

Pathophysiology of Feline Chronic Gingivostomatitis & Juvenile Gingivitis: Insights Into Novel Medical Management

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Editor's Note

The first section has a lot of history and theory. If you are impatient by nature, or a surgeon, save time by reading the last section 'A New Way Forward' on page 5.

If you are interested in immunopathogenesis and how disease causation evolves with increasing knowledge, then start at the beginning.

Introduction

Feline chronic gingivostomatitis (FCGS) is a severe, chronic inflammatory disease of the oral cavity in domestic cats (*Felis catus*). **Clinically, affected cats present with oral pain, drooling, halitosis, difficulty eating (dysphagia or inappetence), weight loss, and poor grooming due to discomfort.** Importantly, FCGS is distinct from simple gingivitis or periodontal disease: by definition, the inflammation in FCGS extends beyond the gingival margin to involve the oral mucosa and caudal stomatitis. Furthermore, the extent of inflammation is greatly disproportionate to the amount of tartar and plaque present. Current evidence suggests that FCGS results from an inappropriate or exaggerated immune response to chronic antigenic stimulation in the mouth. Proposed antigenic triggers include plaque bacteria (oral microbiome), viruses, and even dietary components or allergens.

Feline calicivirus (FCV) has long been implicated as a major factor, and other infectious agents (feline herpesvirus, feline immunodeficiency virus, feline leukemia virus, etc.) and stressors have also been associated with FCGS (discussed further below).

This article will examine in detail the roles of the oral microbiome, dietary factors, viral infections, and immune dysregulation in the pathophysiology of gingivostomatitis in cats (including the juvenile gingivitis variant).

The Feline Oral Microbiome in Gingivostomatitis

The oral cavity of cats harbors a rich and diverse microbiome, composed of numerous bacterial species (and to a lesser extent fungi and other microbes) that normally exist in a balanced ecosystem. When this balance is disrupted – for example, by inadequate oral hygiene, underlying disease, or immune disturbances – dysbiosis can occur, allowing pathogenic or opportunistic bacteria to overgrow. Cats with FCGS often show evidence of periodontal disease (tartar/calculus accumulation, gingivitis, alveolar bone loss) indicating chronic plaque buildup. A key feature of FCGS is that the amount of inflammation is greatly disproportionate to the amount of tartar present.

Recent studies using genomic sequencing have confirmed that cats with FCGS have an altered oral microbiome compared to healthy cats. Genera such as *Porphyromonas*, *Treponema*, and *Fusobacterium* (obligate anaerobic bacteria often associated with periodontal disease) were found to be significantly more

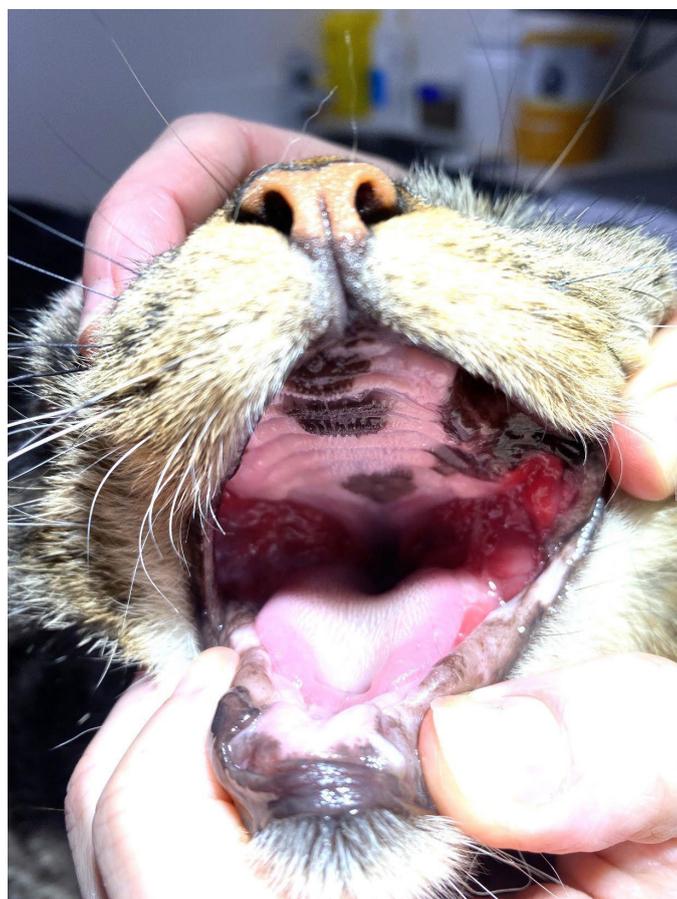


Figure 1. FCGS in a cat; extensive disease of the caudal pharynx persisted despite full mouth extraction

abundant in the mouths of FCGS-affected cats than in healthy controls. *Porphyromonas gulae*, a species related to the *Porphyromonas* bacteria that cause periodontal disease in dogs and humans, has been isolated from cats with stomatitis.

One notable finding was that *Bergeyella zoohelcum* (a Gram-negative bacterium) was abundant in healthy cats and proposed as a biomarker of a normal feline oral microbiome. Overall, microbiome data implies that FCGS involves a state of oral dysbiosis. The inflammation and tissue damage in FCGS could create an environment favouring anaerobes, while the overgrown microbes provide continual antigenic stimulation that drives further inflammation.

