SPECIAL ANNIVERSARY EDITION II
*Control & Therapy Series*, June 2015 | Issue 279

# Centre For Veterinary Education

# Celebrating our Leaders

## 2015 TG HUNGERFORD AWARD

CELEBRATING 50 YEARS OF SERVICE
TO THE VETERINARY PROFESSION IN 2015

Follow Tom Hungerford's 'goanna track to success'...

# C&T
**CONTROL AND THERAPY SERIES**

JUNE 2015 ISSUE 279
Australia's Leading Veterinary Forum

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# FROM THE DIRECTOR

The striking cover in black & gold of our first C&T for 2015 attracted a lot of attention and even the comment that it looked like every copy should have been accompanied by a bottle of Johnnie Walker Black Label Scotch whiskey!

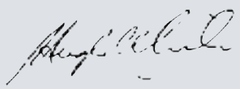
Our 50th year continues to proceed well, with strong attendance at recent events in Launceston, Adelaide, Sydney and Brisbane. Each year we strive to provide interesting programmes across Australia, to support our members in particular, and the veterinary profession, in general with varied programmes offering choice and flexibility.

In April, we held a two day pharmacology seminar in Sydney, in association with the Pharmacology Chapter of Australian and New Zealand College of veterinary Scinetists (ANZCVS). At the end of each day there was a panel discussion where unanswered questions were posed and some lively debate took place. One of the more engaged members of the audience has written two articles for this addition. Aine Seavers is one of our regular contributors and in this publication continues to challenge all vets to think more deeply about everything they do in day-to-day practice.

A dinner was held in Sydney after the pharmacology seminar for the presentation of the TG Hungerford award to Dr Stephen Page for his contribution to continuing veterinary education over many years. Jill Maddison (a classmate of Stephen at Vet School) spoke warmly about how fitting Stephen was as a recipient of this award. The award was presented by Prof Rosanne Taylor , the Dean of the Faculty of Veterinary Science at the University of Sydney. Stephen then gave a humorous and entertaining reply. Jill's more formal citation is published in this C&T, along with Stephen's considered reply. If you want to view the more light-hearted recording of this event, I strongly recommend you view it in the eBook.

This June C&T contains an eclectic collection of articles ranging from horses and goats, to dogs and cats, as well as three great Perspectives. Many of the articles have been written by regular C&T contributors, but we continue to encourage others in the profession to send us articles. There must be at least one interesting case waiting to be written up in everyone's files?

As Stephen Page stated in his acceptance of his award, forums like C&T provide a rich source of clinical anecdotes, which have been regarded by some as sitting at the bottom of the evidence base pyramid, but over recent years have been acknowledged as flagging important observations and topics for valuable research. '*In 1992, as EBM was emerging, Pickering wrote a great opinion piece in the BMJ entitled "The negligent treatment of the medical anecdote". He defined anecdote as "a brief account of any curious or interesting incident" (does that sound familiar?) and concluded that "that habit of curiosity, of critical regard and appraisal of their work, is being lost" – to the detriment of clinicians.'* See page 6 for the full article.



Dr Hugh White,
The Director of the Centre for Veterinary Education

## Course dates

### Major Conferences

**Soft Tissue Surgery Conference** *Also see workshop
Monday 15 – Thursday 18 June | Melbourne

**Clinical Dermatology Conference**
Monday 14 – Friday 18 September | Port Douglas

### Seminars

**Ophthalmology Seminar – *Theory and Practice***
Saturday 25 July | Sydney Also see workshop

**Canine Internal Medicine Seminar**
Sunday 11 October | Port Macquarie

**ECOCPD – Small Animal Radiology Seminar**
Saturday 31 October | Melbourne

### Hands-on Workshops

***Soft Tissue Surgery: Wound Management Workshop**
Friday 19 June | Melbourne

**Basic Echocardiography Workshop**
Saturday 18 & Sunday 19 July | Brisbane

†**Ophthalmology Workshop – *Theory and Practice***
Sunday 26 July | Sydney

**Basic Echocardiography Workshop**
Saturday 25 & Sunday 26 September | Melbourne

**Stress Free Surgery Workshop**
Saturday 17 October | Sydney

**Diagnostic Ultrasound Workshop**
Friday 6 November | Sydney

### TimeOnline – Online CPD

**Practical and Advanced Dentistry**
Monday 8 June – Sunday 5 July | Online

**Reptile Medicine**
Monday 22 June – Sunday 19 July | Online

**Feline Anaesthesia**
Monday 13 July – Sunday 9 August | Online

**Avian**
Monday 27 July – Sunday 24 August | Online

**Demystifying ECGs**
Monday 10 August – Sunday 13 September| Online

**Anaesthetic Complications**
Monday 24 August – Sunday 27 September | Online

**Feline Emergencies**
Monday 7 September – Sunday 4 October | Online

**Small Animal Behaviour**
Monday 21 September – Sunday 18 October | Online

**Wildlife**
Monday 12 October – Sunday 8 November | Online

**Respiratory Failure**
Monday 26 October – Sunday 22 November | Online

For new TimeOnline courses visit our website...
**www.cve.edu.au/timeonline**








# Centre for Veterinary Education

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### PodcastPLUS – Free to CVE Members

