.

Due to the nature of FCGS, it is understood that there is a "wind-up effect" from the pain of having an inflamed mouth for a long time. If not contraindicated, the administration of a cyclohexylamine such as ketamine (1 to 2 mg/kg IV) is recommended and can be administered during induction or intraoperatively as needed for pain. Ketamine will help reduce the effects of windup, unblock receptors, and create a synergistic analgesic effect.

Another major component to pain management is providing intraoral nerve blocks for these patients undergoing a comprehensive oral health and assessment treatment plan. If not contraindicated, dexmedetomidine can be added (1 µg/kg to bupivacaine (0.5% solution up to 5 mg) as a nerve block. This block will enhance the efficacy and duration of the local anesthetic but may be associated with dose-related adverse effects, such as hypertension and bradycardia.

Another intraoral nerve block combination is buprenorphine (0.015 mg/kg) added to bupivacaine (0.5% solution up to 5 mg). The addition of buprenorphine to bupivacaine is known to potentially extend the duration of analgesia up to 48 to 96 hours after surgery.

For the postoperative phase, oral buprenorphine is a drug of choice to send home with a patient recovering from FCGS. In a recent randomized crossover study featuring cats with FCGS, the subjects of the study were given buprenorphine via oral mucosal absorption, the result being a significant effect on reduced pain scores in affected cats and a decrease in plasma concentration between individuals. The subcutaneous sustained-release formulation of buprenorphine is another choice for painful patients after oral surgery and will provide 24-hour pain relief for up to 3 days.

SUMMARY
Although the exact etiology of FCGS remains a mystery, we have a better understanding of this condition today thanks to ongoing research and studies. Educating our clients about this debilitating disease is of the utmost importance. Early detection and treatment can be the difference between a patient suffering in silence and one that is able to undergo therapy and achieve remission. Surgical management of this disease in conjunction with medical management is still considered the gold standard of care for these patients.

References


24. Sheena Davis. Sheena is the founder and owner of Big Apple LVT Consulting & Education, with more than 16 years of clinical experience in both specialty and general practice. She is a peer-reviewed author, course designer for the Veterinary Cannabis Guide Program, library/media curator for the Veterinary Cannabis Society, and frequent guest lecturer for conferences and events. She achieved dentistry VTS and Veterinary Cannabis Counselor certification in 2020.

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