Dietary Factors & Oral Health

Dietary and nutritional factors can influence the oral environment and potentially play a role in gingivostomatitis, although direct causal links are not yet well defined. In one epidemiological survey, it was noted that food residues in the mouth predispose cats to microbial proliferation and dental plaque build-up, which in turn triggers gingival inflammation. Some veterinarians advocate that incorporating dry food or dental diets may help mechanically reduce plaque, though this alone is insufficient to prevent FCGS in susceptible cats, while other colleagues think that a high carbohydrate diet actually favours multiplication of undesirable bacteria. Beyond plaque, there is speculation that food allergens or additives could play a role in oral inflammation for some cats. Nutritional status in general can modulate immune function. Poor nutrition could further impair oral mucosal healing and immune response, creating a vicious cycle. In summary, while diet is not considered a primary cause of FCGS, it influences oral hygiene and possibly immune responses. More research is needed to determine if any specific diet can meaningfully prevent or mitigate feline gingivostomatitis.

Viral Agents & Feline Gingivostomatitis

Feline calicivirus (FCV) is the viral agent most strongly linked to FCGS. In chronic gingivostomatitis, FCV has been detected at high frequency in affected cats, suggesting a persistent infection or carrier state might trigger ongoing inflammation. This implies that FCV presence correlates with the occurrence and severity of stomatitis.

Interestingly, experimentally induced lesions did not invariably progress to chronic disease, indicating that while FCV can trigger stomatitis, additional factors (or host idiosyncrasies, likely genetically programmed e.g., less than optimal immune response) are required for the chronic, immune-mediated condition to develop.

Despite decades of association, it remains debated whether FCV is a primary cause of FCGS or a co-factor. In a recent cohort of 61 stomatitis cats, the percentage of cases positive for calicivirus antigen was high, suggesting active viral presence. **The working hypothesis is that chronic FCV infection in the oral tissues provides constant antigenic stimulation and mucosal damage, which triggers the cat's immune system to mount an excessive, inappropriate inflammatory response.** In a situation reminiscent of FIP, the immune response causes florid inflammation, but perhaps because of missing key component of cell mediated immunity, the virus persists in the tissues despite ongoing inflammation. Notably, no particular 'virulent' biotype of FCV specific to stomatitis has been confirmed—rather, chronic FCV carriers often harbor antigenically variable virus strains (due to mutation under immune pressure), which may help the virus persist by evading the host's immune response.

Other viruses have also been implicated in FCGS, especially those that affect the immune system. Feline herpesvirus (FHV-1) primarily causes respiratory and ocular disease, but it can rarely cause oral ulcerative lesions as well. Given that routine feline vaccines protect against both FCV and FHV, **it is notable that inadequate vaccination was identified as a risk factor for FCGS in at least one study. In the authors' experience, many cats with FCGS originated from shelters or rescue organisations where early vaccination was incomplete, consistent with early exposure to calicivirus being critical to the later development of this syndrome.**

Chronic retroviral infections can predispose cats to severe stomatitis as well. Some authorities suggest cats with FCGS should be tested for FIV/FeLV, as positivity is not uncommon. In general, FIV-infected cats are known to often suffer severe gingivitis/stomatitis as part of their chronic infections. Importantly, cats co-infected with FCV and feline foamy virus (a retrovirus, sometimes found in multi-cat environments) or co-infected with FeLV tend to have poorer response to stomatitis treatment.

Overall, viral agents—especially FCV—are considered major contributors to FCGS pathogenesis. However, not every FCV carrier develops stomatitis, and some stomatitis cats do not have detectable FCV on PCR testing (pointing to other causes, poor sampling, or potential problems with selection of PCR primers). The interplay between viral infection and host immune response is critical, as described next.

Immune Dysregulation & Inflammation

A hallmark of feline gingivostomatitis is an immunopathologic reaction in the oral tissues. Both CD4+ helper T-cells and CD8+ cytotoxic T-cells are

present, with studies noting an overrepresentation of activated CD8+ T cells in blood and tissue of FCGS cats. This suggests that the disease is driven by antigen-specific immune responses (T and B cell responses to oral antigens) that become pathogenic. Chronic inflammation is thought to be a result of the immune system attacking oral tissues or persistently activated by antigens in dental plaque and/or viruses.

Pro-inflammatory cytokines are abundantly expressed in FCGS lesions. IL-6 and IL-8 are key cytokines in driving neutrophil infiltration and acute phase inflammation, and their strong activation in FCGS mucosa confirms a highly inflammatory microenvironment. In one study, pathways related to innate immunity (neutrophilic inflammation) were also enriched, highlighting that both the innate and adaptive arms of the immune system are engaged in FCGS.

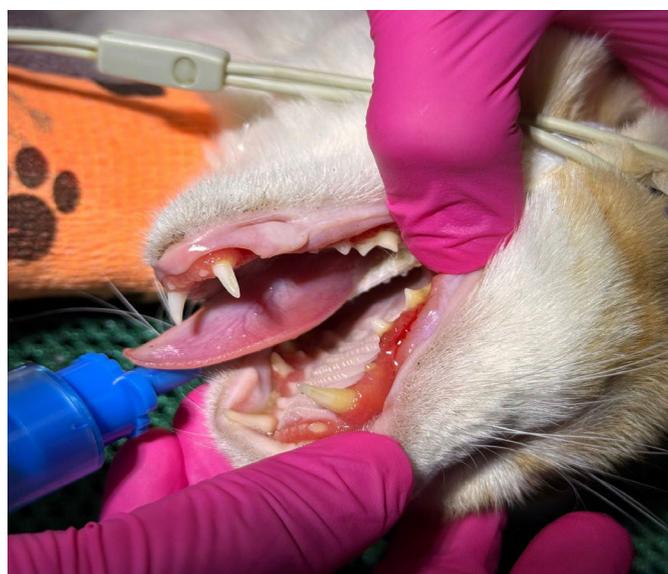


Figure 2. A young cat with 'juvenile gingivitis' due to calicivirus. Gum tissue was RT-qPCR positive for calicivirus, as one might expect.