**Diseases in Wild Birds**
Tuesday 30 June | Online

**Bovine Anaemia, Jaundice and Red Urine: is it Theileriosis?**
Tuesday 28 July | Online

**Hindlimb Lameness – *Seeing the Trees***
Tuesday 24 August | Online

**Sudden Death – *Investigating Causes in Cattle***
Tuesday 29 September | Online

**Pharmacology – *Popular Veterinary Nutritional Supplements***
Tuesday 27 October | Online

Check our website for upcoming PodcastPLUS topics...
**www.cve.edu.au/podcastplus**

### Calendar Key

- 2016 DE Super Early Bird Ends
- 2016 Early Bird Ends
- Major Conferences
- Seminars
- Hands-on Workshops
- TimeOnline start dates
- PodcastPLUS
- School holidays (NSW)

CELEBRATING 50 YEARS OF SERVICE TO THE VETERINARY PROFESSION IN 2015

## Follow Tom Hungerford's 'goanna track to success'...

The C&T is the brainchild of Dr Tom Hungerford, one of the founders of the PGF* (established in 1965) and the first Director (1968-1987), who wanted a forum for uncensored and unedited material.

> ***'...not the academic correctitudes, not the theoretical niceties, not the super correct platitudes that have passed the panel of review... not what he/she should have done, BUT WHAT HE/SHE DID, right or wrong, the full detail, revealing the actual "blood and dung and guts" of real practice as it happened, when tired, at night, in the rain in the paddock, poor lighting, no other vet to help.'***

The first *C&T*, contributed by Dr R M Kibble from Kurring-gai Animal Hospital, Turramurra North, NSW was on 'Infertility – Uterine Conditions' and was published on 29 April 1969. CVE Members are reminded that this and other C&Ts, Perspectives, Proceedings and veterinary publications are available to CVE members through the CVeLibrary. Contact cve.enquiries@sydney.edu.au or call us at +61 2 9351 7979 if you've forgotten your Username and Password for access.

## Thank you to all contributors

### ...and more C&T articles and Perspectives are needed

Thanks to every author who contributed articles or comments to the *Control & Therapy Series* (C&T) and to those who supplied images and visuals. Without your generosity the Series would cease to exist.

## WINNERS

MAJOR PRIZE

Entitling the recipient to one year's free membership of the CVE:
RESTRAINT OF HORSES IN THE PADDOCK OR 'PORTABLE CRUSH' by Nick Scott

CVE PUBLICATION PRIZE WINNER

Entitling the recipient to a CVE proceedings of their choice: www.vetbookshop.com
FELINE PLASMA CELL PODODERMATITIS – A PATHOLOGIST'S EYE VIEW by Melanie Dobromylskyj

And in March 2015 Issue 278, apology for the omission:
ACROMEGALY IN A MALE DOG by Shelley Wiltshire

*The Post Graduate Foundation in Veterinary Science of The University of Sydney (PGF) was renamed The CVE in 2008.

## Thank you to our C&T industry supporters

Your financial support sponsors the production of the *C&T Series* in high quality colour print format as well as the complementary digital eBook version (facilitating the inclusion of film clips, downloads, rollovers and enlarging of images) and postage costs.





## 2015 T G HUNGERFORD AWARD RECIPIENT

# DR STEPHEN PAGE

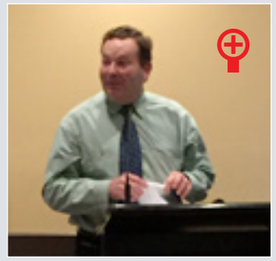
***Citation prepared by Jill Maddison, Richard Malik, Aine Seavers and Anne Fawcett. Delivered by Jill Maddison.***

Stephen graduated from the University of Sydney BVSc with First Class honours in 1980. Following graduation he was an intern then resident at the Rural Veterinary Centre Camden, culminating in the award of Master of Veterinary Clinical Studies. He then embarked on a life-long career pathway in industry which culminated in his term as head of research in the Asia Pacific Region for Pfizer Animal Health. Throughout his career, Stephen has made enormous contributions to both small and large animal veterinary pharmacology in Australia, Europe and the USA. He was instrumental in bringing selamectin successfully to the market in Australia whilst achieving a Masters of Applied Science in Environmental Toxicology. His work is characterised by exceptional scientific rigor and breadth, but this work does not form the only basis of this nomination.

