Feline UPDATE
Winter 2012/2013
The Feline Centre
Pfizer Animal Health
The Feline Centre Langford and Pfizer Animal Health working together for the benefit of cats

Feline Update Goes Online for Silver Anniversary of Feline Fellowship!

by Prof. Tim Gruffydd-Jones
Professor of Feline Medicine, University of Bristol.

Figure 1: Feline Update in its three styles over the past 25 years.

This edition of Feline Update marks an amazing occasion. It is 25 years since the Feline Centre at the University of Bristol School of Veterinary Sciences developed a collaboration with Pfizer Animal Health and the first edition of the Update appeared.
We are using this special anniversary to make some important changes to Feline Update- particularly the way it is delivered to veterinary surgeons and how you can access it.

This is the first time the Update has appeared in electronic form, and this will be the last occasion that you will receive Feline Update in paper format. In future the Update will embrace the I.T. revolution and will be provided just in electronic format.

Please take a moment to use the link **www.felineupdate.co.uk** to access the Update on the new Feline Centre website and to register to receive notification of new Updates and other information relevant to your interests in feline medicine. In future you will receive email notification when new editions of the Update are produced, along with other useful information, such as news of CPD meetings.

There will be a number of advantages to the new electronic format. There will be more flexibility over the timing of the new editions and if an important, topical issue arises, we shall be able to provide you with information with the minimum of delay. Some vets have had to share the practice copy of the Update- now every veterinary surgeon who registers will able to see their own copy.

The Feline Update will be archived on the website and you will be able to access these easily. We shall be gradually transferring earlier editions of the Update to electronic form and these will all appear on the website. We aim to produce an indexing system which will enable you to track down articles on particular topics. The appearance of the electronic form of Feline Update coincides with the new Feline Centre website **www.thefelinecentre.co.uk** which is 'hosted' on the Langford Veterinary Services (LVS) website: **www.langfordvets.co.uk** We expect this to be expanded over the coming months to include such items as short articles on topical issues, news of CPD events, short video tutorials, and even webinars.

The intention of the Update has always been to keep veterinary surgeons up to date on topics which are practically relevant to their day to day work in feline practice. We have been very encouraged by the positive feedback we have received. There have been changes in the format and content over the years in a response to the feedback from vets in practice. New formats have been introduced such as Q&A articles on controversial topics, case reports and top tips which have proven popular.
In the 25 years since the Update first appeared, there have been 50 editions produced. The Update also has an international profile and has been translated into numerous languages!

This is perhaps an occasion to allow a little nostalgia in looking back at Feline Update. The link between the Feline Centre first began with Solvay-Duphar (one of the previous companies which now form Pfizer) with a collaborative study of *Chlamydophila felis.* A vaccine was marketed by the company in the USA, but little was known of the importance of this organism as a cause of disease in cats in the UK. Solvay-Duphar funded an investigation undertaken by Jo Wills as her PhD study to develop diagnostic tests to screen for infection to determine its importance as a cause of disease and reassess the efficacy of the vaccine in providing protection. It was from this relationship that the Feline Fellowship was established and the Update grew. There have been major changes over the years. Solvay-Duphar was taken over by Fort Dodge which was subsequently bought by Pfizer. In recent years The Feline Centre has become part of Langford Veterinary Services (LVS), a subsidiary of The University of Bristol. Two 'constants' throughout the history are myself, Tim Gruffydd-Jones, from The Feline Centre, a lecturer at the time and now Professor of Feline Medicine, and John Hanley who was Head of Marketing with Solvay-Duphar but is now Vice President of Pfizer Animal Health. One other individual who has been an important member of the Feline Team throughout this period is Pam Dennis. She has been one of the virologists who support our special feline infectious disease diagnostic lab which is part of the LVS diagnostic service. In the early days Pam played an important part in setting up *Chlamydophila* isolation and serology for diagnostic screening, and appeared on the cover of the very first Feline Update. More recently she has been one of the key members in the Molecular Diagnostic unit which uses PCR for screening for infectious agents and has more recently expanded to offer feline genetic tests.

An important part of the Feline Fellowship has been to provide young veterinary surgeons with the opportunity to develop their interest in feline medicine. In particular it provides an opportunity to become involved in a feline project and gain an insight into research.

We have been fortunate to have had an outstanding group of Feline Fellows, most of who have continued their interest in feline medicine and made major contributions to the subject. Do you recognise some of these names and faces?!

1987

Dr Cherida Hopper. Retired Research Fellow in Social Medicine Department of the University of Bristol.

1988-90

Dr Andy Sparkes. RCVS Specialist in Feline Medicine, Veterinary Director of FAB/ISFM.

1991

Hilary O'Dair. Feline Dermatology referral service in south west England.

1992

Lorraine Fleming *(nee Waters).* Ophthalmologist at Grove Referrals, Norfolk and Director of Eye Know How Ltd.

1993

Dr Kit Sturgess. RCVS Specialist in Small Animal Medicine.

1994

Prof. Danielle Gunn-Moore. RCVS Specialist in Feline Medicine, Professor of Feline Medicine and Head of Companion Animal Sciences, University of Edinburgh.

1995

Dr Ann Robinson. European Associate Technical Director, Companion Animals, Pfizer Animal Health.

1996

Dr Sarah Caney. RCVS Specialist in Feline Medicine, Director of Cat Professional.

1997-98

Caroline Blundell. Principal of The Oxford Cat Clinic.

1999

Janine Huebner.
Diagnostic Virologist, Germany.

2000

Wanda Owen.
Goddard Veterinary Group, London.

2001

Paula Fisher.
Queen's West Animal Hospital, Canada.

2002-05

Dr Rachel Dean.
Clinical Associate Professor in Feline Medicine, Director of the Centre for Evidence-based Medicine, University of Nottingham.

2006-07

Anita Schwartz.
Previous Resident in Feline Medicine, University of Edinburgh School of Veterinary Science.

2008-09

Gabriele Habacher.
Raddenstiles Veterinary Surgeons, Devon.

2010

Samantha Taylor.
RCVS Specialist in Feline Medicine, European Veterinary Specialist in Internal Medicine.

2011

Anna Brunetti.
Veterinary Surgeon in small animal practice in Manchester.

2012

Philippa Welsh.
Current Pfizer Feline Fellow at University of Bristol Feline Centre.

