

Feline Chronic Gingivo-Stomatitis (FCGS)

Introduction



The condition currently, and most commonly, known as *Feline Chronic Gingivo-Stomatitis (FCGS)* is a relatively common and frustrating problem to the small animal practitioner. A number of synonyms are found in the literature for the same conditions. Examples are “Feline Lymphocytic Plasmacytic Stomatitis”, Plasma Cell Stomatitis”. The reported incidence varies with severity but a figure of 3% of all feline dental conditions for the most intractable cases may be considered reasonable. Many cases prove to be extremely

frustrating with a number of different combination treatments in current use.

The syndrome is characterised by persistent and severe inflammation and ulceration of the oral soft tissues. Many times this includes the pharyngeal and lingual mucosa.

The three sites are:

- *Caudal Stomatitis: Tissues in the caudal oral cavity bordered medially by the palatoglossal folds and fauces, dorsally by hard and soft palate and rostrally by the alveolar and buccal mucosa*
- *Alveolar Stomatitis: Mucosa overlying the alveolar processes of the teeth extending from the mucogingival junction to the vestibular sulcus and floor of the mouth.*
- *Labial/Buccal Stomatitis: inflammation of the lip and/or cheek mucosa*

The condition is often present in the absence of significant accumulation of calculus on the teeth. Inflammation in these areas occurs commonly around the time of kitten vaccination or when temporary teeth eruption, when permanent teeth erupt or, most commonly, much later in life.

Purebred cats have long been considered to be more susceptible although recent work disproves this theory. There is also an inverse relationship between the age of onset of disease and the number of cats in the household and this may implicate social stress or increased exposure to infectious agents as predisposing factors.

This syndrome is best considered as part of a full oral cavity examination and the presence of Tooth Resorption (TR's) lesions frequently adds to and confuses the picture. Additionally, it is clear that carriage of calici virus is a co-factor in the induction or progression of the complex. Although the relationship between calici infection and FCGS appears strong, there is also a reported incidence of 50% of cats infected with FIV also having FCGS. Another source indicates that around 15% of cats with FCGS are positive for FeLV/FIV. (*Knowles 1989*)

One consistent feature of all cases is a hypergammaglobulinaemia. This implies B lymphocyte proliferation and therefore *no humoral immune response depression*. It is probable that *affected cats are intolerant to even small quantities of bacterial plaque* on the tooth surface and elsewhere in the mouth. The main problem is that not all FCGS cases are alike. Some respond to routine periodontal therapy and improved hygiene while others will respond poorly to any treatment. The implication is that some cats have a very low threshold to the trigger factors(s) whilst others have a higher threshold approaching the level for normal cats. *Most intractable cases (87%) improve with elective tooth extraction and a few cases (13%) do not respond to any treatment.* (*Hennet 1997, Girard & Hennet 2005, Hennet 2010*)

Clinical Signs

The main sign in all cats is dysphagia and pain due to extensive oral inflammation and ulceration of soft tissues.

Inflammatory lesions can be focal or diffuse and may involve all oral tissues - most commonly the tissues lateral to the palatoglossal folds, gingiva and mucosa overlying the cheek teeth. Other tissues in the pharynx, tongue and the mandibular molar salivary glands are also affected in severe cases.

Other reported signs are:

- *Anorexia and/or dysphagia*
- *Severe halitosis.*
- *Weight loss - chronic or acute*
- *Lack of (or an inability) to groom.*
- *A reluctance to eat hard food is common.*
- *Submandibular lymphadenomegaly – often dramatically increased in size and painful when palpated.*
- *Variable, sometimes minimal, accumulation of plaque and calculus.*
- *Teeth may be missing, affected by “tooth resorption” or suffering from furcation exposure and excessive mobility after recession of the periodontal tissues.*

Aetiology

There is no simple aetiological agent for this syndrome. Certain factors are known to have an effect but the most commonly held view is that these cats suffer from an immunological over-reaction to low levels of oral antigens – dental plaque mainly. Factors involved are:

Breed: Some breeds may appear to have more affected individuals with Siamese, Burmese, Abyssinian, Persians, Tonkinese, and Main Coons all over represented. Mixed breed cats make up the majority of cases seen in the author's practice by 2:1.