In addition to his industry roles, and later a number of different private consultancies, Stephen has been dedicated to fostering the disciplines of veterinary pharmacology and therapeutics within Australia. He has worked especially effectively with the Australian College of Veterinary Scientists (ANZCVS) and its Pharmacology Chapter, being an examiner and head examiner in this subject for many years. He regularly presents at Science Week. The Pharmacology Chapter is unique in providing detailed notes and study guidelines for ANZCVS membership (MACVSc) candidates. Stephen was instrumental is developing this resource, by badgering and co-opting interested members of the chapter. Likewise, he was pivotal in the development of the 'Block Course' to assist MACVSc candidates to prepare for their examination.

Stephen made a seminal contribution to arguably the most popular veterinary pharmacology text available, in concert with Dr Jill Maddison and Professor David Church. Critically, this text is clinically focused and based not just on drugs and body systems, but also on clinical problems. Highly readable and a great seller internationally, it's onto its second edition.

Together with Associate Professor Paul Mills, he played a critical role in obtaining a $250,000 grant from the Australian Learning and Teaching Council for the development of a national pharmacology curriculum, the Veterinary Clinical Pharmacology Network, a portfolio of clinical case scenarios illustrating key pharmacological principles. The Australasian Veterinary Schools and Dr Amanda Craig from the School of Pharmacy at Canberra University will be involved in its implementation.



Stephen is head of the **Therapeutics Advisory Committee** of the Australian Veterinary Association (AVA), an onerous role and largely *pro bono*, which plays an absolutely vital role in interfacing between drug manufacturers, veterinarians in the field and government regulators. Tirelessly, Stephen is extremely effective in terms of: contacts; insight into the pharmaceutical industry and the veterinary profession; his ability to think strategically and wisely about difficult issues; his diplomacy; and finally his ability to be effective and to bring about change. Permethrin intoxication of cats, an emergency feline intoxication problem in Australia recently was attributable to the availability of these products without advice at supermarkets and pet barns. Stephen provided not only intellectual and moral support to colleagues concerned with this issue but also the intellectual and theoretical frameworks to tackle the problem. An AVA task force subsequently researched the advertising, marketing and labeling of these product and published an editorialized lead article in the *Journal of Feline Medicine and Surgery* (Appendices 1 & 2). Stephen, typically, took this further by networking with key opinion leaders in Europe, and making a detailed submission to the USA Environmental Protection Agency in relation to this issue. Stephen contributes to the *Control and Therapy Series,* teaches part time in a number of Masters Programs offered by the Faculty of Veterinary Science of the University of Sydney and develops close interaction with veterinary colleagues in developing nations. He frequently assists practitioners in his own time by conducting high quality, in-depth and extensive literature reviews to assist in solving clinical problems. He consistently encourages colleagues to take a balanced, scientific approach to often emotive issues.

Stephen is an unassuming, extremely hard working quiet achiever and a truly original thinker. He cuts directly to the heart of an issue and provides extraordinary insight and scholarship. His innate personal humility, tolerance of human diversity and intense enthusiasm for all things veterinary make him among the most respected and approachable of men by clinicians in the field. Outside the boundaries of traditional academic veterinary medicine, Stephen is essentially a true scholar with a vast personal and professional knowledge base that he is happy to share. He is a most caring and patient teacher with a deep love for the veterinary profession, especially veterinary pharmacology.

# TG HUNGERFORD AWARD ACCEPTANCE SPEECH

**Stephen Page**
BSc(Vet)(Hons) BVSc(Hons) DipVetClinStud MVetClinStud MAppSc(EnvTox) MANZCVSc(Pharmacol)
Advanced Veterinary Therapeutics, Newtown NSW

To be the recipient of such a prestigious award is a massive honour and a huge surprise. Tom was extraordinarily prescient in his inexhaustible thirst for knowledge and its dissemination and a great role model for me (and many others). It is always a privilege to be able to help others and a very rewarding experience. To be recognised for my contributions is extremely humbling. However, I feel that my work is only just beginning, building on many years of conversations, research and unique experiences.
I continue to have a truly wonderful adventure as a veterinarian. I feel like the fourth Prince of Serendip, travelling from one unexpected and exciting frontier to another, discovering new things along the way. I was helped and influenced extraordinarily in my formative undergraduate days, Brian Farrow and David Watson for small animals, David Hutchens for horses, Bob Love for pigs - all so clear in their thinking, all helped lay foundations that could then be tested when as an intern and resident I was responsible for facilitating the learning of students, all of us separated by so little experience. I quickly learned that questions from enquiring minds are an invaluable and limitless source of cognitive stimulation. Finding answers to questions has been my lifelong quest.