RENAL FINE NEEDLE ASPIRATION AND BIOPSY

by Dr Natalie Finch
BVSc PhD MRCVS

FAB Sponsored Senior Clinical Training Scholar in Small Animal Medicine

CHRONIC KIDNEY DISEASE (CKD)

Chronic Kidney Disease causes significant morbidity and mortality in the feline patient, particularly the senior cat in which the prevalence of the disease is known to be much higher. CKD is not a single entity, but rather encompasses a range of disorders which cause a decline in renal function. Acute kidney injury secondary to nephrotoxins, pyelonephritis or ischaemic injury may also progress to CKD. A diagnosis of CKD in cats is generally based on abnormalities in blood and urine testing and sometimes by diagnostic imaging studies. Renal biopsy or aspirates may be useful in determining a definitive diagnosis, elucidating mechanisms of injury and aetiopathogenesis, and providing information regarding severity of disease which may aid in establishing prognosis.

A previous study of cats with confirmed CKD in which histopathological examination of renal tissue was performed documented tubulointerstitial nephritis of unknown cause in over 50% of the cats.[1] Renal biopsy or aspiration is unlikely to be of benefit in such cases as the long-term management will not be altered by the biopsy results. Therefore, it is generally recommended that renal biopsy or aspirates in cats in International Renal Interest Society (IRIS) stage III and IV CKD should be avoided. However, there remain a small number of patients which are non-azotaemic or only mildly azotaemic in which renal biopsy or aspirates may be helpful. Renal biopsy or aspirates may be indicated in investigations of patients such as those with renomegaly, irregular kidneys, infiltrative disease or persistent proteinuria with no other identifiable cause. The collection of renal tissue from a patient should only be performed when it is considered that identification of pathological changes may have potential utility in modifying therapeutic options for the patient. However, the risk of the procedure must always be weighed up against any potential benefit, especially in cats with more advanced CKD.

RENAL BIOPSY

Renal biopsy may be more helpful in diffuse disease processes. There are several techniques available for renal biopsy. The percutaneous transabdominal approach is probably the most commonly employed and is usually performed under ultrasound guidance. Various needles can be used, such as a Tru-cut biopsy needle or alternatively spring-loaded disposable biopsy needles or a long large gauge needle. In addition, renal biopsies can be obtained laparoscopically or surgically. Laparoscopic and surgical approaches allow direct visualisation of the kidneys and peritoneum but are more invasive than the percutaneous approach.

The aim of a renal biopsy is to obtain tissue from the renal cortex. This is because there can be damage to large vessels resulting in significant haemorrhage or areas of infarction if the corticomedullary junction is crossed.
If using the ultrasound guided percutaneous technique, visualisation of the kidney in sagittal or dorsal plane is recommended and the cortex should remain within the plane of view in which the biopsy needle will be directed.
The skin over the biopsy collection should be cleaned and ideally sterile coupling gel used for the ultrasound probe. Some clinicians prefer to make a small skin incision to facilitate passage of the biopsy needle through the cutaneous tissue. The biopsy needle is inserted through the renal capsule and directed within the renal cortex.
Care should be taken particularly with spring-loaded biopsy needles to ensure that the needle remains in the cortex when collecting the sample. For more detailed information regarding collection are renal biopsies, readers are directed to a review article.[2]

RENAL FINE NEEDLE ASPIRATION

Fine needle aspiration may be best utilised in cases in which a focal mass is visualised in the kidney on ultrasound examination. It may also be helpful if there is a clinical suspicion of diffuse lymphoma involving the kidneys *(see fig.1)*.
It is generally unhelpful in cases of glomerular disease and interstitial nephritis.
Percutaneous fine needle aspiration of the kidney should be performed under ultrasound guidance.
Aspirates can be obtained blind but this is not recommended. A 21 to 23 gauge needle is generally recommended with the length dependent on the expected depth of the kidneys within the abdomen. The needle is inserted into the renal capsule similar as to when obtaining a renal biopsy and directed within the cortex. The needle is removed to and fro within the kidney. Negative pressure and suction using a syringe is not required as cells exfoliate relatively well. The needle contents are expelled onto a microscope slide and the smear prepared using standard smear preparation techniques. A major disadvantage of renal aspirates is that small sample size may limit the cytological interpretation of renal aspirates.

POTENTIAL COMPLICATIONS OF RENAL BIOPSY AND FINE NEEDLE ASPIRATION

The procedures should only be performed in patients which are clinically stable. Both renal biopsy and collection of aspirates are required to be performed under sedation or general anaesthesia to ensure adequate immobilisation of the patient.
Sedation or general anaesthesia may also be of concern in a patient which may already have compromised renal function. Only clinicians competent and confident in performing the procedures should undertake the collection of samples. Complications associated with renal biopsy or aspiration includes haemorrhage (which may be severe enough to require blood transfusion), hydronephrosis secondary to renal pelvis obstruction, renal infarction, renal infection and death.
Complications have been reported in 18.5% of cats undergoing renal biopsy[3] however, this study did include cats with more severe kidney disease; in cats with less severe disease the complication rate may be lower. The mortality rate associated with renal biopsy in cats has been reported to be 3.1%.[3] The risk of haemorrhage is increased in patients with prolonged clotting times or thrombocytopaenias. Evaluation of coagulation status and platelet count is recommended to be included in the diagnostic work-up prior to performing the procedure to minimise these risks.

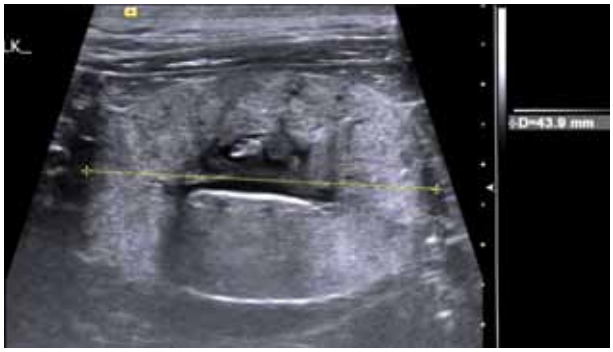


Figure 1: Ultrasound image of a kidney from a cat with renal lymphoma *(courtesy of Virginie Barberet, University of Bristol).*

Histopathological changes within the kidney considered to be related to performing a renal biopsy have been documented following the procedure although obtaining renal biopsies is not reported to have any effect on renal function in healthy cats.[4] Similar data is not available for cats with pre-existing kidney disease.