Why do certain cats develop this maladaptive immune response? It may be that some individuals are genetically predisposed to an overzealous immune reaction. The presence of periodontal disease or retained roots can provide a nidus for chronic inflammation, which is why extracting teeth often helps (removing the major sources of plaque-antigen stimulation), indicating that in those cats, the immune system remains triggered by remaining antigens or perhaps has become self-perpetuating. The overproduction of immune mediators (like cytokines, prostaglandins, matrix metalloproteinases) leads to destruction of gingival connective tissue and bone (periodontal ligament and alveolar bone are often lost in chronic cases). The result is a painful, ulcerative oral environment where normal mucosal barriers are broken down, and secondary bacterial infections can further complicate healing.

Importantly, FCGS is not simply periodontitis—it is an immune-mediated mucositis that goes beyond what typical tartar-induced gingivitis would cause.

Immune dysregulation is underscored by the fact that immunosuppressive medications often provide relief (albeit temporary) and by the success of immune-modulating therapies (like cyclosporine or stem cells, as discussed later).

Juvenile Gingivitis & Early-Onset Periodontal Disease

Juvenile gingivitis (sometimes called juvenile hyperplastic gingivitis) is an oral inflammatory condition occurring in young cats, typically under 1 year-of-age, around the time the permanent teeth erupt. Clinically, these young cats exhibit marked gingival redness, swelling, and sometimes a proliferative or hyperplastic gum line soon after the adult teeth come in (Figure 2). There may also be a rapidly progressive component where periodontal attachment loss occurs early (juvenile periodontitis) in severe cases.

The pathophysiology of juvenile gingivitis is not fully understood, but it is thought conventionally to be an exaggerated inflammatory reaction to the normal bacterial colonisation that accompanies tooth eruption. There is speculation that this could be partly immune-mediated or even involve viral triggers, and the authors think calicivirus infection (as a chronic viral carrier) is actually the key underlying disease process. Many authors believe juvenile gingivitis is multi-factorial, with plaque bacteria being the primary driver but immune system quirks making the response unusually severe. Notably, despite the intense inflammation, juvenile gingivitis often is self-limiting.

Traditionally, management of juvenile gingivitis has focused on aggressive plaque control and supportive care during the period of susceptibility. In cases with gingival overgrowth, surgical gingivectomy can remove excess tissue and reduce pseudopockets. If the condition fails to respond to these measures and progresses, some cats may require extractions of the affected teeth to control pain and disease progression. In contrast, the authors believe this dogma is incorrect, and the principal treatment should be directed at the underlying calicivirus infection, with no requirement for gingivectomy and the like.

The relationship between juvenile gingivitis and adult FCGS is not definitively established—not all juvenile cases go on to develop chronic stomatitis. Both conditions share the feature of immune hyper-responsiveness to oral antigens, though juvenile gingivitis is often transient whereas FCGS is chronic and persistent.

Therapeutic Responses to Pharmacologic Interventions

Management of FCGS is challenging and, according to the literature, often requires a combination of dental, surgical and medical approaches. About 50–60% of cats achieve clinical remission of stomatitis after extensive extractions, and another ~20–30% improve substantially, although they are not completely cured. These refractory cases (and partial responders) require ongoing medical therapy to control inflammation and pain.

Traditionally, the mainstay of medical therapy has been immunosuppressive and anti-inflammatory drugs to 'tamp down' the overactive immune response. However, chronic steroid use gives rise to significant side effects (diabetes, immunosuppression, muscle wasting, etc.) and invariably loses effectiveness over time.

Interferon Therapy & Immune Modulation

Recombinant feline interferon-omega (rFeIFN- ω) has emerged as a therapeutic option for FCGS, particularly in cases associated with calicivirus. Feline IFN- ω is a Type I interferon (like IFN- α) that has been licensed in some countries for treatment of feline viral diseases. In FCGS, interferon can be applied either by injection or oro-mucosally (sprayed in the mouth). Experimental studies suggest rFeIFN- ω is roughly as effective as corticosteroids in managing stomatitis lesions, with the advantage of an antiviral mechanism that could eventually reduce calicivirus load. Indeed, the antiviral effects of omega-interferon might have been underestimated in determining the reason it is effective in these cases, if given for a sufficiently long duration of therapy.

Apart from interferon, the immunosuppressant cyclosporine has shown efficacy in chronic stomatitis. Since FCGS is T-cell mediated, cyclosporine can help 'calm the immune attack' in the mouth. Cyclosporine is often used in stomatitis cats that are refractory to steroids or when steroids are contraindicated. The success rate varies, but some cats maintain long-term remission on cyclosporine. A common concern is whether cats treated with cyclosporine are at risk of developing toxoplasmosis, and commonly clindamycin is given at the same time to try to prevent this happening, and also for its effect on anaerobic bacteria in the lesions.

Importantly, antibiotics are frequently administered to FCGS cats, but usually as adjunct therapy rather than a definitive solution. However, long-term antibiotic therapy risks fostering resistant bacteria and usually does not cure FCGS since the primary issue is immune dysfunction.