I have an insatiable thirst for knowledge and can never resist sharing what I learn with others. And I am continually surprised how many people just love to find out new things too. I can never discard information either, so many times new and curious links eventually emerge that lead me in new directions. Fortunately the garage I use to store the massive pile of information I hoard is digital. And I have to thank Bill Clinton for introducing PubMed and the start of public access, and the Australian Government for making the Cochrane Library free to Australians.

I am easily distracted by new information and interesting things and was drawn very early to the Post Graduate Foundation. I can't quite remember what sparked my interest in drugs and pharmacology, but having survived the 60s and seen so many discoveries – notably the discovery of endorphins and a potential link between Western and Traditional Chinese Medicine, the first antihypertensive drugs, the benzodiazepines, dopamine as a treatment for Parkinson's Disease, so many more, - it might have been inevitable. There were a number of pharmacology and toxicology symposia at the Stephen Roberts Theatre (where has it gone?) and they added to my growing interest and led me to prepare for Membership of the ACVSc via the pharmacology chapter. My first professional presentation and publication in a proceedings was to the Chapter of Pharmacology – more than 30 years ago. The subject was about emerging drugs for use in veterinary practice. It is amazing to see what became of those predictions in 1983!

That early adventure led to recruitment by the animal health pharmaceutical industry – not intended but a wonderful place for somebody easily distracted and passionate about information and making a difference. Every year there was something completely different, anthelmintics for sheep, ectoparasiticides for sheep and cattle, anticoccidial agents, intramammary products for cattle, non-steroidal anti-inflammatory agents for dogs. Just when a topic was becoming familiar it was time to start from the beginning in a new area. It was a formidable but exhilarating experience and I realised that those following this path should not have to spend the time I expended identifying and retrieving the literature – better precious time was spent studying and learning. The Veterinary Pharmacology Study Course was born and is now more than 25 years old and has probably helped well over a 100 emerging veterinary pharmacologists. The Chapter of Pharmacology is now working closely with CVE in the next generation of continuing education resources, setting up the Veterinary Clinical Pharmacology Network – a resource that is getting closer to launch every day.

I was especially proud and honoured to have Jill (Maddison) provide the background to my award. Jill has had a similar journey in a parallel universe; she has that same insatiable thirst for knowledge and for sharing the enthusiasm that results. Jill and David and I are now thinking about the third edition of Small Animal Clinical Pharmacology – a trio of enthusiasts, herded so well by Jill.

I had cultivated an interest in adverse drug reactions while in industry which led to increasing interest in tissue residues in livestock, contaminants in feed and the various impacts of poisonous plants and other environmental toxicants. When the University of Sydney was preparing to begin an online Masters course in Veterinary Public Health Management I was asked to help facilitate the modules on hazards to animal and human health and on food safety. More interaction with students from all over the world eventuated as did many opportunities to expand my own knowledge horizon. Students working with FAO later invited me to work in Nepal providing training on risk analysis and to work in Thailand and Japan on food safety risk analysis. Being paid to work in Kathmandu, Chiang Mai and Tokyo was an exceptional experience and helped expand my veterinary network.

I continue to meet extraordinary people along the way. Just when I think I have reached a plateau, a new challenge emerges. Richard Malik's call to action to prevent permethrin intoxication of cats beckoned me to join the team that was forming - and a new and wonderful adventure commenced. CVE was able to survey vets and a mammoth hidden cause of deaths was revealed. Actions were taken, the results were published, international collaborations were formed, product labels were changed, awareness of the issue was increased and hopefully many feline lives were saved.

My veterinary path has been far from linear; I never plan ahead, things just happen, and I continue to observe and wonder and find inspiration from colleagues and students.

My path started before the launch of evidence based medicine (EBM) and has continued within the age of EBM and I have witnessed a number of changes. By the way, how was diagnosis and treatment undertaken before EBM – surely it was not evidence free? Human and veterinary medicine had been successfully helping the unwell for millennia – or maybe it was only a perception of success? (Human perception or risk, framing and susceptibility to logical fallacies is another interest, but that might be a topic for another day.)

This brings me to Control & Therapy, another great initiative from Tom that has been collecting practice wisdom for 50 years, a magnificent repository with an international audience.