FURTHER CONSIDERATIONS RELATING TO RENAL BIOPSY AND FINE NEEDLE ASPIRATION

A study evaluating agreement between histopathological diagnosis made at post-mortem and that made by renal biopsy reported agreement in 60% of dogs and 35.7% of cats.[3] A recent study evaluating concordance between final diagnosis and that made on renal fine needle aspirates reported 54% of results in cats to be in agreement, however, this increased to 79% in cases of renal neoplasia.[5] In this study 30% of samples were considered to be inadequate for cytological evaluation.

When submitting renal tissue for histopathological examination it is advisable to seek the expertise of a renal pathologist. Submission of samples to a specialist nephropathologist will ensure that any significant changes are detected and correctly characterised to yield the most information. A specialist pathologist will also be able to examine renal tissue with traditional light, electron and immunofluorescent microscopy, provided that the sample has been processed in the correct way. In addition, special staining techniques can be applied to the samples. Diagnostic veterinary renal pathology centres are generally able to provide packages containing the appropriate instructions, materials, fixatives and submission pots for sample collection. Further information regarding recommended histopathological examination and special staining techniques is available in a recent review article.[6]

WSAVA RENAL STANDARDISATION STUDY GROUP

Renal biopsy may be helpful in increasing our understanding of the pathology of renal diseases. A scheme is currently under way to attempt to establish a consensus on characterisation of glomerular disease in proteinuric canine patients and correlate this with clinicopathological findings and long term outcome. Future work will include standardisation of feline renal disease. Information regarding the Renal Standardisation Study Group can be found by visiting the WSAVA website: **www.wsava.org**. In addition, details of centres providing diagnostic renal pathology services can also be found on the website.

SUMMARY

Renal biopsy or fine needle aspirates may be helpful in obtaining a diagnosis particularly in certain disease processes such as neoplasia or in severe proteinuria in cats. However, they are not benign procedures and there are risks and complications associated. The diagnostic utility of renal biopsy or aspiration currently remains controversial. Future standardisation schemes may be helpful in providing further information regarding the collection of renal biopsies in cats. The most important question may be whether the information obtained through performing renal biopsy or aspirates alters patient management and care. Prospective studies to answer this question remain to be performed in cats.

References and further reading

1. *DiBartola SP, Rutgers HC, Zack PM, et al.* Clinicopathologic findings associated with chronic renal disease in cats: 74 cases (1973-1984). J Am Vet Med Assoc 1987;190: **1196-1202.**
2. *Vaden SL.* Renal biopsy of dogs and cats. Clin Tech Small Anim Pract 2005;20:**11-22.**
3. *Vaden SL, Levine JF, Lees GE, et al.* Renal biopsy: a retrospective study of methods and complications in 283 dogs and 65 cats. J Vet Intern Med 2005;19: **794-801.**
4. *Drost WT, Henry GA, Meinkoth JH, et al.* The effects of a unilateral ultrasound-guided renal biopsy on renal function in healthy sedated cats. Vet Radiol Ultrasound 2000;41: **57-62.**
5. *Klosterman. ES HJ, Kurosowa. TA, Moore. GE, Heng. HG, Pressler. BM.* Diagnostic utility and concordance with final diagnosis of renal aspiration in dogs and cats. Journal of Veterinary Internal Medicine 2011;25: **718-719.**
6. *Lees. GE, Cianciola. RE, Clubb. FJ.* Renal biopsy and Pathologic Evaluation of Glomerular Disease. Topics in Companion Animal Medicine 2011; 26: **143-153.**

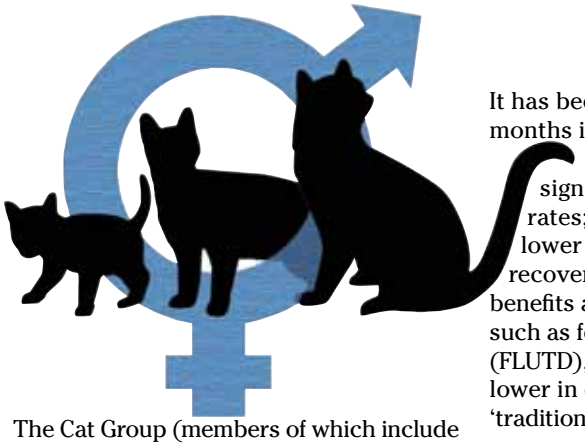
Neutering pet cats at four months of age *(or less)*

by Philippa Welsh *BVSc (hons) GPCertFelP MRCVS Pfizer Feline Scholar.*

Introduction

Neutering has long been recommended by vets to be carried out at six months of age, but this appears to have been an arbitrary age with no evidence base and seems to be purely due to tradition.

Neutering of cats is essential for population control and for reducing sexually dimorphic behaviours such as urine spraying and aggression. It has been shown that neutered cats live longer, are less likely to suffer from mammary carcinoma, are less likely to get some infectious diseases (such as FIV and FeLV), and the inherent risks of pregnancy are avoided. Research carried out at the University of Bristol showed that although over 90% of cats are neutered at some stage in their lives, almost 20% of female cats had had a litter before they were neutered and the vast majority (around 75%) of these litters were unplanned. Although puberty is more typically between five and eight months of age, pregnancy can be seen in queens as young as four months of age. The timing of neutering is therefore essential to prevent unwanted litters.



The Cat Group (members of which include British Small Animal Veterinary Association [BSAVA], International Society of Feline Medicine [ISFM], Governing Council of the Cat Fancy [GCCF], Cats Protection [CP], Royal Society for the Prevention of Cruelty to Animals [RSPCA], Blue Cross, People's Dispensary for Sick Animals [PDSA]) produced recommendations in 2006 advising neutering of cats at four months of age. However, a very recent study (unpublished data) shows that only just over 20% of vets recommend neutering at four months of age, and less than 15% of client owned cats are neutered at this age.

It has been shown that neutering at four months instead of the traditional six months is associated with significantly lower complication rates; with shorter surgical duration, lower surgical morbidity and quicker recovery rates. There are long-term benefits as well: the incidence of diseases such as feline lower urinary tract disease (FLUTD), gingivitis and feline asthma are lower in earlier neutered compared to 'traditional age' neutered cats.

Veterinary surgeons play a crucial role in advising clients to make the right choices for their cats. Many cat owners are unaware that a cat can become pregnant or start urine spraying before six months of age, or that having their kitten neutered at a younger age is safer.

Terminology: There is no consensus as to terminology to be used when relating to the age of neutering. It has been proposed that the term 'early neutering' should now refer to neutering of kittens between 6 and 14 weeks, and 'conventional age neutering' to kittens of 14-16 weeks of age.