Environmental Factors: Colony cats or those in multi-cat households appear to be more commonly affected. **Stress** is considered the main factor plus the close proximity of animals allowing transmission of microorganisms also being significant.

Plaque bacteria: The oral bacteria present in the plaque matrix drive the abnormal non-specific inflammatory response. Although individuals are thought to be plaque intolerant, there is a variable threshold to the bacterial load among these individuals. Specific bacteria as seen in periodontal disease have been reported in these cats and *Pasteurella* and *Prevotella* species are more highly represented than others. Around half the cats seen by the author harvested pure cultures of *Pasteurella multocida* (*Dolieslager 2011*).

Feline Calici Virus: Many clinicians, including the author, find a level approaching 70% of chronically affected individuals (> 6months) showing positive testing to virus isolation following oropharyngeal swabbing for Feline Calici Virus. The significance of this within the syndrome is not known. It is possible that the virus damages cell membranes allowing easier antigenic penetration by other agents. However, other co-factors are required before this virus can cause disease as FCV carriage in the cat population is around 30% (*Zicola 2009*). One research study (*Hennet & Boucraut-Baralon 2005*) considered that chronic palatoglossitis lesions, as opposed to buccostomatitis lesions, to be calicivirus associated.

FIV particularly may have a role in producing oral lesions by predisposing the cat to secondary infections. Both FIV and FeLV may contribute to an aberrant immune response to oral antigens but a recent study (*Dolieslager 2011*) showed a group of FCGS cats to have 4% prevalence for positive FIV and FeLV which is similar to the UK cat population as a whole. However, this is not the hyperimmune response that characterises the main syndrome.

Dental Disease: The presence of any concurrent dental disease is important. Either periodontal disease or Tooth Resorption lesions (TR's) or both can have an exacerbating effect on the syndrome.

Diagnostic Testing

A standard diagnostic approach is advocated for all cats affected. Some of this can be considered optional in some cases and some are essential and are marked in list appropriately as “E” or “O”.

- **Full general and dental history:** including recent and past treatments for the mouth (E)
- **General health assessment** (E)
- **Full examination of head and neck** – (E)
- **Score the mouth using the Stomatitis Disease Activity Index (SDAI) sheet** – (E)
- **Routine Haematology (O) and Biochemistry (E)** screening for underlying systemic disease. One study (*Hennet 1997*) reported 10% of affected cats with chronic renal failure. Any underlying systemic disease may significantly affect the prognosis or the safety of anaesthetic protocols and other drugs (e.g. long term NSAID's)
- **Virus testing:** for FIV, FeLV. Oral swab for FCV and FHV (E)
- **Bacteriology (O):** for both aerobic and anaerobic bacteria. A high proportion of cats tested show pure cultures of *Pasteurella multocida* (*Dolieslager 2011*).
- **Biopsy (O)** of affected areas - necessary to eliminate neoplasms (e.g. Sq. Cell Carcinoma, Lymphoma etc) and other immunopathologies. Very important if lesions not symmetrical.
- **Dental chart and full mouth dental radiographic survey (E)** to assess periodontal status of teeth, bone quality and locate broken root tips or tooth resorption lesions.

Management & Treatment

The main aim is to restore the balance between the immune response and the oral antigen burden. In effect this means zero tolerance of both existing dental disease and of bacterial plaque.

First Line Treatments

These treatments are for all cats and should be performed first. The aim is to reduce the antigen burden and assess how able the patient is to return to normal tissue state with normal hygiene measures with the emphasis of plaque reduction.

Antibiotics - may be necessary pre-operatively to control excessive inflammation and improve quality of soft tissue before and after surgery. These antibiotics must work on *Pasteurella* spp and it should be noted that many cats appear to be clindamycin resistant (*Dolieslager 2011*). A useful first line treatment is *Amoxycillin/Clavulanic Acid* at 12.5mg/kg *bid*.