Antiviral Therapies (Including Molnupiravir & EIDD-1931)

Given the strong association between feline calicivirus and chronic stomatitis, it makes sense that antiviral therapy directed at FCV might ameliorate the disease. Recent advances—some spurred by SARS-CoV-2 (COVID-19) research and feline infectious peritonitis (FIP) treatments—have identified antivirals that are effective against RNA viruses in cats.

One of the newest candidates is molnupiravir, a broad-spectrum antiviral that acts as a nucleoside analogue to induce lethal mutagenesis in RNA viruses. Molnupiravir is actually a prodrug given to improve bioavailability over its primary metabolite, the nucleoside EIDD-1931, which is converted to the active antiviral nucleotide triphosphate, which is the active antiviral.

In a pilot trial (2025), eight FCV-positive cats with chronic gingivostomatitis that had failed full-mouth extractions were enrolled to receive molnupiravir or placebo. By the end of the trial, 4/5 treated cats showed improved oral lesion scores and 2/5 had a marked decrease in calicivirus shedding, whereas none of the 3 untreated control cats showed improvement. This work was presented at the ACVIM forum in June. These results are very promising: they suggest that suppressing FCV replication with an antiviral can lead to clinical remission of stomatitis in at least a subset of cases. Further research with larger samples and longer follow-up is needed, but this proof-of-concept indicates antivirals deserve a place in the FCGS treatment arsenal when viral infection is confirmed.

Besides molnupiravir, other antivirals and antiviral strategies have been explored. Broad-spectrum antivirals like GS-441524 (a nucleoside analogue used to treat FIP) theoretically could also have activity against FCV, but this remains speculative. If a stomatitis cat is positive for FIV or FeLV, managing those conditions (e.g., antiretroviral drugs like AZT for FIV, or interferon for FeLV) might indirectly help the oral disease by improving overall immune function, though evidence is anecdotal.

In summary, antiviral therapy targeting FCV is an exciting new avenue for FCGS management. As these treatments are refined, they hold promise for cats that suffer chronic oral inflammation associated with persistent viral infection. **Our unpublished work in Sydney over the last three years has confirmed that molnupiravir is a highly effective treatment for cats with FCGS, although we use it in concert with doxycycline to manage the bacterial dysbiosis and low dose meloxicam to reduce the over-active inflammatory component within the lesions.**

Emerging Therapies: Mesenchymal Stem Cells

One of the most promising emerging therapies for refractory FCGS is the use of mesenchymal stem cell (MSC) therapy. MSC can secrete cytokines and factors that dampen overactive immune cells, promote tissue healing, and even effect antiviral supportive actions by improving the host's immune response. Initial pilot studies about a decade ago showed dramatic improvements in cats with stomatitis that received intravenous stem cell therapy, especially those that had not responded to other treatments.

In a 2023 long-term study by Soltero-Rivera et al., cats were observed for 2–9 years post-treatment. Importantly, many of these cats had been candidates for euthanasia due to unrelenting pain prior to MSC therapy, and after treatment they experienced a restored quality of life. Approximately one-third of cats treated did not improve significantly (true non-responders), indicating MSCs are not a panacea for all cases. Adverse effects of MSC infusion were relatively minor: about 34% of cats had transient reactions like fever or vomiting around the time of infusion, but these were self-resolving transfusion-like reactions, and no long-term negative effects were noted. Autologous cells may have slightly faster efficacy in some reports, but allogeneic cells are more practical to use in clinical settings (they can be banked and readily administered without the need for harvesting from the current patient).

Mechanistically, MSC therapy in FCGS is thought to work by modulating the immune response. Essentially, they help turn off the chronic inflammatory response by restoring immune balance. A fascinating development is that a specific allogeneic MSC product (using uterine-derived MSCs from spay-neuter clinic donors) has been in advanced clinical trials and was recently on track for conditional FDA approval as a treatment for feline stomatitis. Veterinary stem cell companies and academic centers (e.g., UC Davis, which has spearheaded much of the FCGS MSC research) are optimistic that this therapy will become a standard of care for refractory cases.

Beyond stem cells, other emerging or adjunct therapies include laser ablation of inflamed tissue, plasma-rich protein injections to promote healing, and novel immunotherapies (such as IL-2 or IL-10 modulation).

In conclusion, stem cell therapy represents a significant breakthrough for a subset of stomatitis cats that do not respond to conventional treatments. As with any innovative therapy, cost and access are considerations,

but the potential to cure or induce long-term remission in a disease that was previously often an end-of-line scenario (euthanasia due to intractable pain) is a remarkable advancement in feline medicine.

Conclusions

Feline gingivostomatitis is a complex syndrome with multifactorial pathophysiology. The feline oral microbiome in FCGS shifts toward a dysbiotic state rich in anaerobes, which likely fuels inflammation further. Among infectious agents, feline calicivirus stands out as a key player associated with FCGS development, although other viruses like FHV-1 and FIV can influence disease severity and progression.

Juvenile gingivitis in cats shares some parallels by featuring an outsized inflammatory reaction in the young animal's mouth, but it often eventually resolves with maturity and aggressive dental care. Therapeutically, the approaches to FCGS are evolving from purely symptomatic treatment (antibiotics, steroids, extractions) toward targeted interventions: immunomodulators like interferon-omega to curb viral replication and immune activation, direct antivirals like molnupiravir/EIDD-1931 to eliminate the key triggering viral antigens, and regenerative medicine such as mesenchymal stem cells to restore immune equilibrium. Nonetheless, some cases remain frustratingly refractory, highlighting the need for continued research.