PRE -ANAESTHETIC CONSIDERATIONS

1. Preventative health care

Neutering should be carried out after the kittens' first vaccination, and ideally at least two weeks after completion of the full course of vaccination (to allow full immunity to develop prior to staying in the veterinary hospital thus reducing disease transmission).

Booking the appointment for neutering at the time of first or second vaccination keeps neutering at the forefront of the owners mind, and encourages ongoing early veterinary practice to client bonding.

2. Starvation period

Food should be withheld for no more than 3-5 hours before surgery, as hypoglycaemia can be a concern with kittens. Water should be made available until the time of general anaesthesia (or premedication if applicable). Kittens should be offered food as soon as they are standing after surgery. Kittens can easily become hypoglycaemic due to reduced glycogen stores in the liver. In the rare case of a kitten not recovering well from anaesthesia, blood glucose should be checked and supplementation considered (e.g. oral glucose if the kitten can swallow or IV infusion of 5% dextrose solution).

ANAESTHETIC CONSIDERATIONS

- Keep handling and playing with kittens to a minimum; excited animals will resist being restrained and be more difficult to anaesthetise.
- A full clinical examination should be carried out, as with any animal prior to general anaesthesia, and the procedure delayed if there are any concerns. Male cats with retained testicles should have surgery delayed until six months of age. Kittens should be a normal body weight for their age (min. 1kg for 12 weeks old, 1.2kg for 16 weeks old).
- Using single intramuscular or subcutaneous injections for anaesthesia is recommended as this requires less restraint than via the intravenous route.
- Accurately weigh the kitten and consider using body surface area for more precise dosing especially if using the 'quad' protocol *(see Tables 1 and 2)*. It may be necessary to use diluted solutions in order to achieve accuracy (off licence). As very small doses of drugs are needed, the cost of neutering to the practice is reduced with earlier neuters.
- Prevent heat loss – e.g. using bubble wrap or Bair hugger around the kitten, or place on a Vetbed on a safe, well monitored heat pad. Keep the area of clip small, and use warmed skin preparation solution. Minimise the amount of alcohol used on skin. Monitor rectal temperature throughout the duration of anaesthesia and actively maintain it as close to normal as possible. It should remain above 36°C at all times. The ambient temperature of the surgery environment (including the operating theatres and recovery area) should be kept warm. Good, well-organised, preparation is

ANAESTHETIC CONSIDERATIONS *continued*

essential to minimise operating time, for example by ensuring all equipment is ready for use prior to induction of anaesthesia.

- Placement of an endotracheal tube (2-3.5mm non-cuffed ET tube) is always recommended for female kittens, to maintain a patent airway. Kittens have a larger tongue and a narrower airway than adult cats. Oxygen should be supplied to both sexes of kitten, even if anaesthetic depth and relaxation are adequate; use a face mask attached to an anaesthetic circuit to deliver oxygen to male kittens (flow rate 3-4 litres /min). Anaesthetic circuits with a low resistance to air flow and a minimal dead space should be used with high fresh gas flow rates; an Ayre's T Piece with Jackson Rees' modification is ideal.

  Fresh gas flow rate = Circuit factor (2.5 for T Piece) x Minute Volume (where MV = 250ml/kg for small patients)

- Various anaesthetic protocols have been proposed for neutering of kittens *(see Table 1)*. The 'quad protocol' was devised by Alison Joyce of the RSPCA Greater Manchester Hospital, is promoted by the RSPCA and Cats Protection, and has been shown to be safe and effective. The kitten quad is comprised of medetomidine *(1mg/ml solution)*, ketamine *(100mg/ml solution),* midazolam *(5mg/ml solution*) and buprenorphine *(0.3mg/ml solution)* in equal volume, based on body surface area dosing *(see Table 2)*. The 'Kitten Quad Calculator' is available as free iPhone™ App. Midazolam potentiates the effects of the other anaesthetic agents (reducing the doses required and thus reducing side effects such as hypotension), acts as a mild appetite stimulate post op, and potentially has some amnesic effects (this is reported in human children). Due to the inclusion of midazolam, this 'kitten quad' protocol is off licence. Whilst the 'quad' can be reversed, it is not recommended to use atipamazole until half an hour after ketamine administration in order to avoid excitement.
- Reduce stress – housing kittens with littermates in the practice before surgery and after recovery makes kittens more comfortable in their environment. Keep noise and disturbances to a minimum pre and post surgery. Consider doing any kitten neutering first, allowing kittens to be discharged from hospital as soon as possible. This is also important as their immune system is still relatively naïve.
- Kittens should be monitored closely post operatively, at least until able to maintain sternal recumbancy without difficulty. Extubation should occur before the kitten is able to swallow to prevent laryngeal irritation.
- Meloxicam is licenced for use in cats greater than 2kg, and older than 6 weeks, so its use in earlier neutering may be off licence.
- Owners should be made aware of the use of drugs off licence and permission should be sought.

Anaesthetic agent(s)	Dose and route	Comment
Medetomidine + **Ketamine** + **Butorphanol**	80 µg/kg IM 5mg/kg IM 0.4mg/kg IM	• 'Triple combination' • Reversal agent can be used • Good multimodal analgesia • Gives good depth of anaesthesia in kittens over 1.5kg
Medetomidine + **Ketamine**	80 µg/kg IM 5mg/kg IM	• Gives good depth of anaesthesia in kittens over 1.5kg • Reasonable analgesia
Medetomidine + **Ketamine** + **Buprenorphine** + **Midazolam (NL)**	600µg/m^2 IM 60mg/m^2 IM 180µg/m^2 IM 3mg/ m^2 IM	• 'Kitten Quad' • Good depth of anaesthesia • Quick induction and recovery via single IM injection • Good multimodal analgesia lasting 6-12h • Reversal agent can be used
Propofol	Unpremedicated: 8mg/kg IV Premedicated: 6mg/kg IV	• IV difficult in kittens • Pre-med required for analgesia

Table 1: Protocols for general anaesthesia of kittens undergoing early-age neutering *(adapted from Joyce and Yates 2011)* NL - not licensed for use in cats.

Body weight (kg)	Body Surface Area (m^2) = (10.4 x body weight $^{0.67}$)/100	Volume of each drug required for 'quad' (ml)
1.0	0.10	0.06
1.5	0.14	0.08
2.0	0.17	0.10
2.5	0.19	0.12

Table 2: Conversion of body weight to body surface area and dosing regimen for the 'quad' protocol using medetomidine 1mg/ml, ketamine 100mg/ml, midazolam 5mg/ml and buprenorphine 0.3mg/ml solutions *(adapted from Joyce and Yates 2011)*. Note this protocol is not licensed for use in cats.