Use pre-op as required to improve tissues and post-op for a minimum 8-10 days. Ensure owner can comply with treatment. This may mean using an antibiotic in an acceptable form. Powder can be hidden in frozen butterballs or in pilchards with tomato sauce.

Dentistry

- **Dental chart & SDAI score sheet:** a dental chart is an essential record of the mouth. Discourages shortcutting of exam.
- **Scale & polish:** every case starts by improving basic hygiene.
- **Full mouth radiographs:** All teeth present or missing.
- **Treat diseased teeth:** in almost all cases, this means extraction.
- **Initiate chlorhexidine:** twice daily application of chlorhexidine (Parodontyl: Virbac) wiped inside lips twice daily or brushed if cat will allow it.
- **Re-assess case in 7-10 days.**
 - **If better** continue chlorhexidine twice daily and review in 4 weeks and subsequently as required. Note that more frequent scaling and polishing intervals will be necessary – perhaps 3-4 per annum
 - **If no better** move to elective extraction of cheek teeth as soon as possible. Studies over the last 15 years (Hennet 1997, Girard 2005) consistently show the benefit of this procedure with 50% of cases require no further treatment to resolve their signs and a further 37% need low levels of inflammation support but are markedly better than before – see below.

Repeat Scale / Polish

For juvenile patients it is important to avoid permanent anatomic changes in the first two years of life. If the immune system is substandard in the early months, the provision of excellent hygiene can help considerably. Although little calculus may be visible, continued inflammatory changes in either the whole of the gingiva or the marginal gingiva is an indication to repeat the surgical cleaning - especially the hand curettage subgingivally. This may mean professional scaling & polishing every three months.

Second Line Treatments

Elective Tooth Extraction

This is now firmly established; by both peer reviewed publication and dental specialists, as the logical option to take if first line treatment (see above) alone is insufficient to provide resolution of the inflammation. In the author's opinion, if the tissues fail to respond to the best hygiene you can provide within 2-4 weeks, by reduction of inflammation and improvement in

comfort, elective surgical extraction of all the cheek teeth should follow without delay. Owners and many veterinary surgeons are often reluctant to take this step.

Elective surgical extraction of whole cheek teeth quadrants should not be undertaken lightly as there are several complications that may associated with it.

- 1) *The underlying bone may be sclerotic and poorly vascularised.*
- 2) *The roots may be ankylosed to the alveolar bone*
- 3) *Teeth already affected by Tooth Resorption lesions (type 2) may have roots in an advanced state of destruction with no true morphology. For type 1 TR lesions the teeth may be fragile and hard to extract without flaps.*

Operative management of elective extractions

Multiple extractions require consideration as to analgesics, antibiotics and nutrition pre and post-op. Some cats may be best hospitalised for 2-3 days if owners are unwilling or unable to administer medication per os.

Analgesia: Buprenorphine (Vetergesic™: Alstoe) is considered good for moderate to severe pain in cats at 1ml per 15kg every 6 hours. *This can be used either parenterally or per os/sublingual.* Owners can administer this analgesic very easily. An alternative regime in the hospital would be to use a selective μ -agonist opioid such as morphine. Morphine is very useful for severe pain at 0.1mg to 0.2mg/kg im or sc. every 6-8hrs. Beware of dysphoria in cats when high levels are used. Regional analgesia using lidocaine, mepivacaine or bupivacaine is also effective in a multi-modal regime. Some authors advocate a combination of these agents – for example a 1:3 ratio of lidocaine and bupivacaine. Carprofen or meloxicam is useful in addition to, but not instead of, opiates.

Antibiotics: As the primary condition is a hyperimmune reaction to mixed oral antigen, antibiotics by themselves give minimal success. In the perioperative period, they will guard against opportunist infection and should be started pre-operatively. The selected drug should have good activity in bone and on anaerobic bacteria. Clindamycin and/or potentiated Amoxycillin are the drugs of choice in most cases but many *Pasteurella* species are resistant to clindamycin.

Feeding: Nutritional assistance may be necessary short or medium term. It may be necessary to consider pharyngostomy feeding in extreme cases and assisted oral feeding in hospital in others. If fluid intake is suboptimal, this should be addressed also.