But surely the content of C&T is all anecdotal? Amazing how that term has gained a disparaging connotation, particularly during the age of EBM. In 1992, as EBM was emerging, Pickering wrote a great opinion piece in the BMJ entitled 'The negligent treatment of the medical anecdote'. He defined anecdote as 'a brief account of any curious or interesting incident' (does that sound familiar) and concluded that 'that habit of curiosity, of critical regard and appraisal of their work, is being lost' – to the detriment of clinicians. Almost 20 years later the same message was being emphasised – Nunn (2011) wrote that 'not all anecdotes are worthless and not all randomised controlled trials (RCTs) are gold' and in his opinion 'the devaluation of anecdotes in medicine has gone too far'. Enkin and Jadad (1998), prominent epidemiologists from the home of EBM (McMaster University in Ontario) noted that 'if evidence-based health care is to meet its potential, the important role of anecdotes must be acknowledged, studied and utilized'. But why was there such interest in and recognition of the value of anecdotes, those individual observations, those clinical vignettes? The transformation of how the safety of drugs is considered was brought about in great part by the couple of sentences written by Bill McBride in the Lancet in 1961 about his personal observations of a new embryopathy associated with the use of thalidomide by the mother – no RCT, just an individual's clinical observations and intuition. Aronson is a heavyweight in the world of adverse drug reactions and always has something intensely interesting to say. He wrote that 'anecdotal case reports contribute about one-third of the published literature on adverse drug reactions and interactions' and that 'each suspected adverse reaction should be reported in detail and reactions should be reported in sufficient numbers for proper classification and for patterns to be recognized' (Aronson 2005). He realised that a single case should be reported, but that interpretation required many cases – but each case had to be reported – just like permethrin in cats, thalidomide in humans. Somebody had to be first. There is a growing list of those who recognise the fundamental importance of personal experiences and anecdotes. Stuebe (2011) a strong convert to EBM at first, with experience realised that 'adverse anecdotes can transform a clinician's practice patterns in an instant' and are a great complementary source of evidence to integrate with EBM teachings. And not just in medicine but also, and maybe more importantly, in surgery, the anecdotal report can be very impactful (Treasure 2006). Borgstein (1999) wrote that 'the well documented creative clinical anecdote, when we can obtain it, allows us a unique holistic view, not only into the illness process but also into the workings of the diagnostic mind'. One of my favourite authors, Oliver Sacks, is a strong advocate of anecdotes and a wonderful exponent of the narrative style of describing cases. The narrative approach, so important and widespread in past centuries, had all but disappeared, and is slowly re-emerging. Difficult to analyse, but nonetheless can be packed with meaning.

One of the recent (last decade) changes in EBM has resulted from the realisation that RCTs have excellent internal validity; the results can be expected to apply to the population being studied. But the population being studied may be very unrepresentative of the population from which an individual patient is drawn – the external validity of RCTs can be very low.

As Enkin and Jadad noted, 'randomized clinical trials can tell us which treatment is better, but they cannot tell us for whom it is better'. The N-of-1 trial, in which selected treatments are randomly applied repetitively to the same person before analysis, can answer the question of what is best for the individual patient – another change in EBM – the N-of-1 study is now at the apex of the evidence hierarchy, it has been there for more than 10 years, but frequently overlooked.

What is also happening is a realisation that we can learn from the wisdom of the ancient Greeks! What could they possibly have to say about EBM and anecdotes? Braude (2013) provided many insights into this question. Medicine is not distinguished by being a science, but rather, through its timeless concern for the good of the individual patient – the individual patient had been a casualty of EBM version one. He further noted that 'medicine exists as medicine only when it engages in the full range of activities which constitute clinical judgement and which lead to decisive action in the interest of a particular patient'. It is phronesis that enables us to discern which means are most appropriate to the good for a particular individual patient, and it is phronesis that Greek philosophy first described and had been overlooked until recently. I had definitely overlooked it and finding it revealed how to explain the value of those with experience and accumulated intuition – those whose recommendations occupy the lowest level of evidence in the EBM hierarchy. 'The core competency of excellent physicians across the centuries is practical wisdom, what Aristotle called phronesis, the ability to determine what is possible and proper to each unique clinical situation' was noted by LeBlond (2013) who went on to say that 'the increasing emphasis on narrowly restricted expertise and technical proficiency as the foundation for medical careers may create the illusion that objective knowledge and technical competence are sufficient for clinical excellence', 'without an equal emphasis on mindful reflection, true understanding, mature judgement, and wisdom are not possible; physicianship will be replaced by technicianship', and finally, 'we must encourage and mentor learners to strive for practical wisdom what is the core competence of all excellent physicians'. So phronesis – how could I not have stumbled on it in the past, but is definitely part of my future. Jacqui, please put this in a 'break-out box'

Now I can concur with Kumagai (2014) when he advised that 'the goal of education in areas of social relevance in medicine… aspires toward the development of practical wisdom (phronesis) which, when embodied in the physician, links the knowledge and skills of the biomedical and clinical sciences with a moral orientation and call to action that addresses human interests in the practice of medicine.' While we might only have seen a single evidence hierarchy pyramid in the past, there has always been another pyramid, only now coming into focus, the phronesis hierarchy, without which medical or veterinary patients will not benefit ideally and humanity will be missing from care. And it is in the area of phronesis that C&T has played and continues to play such a highly valuable role. Well ahead of its time, very prescient.