SURGICAL CONSIDERATIONS

Castration

- Ensure both testes are present in the scrotum before beginning! Cryptorchid castration should be delayed until six months of age.
- Plucking of fur from kittens of less than 16 -20 weeks can be difficult, so clipping of scrotal fur is recommended.
- Although smaller, there are no differences in the method of castration in young cats. Three techniques can be employed (see 'Further reading' for more detail of these techniques):

  i. Ligation of spermatic bundle with absorbable suture material (either open or closed method).

  ii. Forceps method (or overhand technique)- using curved forceps to create a figure of eight knot in the spermatic cord.

  iii. Ligation of vessels using the ductus deferens (hand-tie).

Ovariohysterectomy

- Consider using a midline incision, which gives good exposure and allows for easy access, should complications ensue.
- Gently expressing the bladder at GA enables better visualisation with a midline approach, reduces the likelihood of damage to the urinary tract, and prevents wetting and chilling of a patient during anaesthesia or during recovery due to urination.

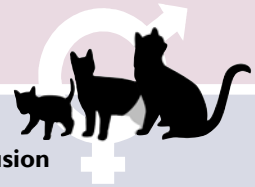
continues overleaf

Neutering Pet Cats at Four Months of Age

ANAESTHETIC CONSIDERATIONS

continued from page 7

- For kittens over 12 weeks, the incision should be made half way between umbilicus and pubis. A slightly more caudal incision is needed in kittens less than 12 weeks of age.
- Ovariohysterectomy should be performed as usual (for more detail see further reading). Significantly more clear abdominal fluid is often seen in younger neuters.
- Intradermal skin sutures avoid the need for Elizabethan collars.



Conclusion

Neutering of cats at six months of age is based on tradition and has no positive scientific evidence base. Neutering pet cats at four months of age is safer in the short term, and has long-term benefits as well. Increasing the number of cats neutered by four months of age by educating cat owning clients will have an important impact on cat population control, and lead to an improvement in the health and welfare of cats in our care.

Further reading

Joyce, A and Yates, D: JFMS (2011)13: **3-10** Help Stop Teenage Pregnancy! Early-age neutering in cats.

Smith, N: The Veterinary Nurse (2011) Vol. 2 Issue 3 **pp121-126** Early Neutering of cats: the risk factors and the benefits.

Little, S: The Cat, Published by Elsevier 2012 **pp1246-1249** Chapter 46: Paediatrics.

Other useful resources:

Cats Protection website: www.cats.org.uk/what-we-do/neutering/enr

Small Animal Surgery, Fossum 3rd edition. Chapter 26: **pp715-717.** Cat group policy statement 2006: *Timing of neutering.* At www.thecatgroup.org.uk or http://www.fabcats.org/cat_group/policy_statements/neut.html

Feline UPDATE *online*
at www.felineupdate.co.uk

for a link to the Cats Protection early neutering video, follow the links from the Feline Update website.

YOUR QUESTIONS ANSWERED:

FELINE EOSINOPHILIC GRANULOMA COMPLEX

Natalie Barnard *BVetMed CertVD DipECVD MRCVS*
European Specialist in Veterinary Dermatology.

WHAT IS FELINE EOSINOPHILIC GRANULOMA COMPLEX (EGC)?

This is a term used to describe a skin problem in cats that involves several different syndromes namely the indolent ulcer (rodent ulcer, eosinophilic ulcer), eosinophilic plaque and eosinophilic granuloma (linear granuloma). This term describes a cutaneous reaction pattern of the skin, which can arise from multiple different causes and should always highlight the need for a thorough investigation and logical diagnostic approach. An allergy investigation is often indicated.

WHAT ARE THE FEATURES OF AN INDOLENT ULCER?

- Usually associated with an underlying hypersensitivity.
- Common in cats.
- The lesion begins as a small crater-like ulcer with raised margin
- Lesion distribution: commonly affects the upper lip, also reported in the oral cavity.
- Can be unilateral or bilateral.
- The lesion may enlarge progressively and become disfiguring.
- Not painful or pruritic.

Fig.1: Indolent ulcer.

- Regional lymphadenopathy: may be present.

WHAT ARE THE FEATURES OF AN EOSINOPHILIC GRANULOMA?

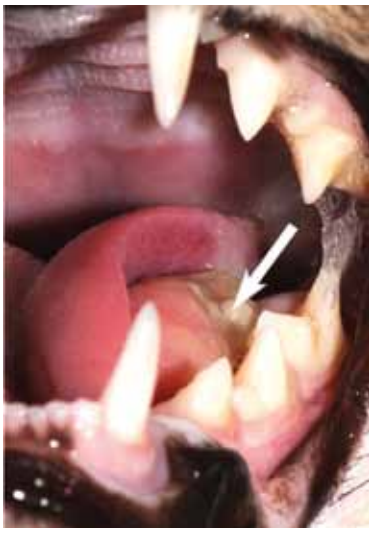


Fig.2: Eosinophilic granuloma.

- Usually associated with an underlying hypersensitivity.
- Common in cats.
- Lesions usually occur singly.
- Can be variable in appearance: they may be raised, firm, linear plaques or papular to nodular, oedematous or firm swellings. The lesions may be erythematous, ulcerated, alopecic, eroded.
- Usually not painful or pruritic.
- Lesion distribution: most common on the caudal aspect of the thigh (linear granuloma) and chin or lip (swelling). Oral cavity.
- Regional lymphadenopathy may be present.
- Lesions in the oral cavity are characterised by papules, nodules, or well circumscribed plaques – usually on the tongue or palate.
- Cats with oral lesions may be dysphagic.

WHAT ARE THE FEATURES OF AN EOSINOPHILIC PLAQUE?

- Usually associated with an underlying hypersensitivity.
- Common in cats – highest incidence in young adult – middle aged cats.
- Single to multiple erythematous, well circumscribed, raised, eroded or ulcerated plaques.
- INTENSELY PRURITIC.
- Lesion distribution: anywhere on the body, commonly ventral abdomen and medial thighs.
- Regional lymphadenopathy: may be present.