Most cats do better at home if the owner is able to provide active help. Favourite soft foods (pilchards in tomato sauce) are necessary for three to five days post-op. In some circumstances it may be necessary to use a convalescence diet immediately post-op such as Hill's a/d™, Waltham Feline Concentration Diet™ or Nutrigel™ (Virbac).

Other Anti-inflammatory or Immunomodulation Therapies

Many drug therapies are been advocated previously for this condition. This is probably due to the historical lack of success. *Most have no proven efficacy.* Some of these are based on low number case reports, anecdote or small-uncontrolled studies. Given that many of these drugs

are highly toxic in cats, familiarity with the drugs is recommended. The internet also provides many owners with information which may or may not carry any reasonable validity.

Interferon Omega

A number of veterinary surgeons report using interferon and some studies are now appearing to indicate that it exceeds the potential of other treatments for this condition.

A consensus statement by a group of European specialists in late 2010 indicated feline recombinant interferon omega is most effectively used in the group of cats which are FCV positive and are long-term non-responders to extraction. Our own studies over three years indicate that, not only is interferon very helpful in reducing inflammation and improving comfort levels, it often also allows practices to drop other treatment regimes.

Results in a recent study of 39 cats indicate that feline recombinant interferon is an effective treatment particularly in the group of cats, which are FCV positive and are non-responders to elective extraction. (Hennet 2011 JFMS in publication).

Oral use: Interferon given per os is believed to work by initiating a cytokine cascade when it comes into contact with cells to provide an immunomodulatory effect over a long period of time. The cascade then has distant effects.

A 10MU vial is initially injected into a 100ml bag of sterile saline and ten fractions of 10ml created, which are then frozen. When frozen they have a reported shelf life of one year. The first 10ml fraction is used to give a dose of 1ml per os per cat per day resulting in a daily dose of 100,000 units of interferon. This fraction can be refrigerated normally and will have a shelf life of three weeks. The owner continues to give 1ml per day using alternate sides until all the fractions are used. Ideally, treatment lasts for 100 days but longer may be required. After three months, the progress should be reassessed using the *Stomatitis Disease Activity Index (SDAI)* scoring system. Cats can be rechecked for calici virus carriage in the oropharynx at this time.

Preliminary results of our own long term study of 29 cats (2009 to 2011)

- Cats presented with FCGS were DSH 62% and pedigree 38%
- Mean age at presentation was 6 years 7 months with 60% male/n and 40% female/n
- Cats positive for FCV on first presentation (virus isolation on oral swab) were 69%
- Of those cats FCV positive, only 13.8% became FCV negative after INF treatment

Success rates were measured using the SDAI score sheets. A successful outcome was considered to be an SDAI score of 5 or less at revisit. A cure was 2 or less. Improvement was defined as a 50% reduction in initial SDAI score. Bear in mind that a “normal” cat with moderate gingivitis would score around 4 on an SDAI sheet.

- **FCV negative cats** – all cats cured at three month revisit. All scoring less than 5 and most (70%) scoring less than 2
- **FCV positive cats** – 75% cats scoring less than 5 and half of these scoring less than 2
 - 25% cats improved. SDAI scores less than half from original presentation

Initial intralesional use: The consensus statement (October 2010) by a group of European specialists indicated *that intralesional treatment is not probably necessary to initiate therapy.*

In some very severe cases an initial treatment total dose of 5 MU injected locally into multiple sites at the junction between healthy gum and a diseased tissue can provide an initial boost to a treatment course. Using a 10MU vial, enough saline or sterile water is drawn into the syringe to provide a reasonable volume for use - normally 1-2ml depending on area to be injected. The contents are administered in fractions of 0.1 - 0.2ml over the areas inflamed. For severe cases, we make five injections in each side of 0.2ml each. In less severe cases, concentrate higher volumes into a smaller area.

Monitoring the cat's weight, along with a number of other indices as per our standard evaluation forms (SDAI), is a useful objective way of assessing response to treatment. An initial assessment form and one for ongoing evaluation is available on request.