It has been and continues to be a privilege to be involved in continuing professional development. It is an extraordinary honour to receive the TG Hungerford Award – especially when my own learning has benefited at least as much but probably more than that of my colleagues and students. It was a privilege to receive the award from Prof Rosanne Taylor who was a student of mine – albeit briefly and many years ago. I hope she can only remember the good things as I struggled with teaching as a newly graduated resident. I can only hope I do better now. There are many more challenges and exciting times ahead and every new project is built on the accumulated experiences of the past, all enhanced by the interactions, collaborations and network of colleagues and friends.

**Note:** Stephen has provided a comprehensive reference list which, due to space constraints, is available in the eBook.

**References**

View the video of the Award ceremony at **www.cve.edu.au/tghungerfordaward**

# LETTER TO THE EDITOR:
## CREDIT WHERE CREDIT IS DUE FOR PET INSURERS

Dear Editor,

Subsequent to my article **Pet Insurance – Problems And Potential in C&T (Issue 276, Sep 2014**) we can report some pleasing progress with pet insurance.

The AVA Pet Insurance Task Force engaged with insurers to discuss veterinary concerns, and organised a series of seminars. Following legal advice, the AVA produced guidelines for vets which are available here: www.ava.com.au/sites/default/files/A3%20-%20A%20veterinarians%20guide%20to%20pet%20health%20insurance%20web.pdf

Encouragingly, insurers are now participating in veterinary conferences where they can interact directly with veterinarians for advice or feedback. Several major insurers are developing **electronic online claims** processes and a trial is about to commence. This should help reduce the perennial and frustrating problem of loss of claim forms in the post (or more likely during processing). We hope insurers will also be receptive to simplification of paper insurance claim forms and claims processes - personally I am still mystified as to why detail on vaccination status is required for every claim when the vast majority of claims are not related to vaccine preventable infectious disease. **The costs of completion of forms are significant to vets** and any **simplification** would be welcome. Many industries face rapid growth and change. One only has to look at the airline industry moving from travel agents and paper tickets to online sales, check in via Apps, mobile phones or online, frequent flyer programs and efficient security screening, all of which have simplified air travel. The vet and insurance industry should work together to make insurance work better. Of course there will be areas where we 'agree to disagree'.

One key objective was that, when requested, insurers offer **review of claims by an Australian registered vet** who is fluent in English and medical terminology. One major insurer, Petsure, has developed a vet hotline, allowing vets to accelerate communication processes without having to battle through call centres.

Insurers are actively seeking feedback from vets. On the subject of denied claims I have been asking them to review their policies on cover for parasitic conditions. Some insurers deny claims on any parasitic disease – few would object when there is a preventative available – such as for heartworm disease or hookworm. There is an obligation on the owner to maintain basic healthcare (or should be). It seems unreasonable, though, when claims are denied for parasitic diseases for which a routine preventative is not available such as GIT disease due to Giardia or neurological disease secondary to Angiostrongylus cantonesis.

We would also like to see **better definitions of pre-existing conditions and no broad exclusions** based on whole body systems. This is a complex area that needs further discussion.

Direct professional feedback from vets to Petsure (one of the major insurers) is welcome via email to vethelpline@petsure.com.au

Sincerely, James Thompson

Disclaimer: I have no personal or financial relationship with any pet insurer.

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# IMPORTANT PUBLIC SERVICE MESSSAGE
## RE: HUMAN TICK-RELATED DISEASES

**Following on from C&T No. 5416 'How Much Do You Know About Human Tick-Related Diseases?', Clinical Associate Professor Sheryl van Nunen has sent us the link to the program, which recently featured on the ABC's Catalyst show, highlighting the dangers of ticks to humans.**

**WATCH NOW in the eBook or go to: www.abc.net.au/catalyst/stories/4177191.htm and please share with your friends and colleagues.**