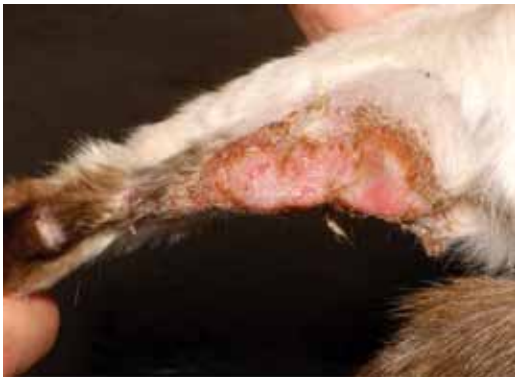


Fig. 3: Eosinophilic plaque.

WHAT ARE THE MAIN DIFFERENTIAL DIAGNOSES FOR EGC?

- Infections – bacterial, viral, fungal.
- Trauma.
- Neoplasia – squamous cell carcinoma, mast cell tumour, cutaneous lymphoma.

HOW DO WE DIAGNOSE EGC?

Diagnosis is usually based on history, clinical findings and ruling out other differentials. In some cases histopathology may be required if there is an unusual presentation, or if it does not respond to treatment. An impression smear from a moist lesion may reveal large numbers of eosinophils, but neutrophils and bacteria may predominate if the lesion is secondarily infected. A skin biopsy is also useful to characterise the lesion and will help rule out some of the differentials. The three types of lesion have characteristic histological appearances.
Cats with an eosinophilic granuloma or eosinophilic plaque may have a peripheral eosinophilia.

Rarely dermatophytosis can present similarly in appearance to a lesion of the eosinophilic granuloma complex, so a fungal culture should be performed to exclude this differential.

Once a lesion of the eosinophilic granuloma complex has been identified then investigation to find the underlying cause should be undertaken. This will usually include a full allergy investigation to rule in/rule out flea allergy, cutaneous adverse food reaction and atopic dermatitis.

MANAGEMENT OF UNDERLYING CAUSES AND TREATMENT OF THE FELINE EOSINOPHILIC GRANULOMA COMPLEX LESIONS

THE MOST IMPORTANT THING IS TO ATTEMPT TO IDENTIFY AN UNDERLYING CAUSE AND MANAGE IT. This is not possible in all cases.

1. Management of underlying causes.

Managing Flea Allergy:

- Treat the affected animal and in contacts.
- Treat the environment.
- If the cat is extremely pruritic then systemic glucocorticoids may be appropriate.

Managing cutaneous adverse food reaction:

- This can be controlled by finding an appropriate diet to maintain the cat on, which may have been determined during the dietary trial period.

Managing atopic dermatitis:

- A combination of steroids, anti-histamines, fatty acid supplements and allergen specific immunotherapy may need to be used. Treatment will be tailored to the individual patient, with the aim being to find the least amount of medication that controls the clinical signs.

2. Treating the lesions of eosinophilic granuloma complex.

Treat secondary infection:

- Often several weeks of antibiotic treatment may be required if the lesion is secondarily infected. This can be determined by performing some cytology and examining it in house. External culture and sensitivity should be considered if rods are seen. Treat with an appropriate antibiotic dependant on what is seen on cytology, for a minimum of three weeks, or until a week after a clear cytological assessment for bacteria. Examples of commonly used antibiotics include cefalexin (at 15-20mg/kg BID) or clindamycin (at 11mg/kg SID). Some lesions are reported to resolve with antibiotic treatment alone.

Inducing remission of the lesion:

- This generally requires treatment with systemic glucocorticoids. An improvement is usually seen in 2-4 weeks of treatment and then treatment should be gradually tapered to the lowest possible alternate day dose and if possible discontinued if you can manage the underlying cause successfully.
- Suggested doses of glucocorticoids:
  - Prednisolone 1-2 mg/kg once daily until remission is achieved (2–8 weeks) then taper to lowest possible alternate day dose.
  - Methylprednisolone 0.8–1.6mg/kg once daily until remission is achieved then taper to lowest possible alternate day dose.
  - Methylprednisolone acetate – in the author's opinion this should only be used in cases that cannot be medicated orally at a dose of 4mg/kg SC or IM every 2-3 weeks. Once the lesions are in remission this should only be used as needed.
- Some lesions are refractory to glucocorticoids treatment and in these cases alternate therapies listed below may be useful.
  - Doxycycline 5-10 mg/kg every 12 hours.
  - Ciclosporin 7mg/kg once daily
- Anti-histamines (Cetirizine 5mg once daily) may be useful as a steroid sparing agent. In humans this is reported to inhibit exocytosis of eosinophils. Adverse effects are rarely reported, but mainly include excitation after administration and sedation.

Prognosis.

This is usually good if the underlying cause can be successfully managed, but cats that have recurring lesions where an underlying cause cannot be determined may require long term treatment with glucocorticoids to keep their lesions in remission. In these cases always try to find the least amount of medication which controls their clinical signs to minimise the risk of unacceptable adverse effects.

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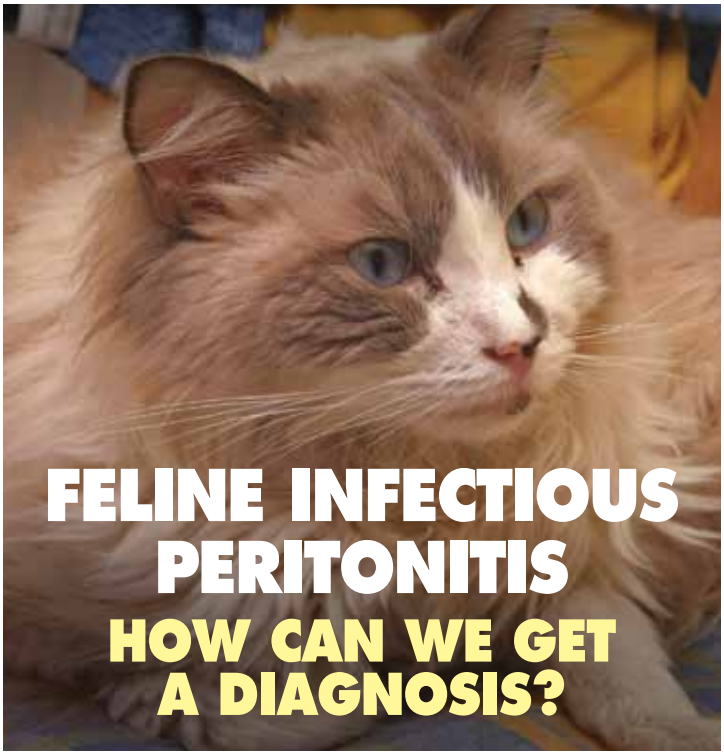

FELINE INFECTIOUS PERITONITIS

HOW CAN WE GET A DIAGNOSIS?