With a better understanding of the pathophysiology, veterinarians can develop earlier diagnostic markers and more effective, specific treatments—turning this once life-long debilitating disease into a manageable or even preventable condition for our feline companions.

Editor's Note

Start overleaf if you just want the basic facts and not the background and history.

A New Way Forward

To reiterate, FCGS is a debilitating inflammatory disease affecting the oral mucosa of cats presenting as ulcerative and/or proliferative inflammatory process extending from the gingiva to the caudal pharynx. **The foundational understanding of gingivostomatitis in cats was established by Pedersen (1991) and further expanded by Ross Harley's PhD research at Bristol Veterinary School (see reference 7 in the bibliography), with both investigators emphasising the critical role of calicivirus.**

Over the past three decades, however, complex and often contradictory findings have emerged, complicating and in some respects hindering the clinical approach to managing FCGS.

After initial primary infection with calicivirus, affected cats mount a robust antibody-mediated (AMI) and cell-mediated immune response (CMI) to clear FCV from oral tissues. FCGS occurs when these processes are unbalanced, so the virus and the inflammatory response to its presence persist. Dietary factors may also play a role, especially when ultra-processed carbohydrate-rich kibble is a major part of the affected cat's diet. Additionally, bacterial biofilms displaying striking dysbiosis have been identified in affected tissues, reinforcing the notion that both viral and bacterial factors trigger an inappropriate immune response which favours disease progression.

CONCLUSION

FCGS is a multifactorial disease influenced by viral infection, immune dysfunction, and environmental factors. A multidisciplinary approach incorporating antivirals, immunomodulation, and adjunctive therapies has the potential to significantly improve clinical outcomes and quality of life for feline patients.

Old Treatment Modalities

Surgical Management

The historical dogma is that full-mouth or partial-mouth dental extractions remain the gold standard treatment, providing long-term resolution or substantial improvement in maybe 60% of cases. Lower success

rates are commonly seen by practitioners who are not experts in performing this radical surgical procedure. Although there is a wealth of evidence supporting this approach, intuitively this would appear to be an unattractive option for most cats and most owners.

Full mouth extraction is an aggressive, painful surgical intervention involving prolonged or multiple general anaesthetics, and can be associated with moderate morbidity, high cost and delayed convalescence. Although most cases are improved, a substantial proportion of cases still have residual disease even after healing has occurred. Presumably, extraction removes chronic antigenic stimulation by elimination of virus-infected tissues, facilitating viral clearance and immune resolution. Some cats, however, continue to exhibit caudal pharyngeal inflammation post-extraction, necessitating additional medical intervention.

Corticosteroids such as prednisolone provide temporary relief but are not viable for long-term management due to adverse effects. If they are used, when the doses are later terminated the condition recurs, sometimes worse than it was initially. This is because corticosteroids favour viral persistence and multiplication!

Cyclosporine has shown excellent efficacy in controlling refractory cases by inhibiting T-cell activation and reducing proinflammatory cytokine expression. It is also used in a conceptually similar condition in dogs, i.e. Canine Chronic Ulcerative Stomatitis (CCUS) or Canine Ulcerative Parodontal Stomatitis (CUPS; but which older Australian vets would refer to as 'trench mouth'), in concert with metronidazole.

Mesenchymal stem cell (MSC) therapy has emerged as a promising option, with studies showing normalisation of CD4/CD8 ratios and resolution of clinical signs in some refractory cases but only following full mouth extraction.

Antiviral Therapy – Way of The Future?

Recent advancements in feline antiviral therapies have produced a paradigm shift in the treatment of FCV-associated FCGS. Molnupiravir (prodrug) and its active metabolite, EIDD-1931, have demonstrated efficacy in eliminating FCV from the oral mucosa, paralleling their success in treating feline infectious peritonitis (FIP). Mefloquine and nitazoxanide have also shown antiviral activity against FCV, warranting further investigation as therapy. **Prolonged treatment courses are necessary to fully clear FCV from gingival and pharyngeal tissues, like protocols used in FIP therapy.**

Additional therapeutic interventions, such as high-energy laser therapy, have shown potential in eradicating viral reservoirs within gingival tissue.

Our Current Recommended Therapeutic Regimen

The tide turned during the resurgence of feline antiviral therapies, which gave veterinarians worldwide a greater confidence in using antiviral drugs. This movement began with the use of famciclovir for herpetic infections caused by FHV-1 and gained momentum with GS-441524 and GC376 for feline infectious peritonitis (FIP).

We believe the most promising agent for treating calicivirus is EIDD-1931 and its prodrug molnupiravir. Research by Jacqui Norris's group indicated that mefloquine also exhibits effective activity against calicivirus, while other teams, including one from the University of NSW and a feline physician (Dr Emily Pritchard), advocate for nitazoxanide.

Our preferred treatment for calicivirus is molnupiravir and its metabolite, EIDD-1931, due to their established efficacy against FIP. All three medications we utilise (EIDD-1931, doxycycline, half-dose meloxicam) can be safely administered to kittens with acute calicivirus, adult cats with acute virulent disease, and those with calicivirus-associated gingivostomatitis.

A combination protocol incorporating low-dose oral meloxicam (to reduce the inflammation), doxycycline (to mitigate bacterial dysbiosis), and molnupiravir or EIDD-1931 (for antiviral action) has yielded excellent results in the hands of the authors. This regimen often leads to marked clinical improvement within 2–3 months, allowing for medication tapering and potential discontinuation.

Mirtazapine (2 mg once a day; oral or transdermal) is frequently included to stimulate appetite in affected cats.