Note that feline interferon omega should always be stored in the fridge and will remain viable once reconstituted for up to 21 days at 4°C. when used for low dose oral administration – not for injection.

Subcutaneous injections: This method of administration has been described previously *but appears to be substantially less effective than submucosal administration* for treatment of FCGS and is not used by the author.

Corticosteroids

These drugs are used, by some practitioners, principally to control inflammation in refractive cases which have had elective cheek teeth extraction and are not sufficiently controlled by feline recombinant interferon. If their use is justified on welfare grounds, the overriding principle must always be to use the minimum effective dose rate. This means using a short acting molecule (prednisolone) at the lowest effective dose rate such as 5mg twice weekly or 2mg every other day tapering downwards. They can be used in conjunction with feline recombinant interferon omega.

NSAIDs

If used, the first choice option appears to be meloxicam. Any NSAID needs to be prescribed with respect to the appropriate guidelines for use of long term NSAIDs in cats (Sparkes 2010). Some new molecules such as robenacoxib may show promise.

Cyclosporine

There is insufficient data to recommend the use of cyclosporine in the management of FCGS syndrome.

Some data has been published on this molecule, as part of a dermatology study, suggesting 4 out of 8 cats treated responded and could be maintained on every second day dosing. However, other studies have been equivocal about the benefits and a placebo-controlled trial in a small number of cats did not show a significant difference from placebo. Some suggestions for use have been provided but monitoring of blood levels to avoid toxicity is

deemed essential due to erratic absorption differences. In general, the currently available data is not sufficient to support a recommendation to use this drug.

Azathioprine/ Chlorambucil/ low dose Doxycycline/ Gold salts:

There is insufficient data to recommend the use of these agents in the management of FCGS syndrome. The potential side effects can be significant and excessive use of generalised immunosuppressive options can be a problem long term.

CO2 laser surgery

There is insufficient data to recommend its routine use in the management of FCGS syndrome. The consensus group felt it may have a possible role with adjunctive pain control.

Additive Free Foods and Additional Nutritional Support

It is necessary to ensure good quality nutritional support to encourage an effective immunological response and post-extraction healing process. Various diets and supplements have been suggested including vitamin preparations and omega-3 EFAs, but there is no study which has data to prove a recommendation for any specific product. The beneficial effects of a recovery food post surgery has been demonstrated in cats with FCGS syndrome. Additive free and hypoallergenic foods have also been suggested but the results are anecdotal at best with no known study proving efficacy.

Vaccine

A multi-site placebo controlled trial is taking place to evaluate the effects of their T-Cell Receptor (TCR) peptides for feline stomatitis. The TCR Peptides are immune modulating biologics, which have been shown to modulate T-helper cell function and Th1/Th2 cytokine profiles. T-helper cells appear to play a central role in feline stomatitis, causing inflammation and inappropriate immune reactions. Preliminary studies in cats have shown significant results in advanced, refractory feline stomatitis.

Summary

This is a poorly defined syndrome of unknown aetiology characterised by focal or diffuse chronic inflammatory response involving the gingiva, oral mucosa, and often the pharynx and tongue.

Commonly described clinical findings include elevated serum globulins and a submucosal infiltrate of plasma cells, lymphocytes, neutrophils, and macrophages. Potentially various viral agents and bacterial species are involved. There is no doubt that atypical hyperimmune responses are the basis of the problem. Multiple mechanisms appear to be acting concurrently.

Successful management of this complex requires a logical diagnostic pathway approach. The need for first line information gathered before treatment alters the host response cannot be over-stated. Once this information is available, a treatment plan and prognosis can be considered. The role of bacterial plaque is crucial whatever the state of the host immune response. Diligent professional scaling, polishing and subgingival debridement - zero

tolerance to any dental disease - underpins any treatment in tandem with aggressive homecare by the owner. Cases failing to respond to simple plaque control should be considered for elective cheek teeth extraction and adjunctive treatments at an early date. Those cases still non-responsive but FCV positive may be helped by interferon therapy.

It is important that the owner is involved at an early stage with discussions as to aetiology, treatment plans and help with homecare. A highly motivated owner is a strong ally in the provision of successful treatment.

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