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Feline infectious peritonitis (FIP) is usually regarded as an incurable disease and an important cause of death in young cats caused by feline coronavirus (FCoV). FCoV infection is endemic amongst cats worldwide. In the UK, around 40% of the domestic cat population has been infected with FCoV and in multi-cat households this figure increases to almost 90% *(Addie 2000, Addie and Jarrett 1992, Hartmann 2005, Sparkes 1992).* FIP usually arises sporadically and unpredictably, with only a small percentage of cats developing FIP within the first three years of entering a seropositive household. Rarely FIP can arise as an 'outbreak' in a group of cats over a short period of time *(Pedersen 2009, Potkay and others 1974).* FIP is extremely distressing to deal with, for both cat owners and veterinary surgeons, because of the difficulties in achieving an ante mortem diagnosis, the fatal nature of the disease, and the difficulties of control of FCoV infection.

What Causes FIP?

During natural FCoV infection the virus replicates within enterocytes, particularly of the colon and to a lesser extent the small intestine *(Kipar and others 2010).* Concurrently viral RNA is variably detectable in mesenteric lymph nodes, liver, lungs and other organs, typically within specialised resident macrophages in the absence of pathology, providing potential sources for recurrent viraemia and persistent infection. Infections are usually asymptomatic or result in transient mild gastrointestinal disease (e.g. diarrhoea). Viral particles are shed in the faeces and subsequently ingested by a susceptible cat. Risk factors for the development of the disease are multifactorial *(see Fig. 1)*, but a detailed discussion of these risk factors and their management are beyond the scope of this article.

In a small number of individual cats the infecting FCoV becomes capable of replicating extensively within monocytes/macrophages leading to pathological changes that culminate in vasculitis and granuloma development in organs *(Kipar and others 2005).* In the early stages of disease the clinical signs may be vague, signs consistent with a systemic inflammatory response, such as lethargy, pyrexia and weight loss, are often present. Subsequently the vasculitis can result in the peritoneal pleural and pericardial effusions seen in the 'wet' form of the disease. In contrast the 'dry' form of the disease is characterised by the organ system most affected by the granuloma formation e.g. neurological dysfunction with central nervous system involvement, uveitis with ocular involvement.

Fig. 1: Risk factors involved in Feline Infectious Peritonitis development and their management.

It has been proposed that the molecular switch permitting the replication in monocytes / macrophages, and the subsequent development of FIP, arises from nucleotide mutation(s) in less pathogenic FCoVs in individual infected cats; known as the "internal mutation" hypothesis *(Pedersen 2009).*

An alternative "virulent/avirulent"hypothesis had been proposed, which stated that distinct populations of enteric and FIP FCoV strains are circulating in cat populations, and that these are independently acquired *(Brown and others 2009).* Recently whole genome sequencing data identified a genetic mutation, common to the >90% FIP tissue-derived FCoVs, and present in none of the asymptomatic faeces-derived FCoVs, *(Chang and others 2012).* This genome mutation provides a very useful potential future target for FIP diagnostics but does not completely confirm the "internal mutation" hypothesis and exclude the possibility of other explanations in other situations. This is because the FCoV genome mutation rate is rapid, meaning that this genome mutation should be generated many times over during the course of a typical FCoV infection in a cat. However FIP only arises sporadically in FCoV-infected cats, suggesting that factors other than the described genetic mutation also play a role in the development of FIP. Host factors are likely to play a role in this.

Diagnosing FIP

FIP can be difficult to definitively diagnose despite a high degree of clinical suspicion based on history, clinical signs and routine laboratory tests.

History & Clinical Signs

The wide range of clinical signs makes FIP a differential in many different clinical cases. However, history and clinical signs can be used to increase the index of suspicion.

- FIP is most common in young cats (<3 years), but a smaller peak also occurs in older cats (>10 years).
- Pedigree cats and cats from multicat households are at increased risk.

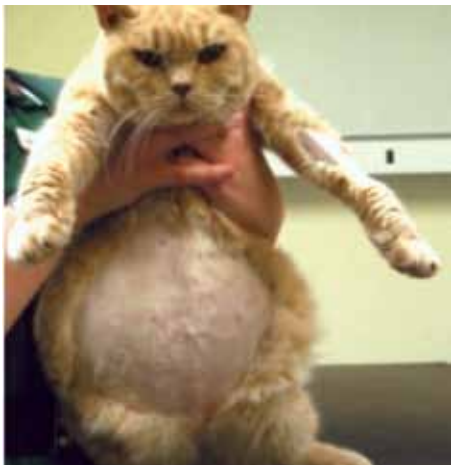

Fig. 2: British Shorthair with 'wet' FIP showing abdominal distension consistent with ascites.

- A recent history of stress (rehoming, neutering, introduction of new cats, vaccination) may be apparent.
- Typical clinical signs of FIP: lethargy, anorexia, weight loss, pyrexia, jaundice, ascites *(see Fig. 2)* and/or pleural effusion and/or pericardial effusion, neurological signs and/or ocular changes etc.

NB: FIP is a progressive disease: clinical signs change over time so it is important to repeat clinical (including ophthalmic and neurological) examinations.

Blood Tests

Haematology and serum biochemistry can support a diagnosis of FIP, and although changes are largely non-specific they can used to increase the index of suspicion.

Haematology

- Lymphopenia (55-77% of cases).
- Neutrophilia (39-55% of cases).
- Mild to moderate normocytic, normochromic anaemia (37-54% of cases).

Serum Biochemistry

- Hyperproteinaemia (up to 60% of cases).
  - hyperglobulinaemia.
  - low or low-normal serum albumin.
  - albumin: globulin (A:G) ratio.

    low (< 0.4) = FIP very likely.
    high (> 0.8) = FIP very unlikely.
  - Hyperbilirubinaemia (21-36% of cases; especially in effusive cases; magnitude increases as the disease progresses).
  - Liver enzymes (ALT, ALP & GGT) often normal or only mildly or moderately elevated.