Much like treating FIP, prolonged treatment courses are necessary to eliminate calicivirus from the gingival and caudal pharyngeal tissues. With input from BOVA Compounding, we have developed a stable drug combination that includes low-dose oral meloxicam to reduce the inflammatory response and thereby make the cats more comfortable, doxycycline to combat bacterial

dysbiosis and for its immunomodulatory effects, and EIDD-1931 for its long-term antiviral action.

We administer these treatments, either directly onto the lesions, or mixed with two equal meals of canned cat food or fresh meat, using a specially designed paste which is palatable and 'adhesive'. The rationale is as follows: we wish to have the drug work initially in the oral cavity and gums at very high concentrations and subsequently be absorbed and target the same tissues by achieving effective blood levels. We chose EIDD-1931 so that the active antiviral would work LOCALLY from the get-go, in comparison to molnupiravir which needs to be activated in the liver to become an effective antiviral agent. Additionally, we often include 2 mg of mirtazapine daily (given separately orally or transdermally) to encourage a strong appetite.

Patients typically show immediate initial improvement, likely due to doxycycline and meloxicam. Over 1-3 months, the benefits become sustained, resulting in substantial recovery, allowing for discontinuation of all the medications.

We have used this approach in cats with residual disease after whole mouth extractions and also in cats with calicivirus-associated gingivitis where full-mouth extractions have not been performed, including cases of juvenile gingivitis. Ideally, these cats should receive thorough dental care and the extraction of any teeth that

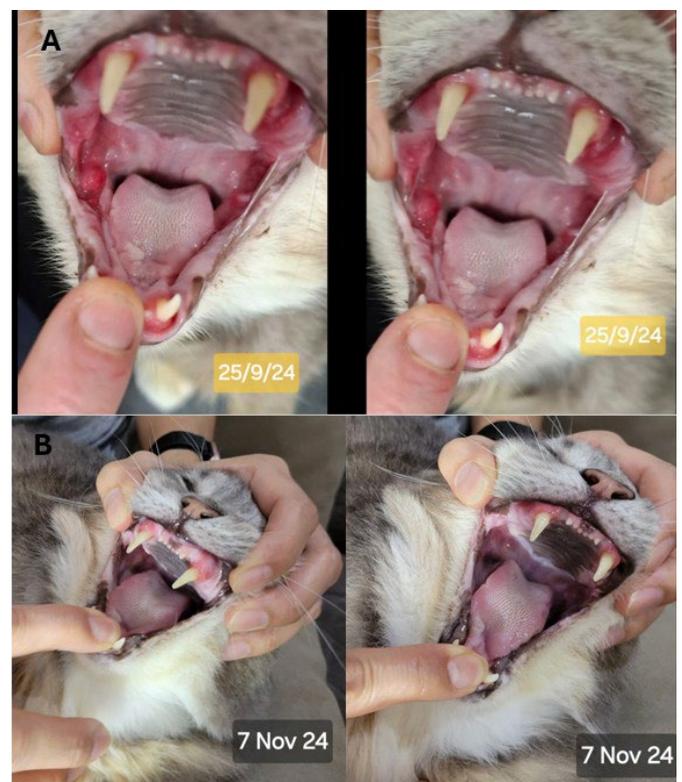


Figure 3. A cat with FCGS before (A) and after (B) therapy with molnupiravir/meloxicam and doxycycline. The cat has continued to do well following discontinuation of all drugs. The dates are provided on the photographs.

are loose or exhibit lytic changes (in alveolar bone or teeth) on dental radiographs. **It can also be used in cats and kittens with acute calicivirus disease, including cats with prominent lingual ulcers.**

It is essential to note that this approach is still a work in progress. Some cats may require higher doses of EIDD-1931, and we may explore the sequential or combination use of mefloquine or nitazoxanide in the future. Continued research and clinical experience will help refine these treatment strategies to enhance outcomes for affected cats. Thorough and comprehensive case notes (that include details of diagnosis, treatment schedule, response to treatment [including photos] and details of suspected adverse events) will allow retrospective assessment and analysis.

Practice Tip

It is worth keeping a tub of this combination paste in the pharmacy* in case you are presented with an acute case of calicivirus disease, whether it be a nasty virulent calicivirus strain, or just a normal calicivirus involved in a kitten with cat flu. This product will provide symptomatic relief and be an effective antiviral, with the proviso that you maintain hydration by force-feeding, syringing A/d or cream treats, or IV fluid therapy to protect the kidneys during administration of low oral meloxicam. The disease course will be markedly foreshortened. If you are not sure if herpetic disease (FHV-1) is present also, add in Famvir at 40 mg/kg BID to TID.

* Vets are legally allowed to order medicines from pharmacies either by prescription (i.e. for an individual animal) or via written order. The written order does not need to comply with the same requirements that a prescription does i.e. no need for animal owner details or a need to be for a specific animal. Vets can order via written order the quantity they need 'for emergency use'. It is the responsibility of the prescribing veterinarian to determine if a medicine is likely to be needed immediately and when it isn't in the animal's best interests to wait the time it takes (often several days) to order and receive a compounded medicine. So, the medicine ordered via written orders, can sit on a vet's shelf until dispensed by the vet. The vet can then dispense and label the amount they give to the owner from the shelf stock. A vet shouldn't dispense an amount of a compounded medicine that will expire before the label says. Some of Bova's products have long shelf lives, others not so long, so it really depends on the formula and the stability data.