*Thank You.*

***Photo courtesy of Anne Fawcett***







# ANTI-MÜLLERIAN HORMONE – A NEW TEST FOR THE DIAGNOSIS OF GRANULOSA CELL TUMOURS IN MARES

**C&T NO. 5465**

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Ovarian granulosa cell tumours (GCTs) account for more than 85% of all tumours of the reproductive tract in mares and 2.5% of all equine neoplasms[1-5]. Typically these tumours are benign and unilateral in nature with the contralateral ovary commonly small and inactive[1, 3, 6]. GCTs are hormonally active and produce variable amounts of inhibin, oestradiol and testosterone[1, 7]. It is therefore common for mares to present with behavioural abnormalities including aggressiveness, stallion-like behaviour, prolonged anoestrous, or nymphomaniac behaviour[1, 3, 7, 8]. However, most mares with GCTs present with anovulatory anoestrus. GCTs display no breed predilection and have been detected in maiden, barren, pregnant and post-partum mares[1, 3, 6, 9-12].

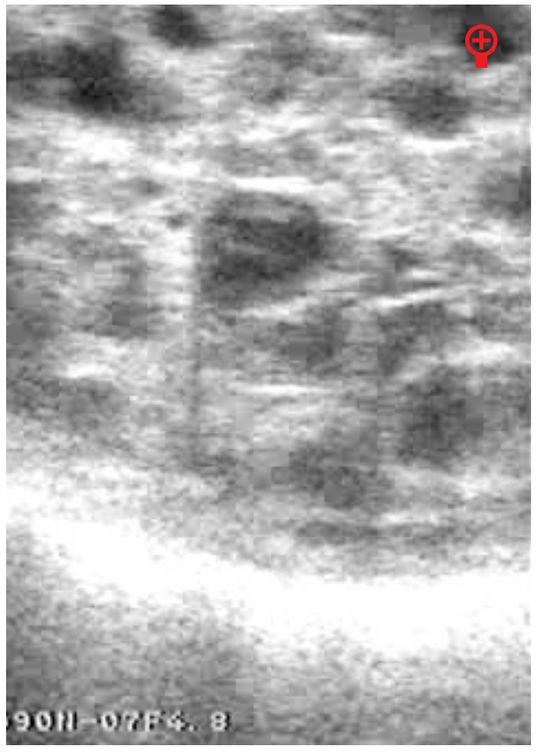

*Figure 1: Ultrasound image of a GCT*

Ultrasound of the affected ovary commonly reveals an enlarged, multicystic structure of honeycomb appearance containing areas of hyperechoic tissue as seen in *Figure 1*. However the appearance of the tumour can be variable, presenting as a solid mass, single large fluid filled cyst or a polycystic core surrounded by a thick capsule, potentially containing focal areas of haemorrhage and necrosis (*Figures 2a,b*) [2, 7]. Histologically, it is common for the ovulation fossa to be obliterated[1, 3, 8].

Clinical signs and ultrasonographic findings alone are not sufficient to confirm a diagnosis of GCT. Differentials for ovarian enlargement in the mare include neoplasia (serous cystadenoma, dysgerminoma, teratoma), physiological processes (pregnancy, haemorrhagic anovulatory follicles (HAF)), or localised pathology such as ovarian haematomas or abscessation[1, 2].

The hormonally active nature of GCTs allows endocrine analysis to be used successfully as a diagnostic aid[1, 6]. The current standard 'GCT panel' quantifies serum concentrations of inhibin, testosterone and progesterone[1, 6]. Increased serum concentrations of inhibin (>0.7ng/mL) and/or testosterone (>50-100pg/mL), combined with decreased circulating progesterone (<1ng/mL) are suggestive of a GCT[7, 13, 14]. However, serum concentrations of these 3 hormones can fluctuate depending on the stage of the oestrus cycle and stage of pregnancy[6, 15, 16]. In addition, in the early stages of tumour development, levels of all 3 hormones can be within the normal range.

Anti-Müllerian Hormone (AMH) is a homodimeric glycoprotein expressed by the granulosa cells of ovarian follicles that has a role in the regulation of follicular development[17, 18]. AMH is highly conserved across species and has been found in all domestic mammals tested so far (horses, cattle, dogs, cats, sheep and goats). Immunohistochemistry has previously shown that AMH is expressed in granulosa cells of normal equine ovaries as well as in GCTs[19, 20]. Serum AMH as a biomarker has thus been investigated as a more sensitive diagnostic aid than previously measured hormones in equine GCTs[6, 19-21].