Additional serum testing

- Protein electrophoresis
  - increased α2- globulins (mostly haptoglobin).
  - increased γ-globulins
- Raised α1-acid glycoprotein (>0.48 mg/ml is abnormal but levels in FIP cases are often markedly elevated at >1.5 mg/ml)

FCoV Serology

Commercial testing of serum FCoV antibodies typically use enzyme-linked immunosorbent assays (ELISAs) or indirect immunofluroescence antibody (IFA) tests. They only test for the presence of antibodies against any type of CoV and cannot differentiate antibodies induced by FIP-causing FCoVs from those not associated with disease. Methodology and antibody titre results can differ between different laboratories (so one cannot directly compare results). A positive FCoV antibody test ***only*** indicates that the cat has been infected with an FCoV and has seroconverted. Seroconversion takes 2-3 weeks. Although cases of FIP tend to have higher antibody titres than non-FIP cases, the degree of overlap makes interpretation in an individual cat difficult. Indeed, most seropositive cats will never develop FIP, and around 10% of cats with FIP are seronegative.

Effusion samples (usually peritoneal or pleural) are very helpful in the diagnosis of FIP. They may be classified as exudates based on their high protein concentration (>35 g/l) but are more of a modified transudate based on their low cell counts (usually <10 x10^9 cells/l).

Body Cavity Effusions

Identification and analysis of effusions can be very useful in the diagnosis of FIP. Ascites is the most commonly encountered body cavity effusion; however, pleural effusion and / or pericardial effusion may be present in the presence or absence of ascites. Repeated imaging (especially ultrasonography) can be useful to detect subtle effusions and direct fluid sampling. Characteristics of FIP effusions include:

- They are usually clear, viscous and straw-yellow in colour.
- Typically they have a total protein concentration of >35 g/l and a predominance (>50%) of globulins.
- Similar biochemical changes to those found in the serum exist in effusions: i.e. low A:G ratios, increased α2 globulins and γ-globulins, and markedly elevated α1-acid glycoprotein levels.
- They are often (but not always) poorly cellular. Cell counts are usually <10, (but occasionally counts higher than 25 x10^9/l have been reported). The cell types most frequently are non-degenerate neutrophils, macrophages and lymphocytes.

NB: Lymphocytic cholangitis, malignancy (e.g. lymphoma) and bacterial peritonitis can produce abdominal effusions of a similar nature to FIP; remember that cytology (neoplastic cells and large numbers of [septic] neutrophils respectively) may help differentiate the latter two diagnoses, whilst lymphocytic cholangitis will be accompanied by at least moderate increases in liver enzymes (esp. ALP and GGT).

Reverse-transcriptase (RT-) polymerase chain reaction (PCR) for detecting FCoV

RT-PCR can detect viral FCoV RNA in blood, effusions, faeces (to detect FCoV shedders) or tissue samples. Current PCR assays detect any FCoV and are not specific for those associated with FIP. The use of RT-PCR to detect FCoV in blood samples showed promise in some studies, although the level of FCoV in the blood of cats affected with FIP can be very low. RT-PCR on effusion or tissue samples is potentially more helpful. Recent studies suggest that FCoV RNA can be amplified by RT-PCR from the vast majority of FIP effusion samples tested, but not from non-FIP effusions *(Held and others 2011, Tsai and others 2011).* Work at the University of Bristol has found similar RT-PCR results using effusion samples, and also of tissue samples, although non-invasive collection of tissue samples is obviously more difficult. In the future RT-PCR performed on tissue samples collected by minimally invasive techniques e.g. Tru-Cut biopsy, may become a useful diagnostic test as it is quicker to perform than histopathology. However, further studies are required to assess the sensitivity and specificity of RT-PCR, as cats with intestinal FCoV infection in the absence of FIP can also be viraemic, whilst those with FIP can have low blood copy numbers and the tissues biopsied may not contain granulomatous lesions. To date there are no commercial RT-PCR tests for the detection of the FCoV genome mutation associated with the FIP-phenotype *(Chang and others 2012),* but this shows promise for future diagnostic tests for FIP.

Histopathological examination of tissues

Routine histopathology

Historically a definitive diagnosis of FIP relied on histopathological examination of affected tissues and the identification of characteristic changes (pyogranulomatous parenchymal foci, perivascular mononuclear infiltrates, fibrinous polyserositis). Samples of tissue, typically from mesenteric lymph nodes, liver, kidney and spleen or less commonly from the thorax (these are harder to obtain), can be collected ante mortem (by ultrasound-guided percutaneous Tru-Cut biopsy, laparoscopy or laparotomy) or at post-mortem. Histopathology has been used as the "gold standard" diagnostic test for the diagnosis of FIP *(Hartmann and others, 2003).* However, routine histopathology is not 100% sensitive: lesions may be missed due to their multifocal distribution e.g. if small

samples are taken, or if non-affected organs being sampled *(Giordano and others 2005)*. Immunostaining for FCoV antigen (see below) can be used to further confirm a diagnosis of FIP, and can be used in cases that have an absence of classical histopathology changes *(Giori and others 2011)*.

Immunological staining of FCoV antigen

Immunohistopathology or immuno-cytology staining of formalin-fixed tissues or effusion cytology samples, respectively, has been used to identify FCoV antigen associated with pathology in tissues or in the cells of an effusion. Positive immunological staining of tissues is said to confirm a diagnosis of FIP (i.e. it is very specific), although a negative result does not exclude FIP as FCoV antigens may be variably distributed within lesions *(Giordano and others 2005)*. Immunostaining of effusion samples has also shown variable sensitivity: a false negative result may be obtained if the effusion is cell-poor (i.e. few macrophages in the sample), or if the FCoV antigen is complexed by FCoV antibodies in the effusion. An abstract at a recent conference *(Held and others 2011)* reported that two of 50 cats without FIP had positive immunostaining on their effusions. However, immunostaining is a useful adjunct test in the diagnosis of FIP. It is available from the Veterinary Laboratory Services, School of Veterinary Science, University of Liverpool, United Kingdom.

Conclusions

Many features of a cat's history, clinical signs and laboratory testing can increase our suspicion of a diagnosis of FIP, potentially to the point that a presumptive diagnosis of FIP can be made, particularly in the face of owner financial constraints or clinical deterioration. A definitive diagnosis can be made in the majority of cats with using histopathology and immunostaining. However, no test is 100% sensitive or specific and it is important not to interpret any clinico-pathology results in isolation. RT-PCR shows promise as an additional non-invasive test for the diagnosis of FIP but further work is required to fully determine its sensitivity and specificity. Detection of the FCoV genome mutation associated with the FIP-phenotype may have the potential to increase the specificity of RT-PCR in the future.

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Feline Update is a co-operative venture between The Feline Centre, Bristol University and Pfizer Animal Health.
Pfizer is pleased to sponsor this CPD initiative, however the views expressed herein remain those of the authors.
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