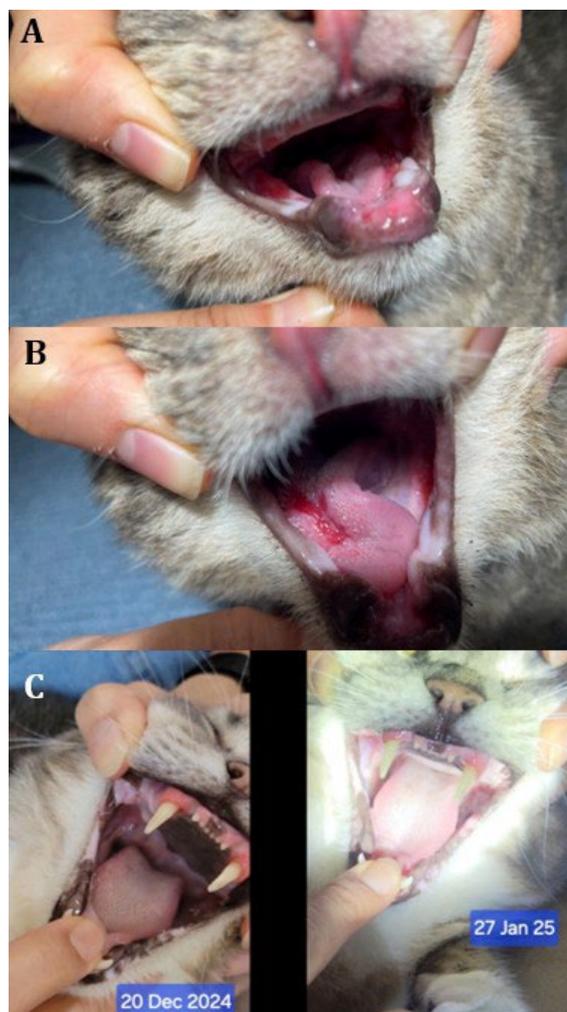


Figure 4. A cat with FCGS and a non-healing lingual ulcer before (A & B) and after (C) therapy with molnupiravir/meloxicam and doxycycline. The cat has continued to do well following discontinuation of all drugs. The dates are provided on the photographs.



Figure 5. A cat with calicivirus-associated juvenile gingivitis before and after therapy with molnupiravir/ meloxicam/ doxycycline. The cat has continued to do well following discontinuation of all drugs.

**Doxycycline (as monohydrate)
EIDD-1931 Meloxicam**
60mg, 204mg, 0.15mg/ml Paste

This product has been compounded by the pharmacist

35ml

For Animal Treatment Only | Chicken Flavour

Wear gloves when handling. Wash hands after administration.
Contains 0.1% butylated hydroxytoluene as preservative

Storage: Room temperature in a cool dry place

BOVA AUS Discard contents after DD/MM/YYYY



Figure 6. Label for palatable paste containing EIDD-1931, doxycycline monohydrate and meloxicam in the optimal ratios for treatment of calicivirus associated stomatitis



Figure 7. A different cat with FCGS/juvenile gingivostomatitis before (above) and after (below) molnupiravir/meloxicam/doxycycline therapy

Therapeutic regimen using the BOVA combination paste product

- | | |
|----------------|------------------|
| 1. EIDD 1931 | 17 mg/kg BID |
| 2. Doxycycline | 5 mg/kg BID |
| 3. Meloxicam | 0.0125 mg/kg BID |

EIDD-1931 204mg/mL, Doxycycline 60mg/mL, Meloxicam 0.15mg/mL

Dose rate – number of clicks (1 click = 0.25mL) per 3 kg of cat, twice a day, with food

- i. A 3 kg cat should get 1 click twice a day
- ii. A 4.5 kg cat should get 2 clicks in the AM, and one click in the PM
- iii. A 6 kg cat should get 2 clicks BID

Each click (=0.25mL) contains EIDD-1931 51mg/0.25mL, Doxycycline 15mg/0.25mL, Meloxicam 0.0375mg/0.25mL.

Presented as 35mL pack size in the Topi-click device with a syringe.

Contextualised Care/Spectrum of Care

This novel management approach focusing on antiviral treatment rather than surgical removal of teeth is currently controversial amongst some veterinary dentists given the current limited evidence base. However, the importance of contextualised care/spectrum of care has become well recognised, acknowledging that there are different ways to approach treatments, depending on specific circumstances of the individual animal and their caregivers, and the context in which care is delivered. This approach emphasises tailoring care to individual circumstances which includes holistic patient specific needs, client preferences, and financial limitations, encouraging a flexible and patient-centred approach.

The authors therefore consider that it is critical that less invasive and less expensive treatment options are able to be offered, in the interests of best patient welfare and affordability to clients, particularly given that these cases tend to be more prevalent in low socioeconomic communities.

Ethical Considerations in Treatment Selection

One of the most debated aspects of FCGS management is the ethical consideration of full-mouth extractions. Ethical decision making with any treatment should include

- i. Treatment efficacy
- ii. Patient welfare impacts (discussed below)
- iii. Other adverse impacts of treatment
- iv. Client preferences
- v. Cost

Most clients would have a strong preference for medical management if it were efficacious. Whilst it is early days in clinical trials, results to date from different researchers across the world are extremely promising. Welfare impacts on patients are substantially reduced if surgical intervention is not required or can be minimised. Some cases may still require dental extractions where there is dental pathology, and full dental evaluation is always recommended, but there may be benefit in reducing inflammation with medical management prior to dental extractions in these cases—a contextualized individual patient approach is advised. Medical management is substantially less expensive which can be a key component in determining whether these cases are successfully managed or not—many owners of these patients simply cannot afford extensive dental extractions. The only concern raised with antiviral therapy by some clinicians is the contribution to resistance of these antivirals. Whilst this is a valid concern, in the authors' opinions this is not an ethical justification to withhold an efficacious antiviral treatment for a viral disease.

Welfare Considerations in Treatment Selection

Applying the Five Domains Model for assessing patient welfare enables a scientific, holistic and objective approach to assessing welfare impacts of management interventions. This involves assessing impacts in the four physical/functional Domains of Nutrition, the Physical Environment, Health, and Behavioural interactions (with other animals, people and the environment) and through evidence from physiology, behavioural science and neuroscience, inferring impacts on the animal's mental experiences.

Surgical intervention has greater negative impacts on patient welfare through the frequency of reduced voluntary nutrition in the peri-operative period, risk of dehydration associated with reduced food intake and general anaesthesia, requirement for hospital admission and the associated anxiety/fear, the requirement for prolonged or multiple general anaesthesia and the associated risks, pain associated with surgery, impacts on behaviour in both the peri-operative period and potential longer term behavioural impacts from full mouth extractions. Conversely, medical management has very few welfare impacts restricted mainly to the impacts of administering medications since the recommended treatment regimens have limited side effects.

In summary, some researchers, including the authors of this article, argue that antiviral therapies offer a less invasive alternative to extensive dental extractions, potentially reducing the need for radical surgical interventions. This may circumvent an extremely expensive procedure associated with substantial morbidity for the feline patient.

Is treatment a choice between medical or surgical approaches or should both be used?

To be clear, the authors are not necessarily suggesting a choice between medical and surgical treatment but rather are recommending a contextualised and individual patient-centred approach to management decision making, which includes the option of antiviral treatment. Dental evaluation is recommended, and some extractions may still be required. **However, it is likely that many patients will benefit substantially from antiviral therapy, and whether any required tooth extractions are performed before or after such therapy should be considered on a case-by-case basis.**



Doxycycline (as monohydrate), EIDD-1931, Meloxicam Paste- How to Use. (Administered with Topi-CLICK Perl® Dispenser)

Doxycycline (as monohydrate), EIDD-1931 and meloxicam paste is a specially compounded preparation designed for the treatment of cats with Calicivirus-associated stomatitis. It is dispensed using the Topi-CLICK Perl®, a precision dosing applicator that allows accurate, consistent oral doses every time. 1 click = 0.25 mL of paste.

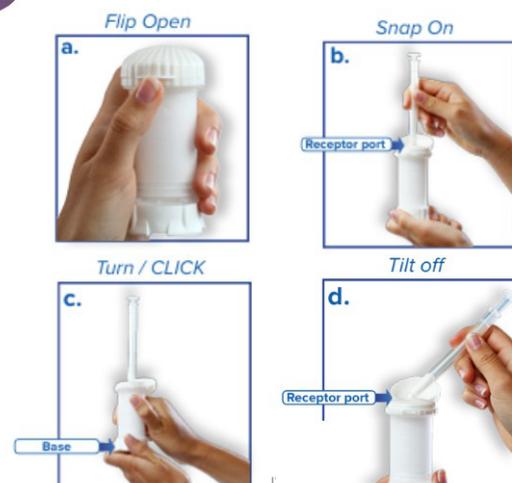
How to administer

1. Open cap (figure a.): Flip open the top cap on the Topi-CLICK Perl® device.
2. Attach the Snap-on Applicator (figure b.) to the base by aligning and snapping it into the receptor port.
Make sure the plunger touches the base.
3. Hold the device vertically and upright.
4. Turn the base until you hear a click, this loads the dose into the applicator (figure c.).
5. Repeat step 4 if another click is required.
6. Remove applicator by gently tilting the applicator off the base – do not pull straight off (figure d.).
7. Wipe the nozzle with a clean tissue and flip the cap back down to close the device.
8. Administer the dose directly into the mouth using the plunger.
9. Gently massage under the chin if needed to encourage swallowing.

Important Notes

- Pregnant women should not handle.
- Wear gloves when handling. Wash hands after administration.
- Store medication at room temperature, away from direct sunlight.
- Wash the applicator thoroughly after use.
- Applicator is dishwasher safe; use with caution to avoid residual medicine transfer when cleaning (max. 30 cycles).
- Follow the dose prescribed by your veterinarian and do not exceed the number of clicks.
- This product contains an antibiotic and an antiviral. Use responsibly to help prevent antimicrobial resistance.

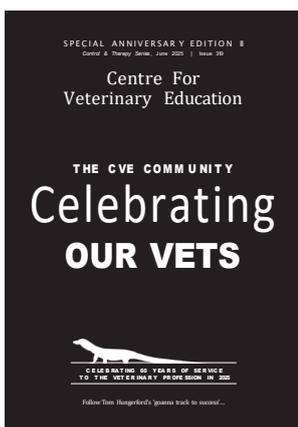
Scan QR code: How-To-Use video



In summary, gingivostomatitis in cats remains a complex and challenging condition influenced by a viral component, immune response discrepancies, and environmental factors. By leveraging advancements in antiviral treatments and adapting therapeutic protocols to address the specific needs of each individual cat, we have the potential to improve the quality of life for many feline patients suffering from this condition.

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This *Control & Therapy Series* article (or an updated version) will be published in the September 2025 issue. It is an independent article, was not commissioned and there are no conflicts of interest to declare.

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