In horses, serum AMH concentrations were first characterised by Almeida et al. (2011) using a heterologous enzyme linked

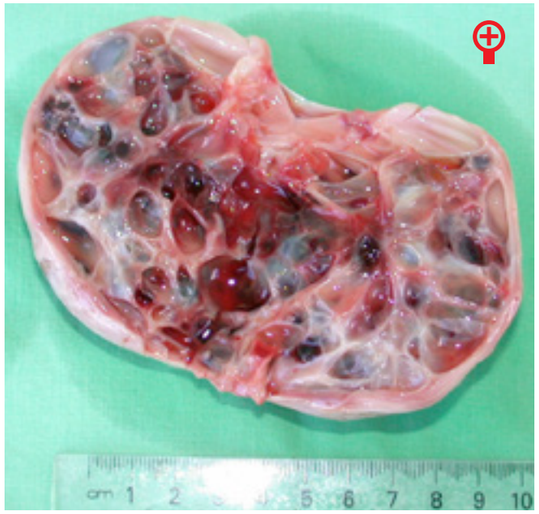

*Figure 2a: Cut section of ovarian GCT*

immunoassay (ELISA) in normal cyclic mares, ovariectomised mares and mares previously diagnosed with a GCT. There were no significant differences in circulating serum AMH concentrations between normal cyclic mares and pregnant mares, thus negating any confounding factors encountered by inhibin, progesterone and testosterone analysis. The concentration of AMH in ovariectomised mares was equal to or less than the limit of detection of the assay, confirming the ovarian localisation of the hormone. AMH concentrations were increased in all mares with histologically confirmed GCTs. This demonstrates significantly increased sensitivity when compared to inhibin and testosterone analysis, with levels elevated in only 73% and 45% of GCT cases respectively if these hormones are measured individually. Ball et al. (2013) conducted further studies, concluding that AMH, when measured in combination with testosterone and inhibin, achieves a sensitivity of 100%[19].

Canterbury Health Laboratories (Christchurch, NZ: E. info@chl.co.nz) and Vetpath Laboratory Services (Perth, WA: Vetpath.reception@vetpath.com.au) currently perform the only AMH assays available for clinical use in Australasia. Though the assays are designed for humans (NZ), and dogs and cats (WA), the manufacturers report that they also cross-react with AMH from other species including the horse. Though each assay may not have full measurement (cross reaction) of the AMH from other species it appears adequate for differentiating the elevated AMH observed in mares with GCTs compared to healthy mares. Both laboratories are currently in the process of establishing individual reference intervals for the mare and therefore it is useful to provide a clinical history with your submission, especially if you have confirmed the diagnosis of a GCT by histology. It is also important to contact the relevant laboratory for specific submission requirements. Note that results are reported as AMH pmol/L; to convert to ng/mL (the unit often quoted in veterinary publications) divide the pmol/L result by 7.14.



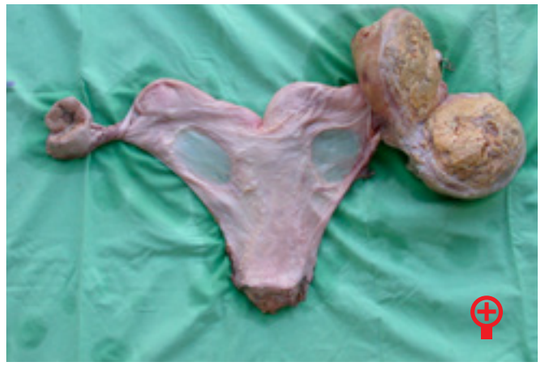

*Figure 2b: Cut section of ovarian GCT* ex vivo

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MAJOR WINNER

The Major Prize Winner is entitled to a year's free membership to the CVE.

# RESTRAINT OF HORSES IN THE PADDOCK OR 'PORTABLE CRUSH'

**C&T NO. 5466**

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When examined rectally or vaginally it is surprising that very few horses will actually kick, but when they do the results can be devastating and even fatal for the person behind them. Unlike cattle, rather than kick back with one hind leg most horses will kick up both legs and 'let fly with both barrels' which can generate significant force.

Without a properly designed horse crush there is considerable danger, but makeshift arrangements like 2 hay bales or reaching over a gate can cause a false sense of security and be even more dangerous. Poorly designed 'crushes' can be even worse; in fact, one of the worst kicks I have ever received was when the handler allowed a mare to jump forward and kick over the flimsy rails that had been arranged behind her.

Likewise, use of the client`s serving hobbles are not much of a solution as they are only placed around the mare`s hocks and still allow a decent kick to be delivered.

Unfortunately, those of us who are in part-time equine practice are likely to have this problem more than those who work on large studs etc. Some operators favour a single sideline which places a large strap around the neck and then a strap is hooked to the hind pastern and the leg is dragged forward almost off the ground and a special quick release buckle attaches this line to the neck strap.

I used this apparatus for a while but found it placed the horse in an unnatural position, particularly for rectal examinations, and was very cumbersome to stow and then get out of the vehicle.

The paired sidelines as pictured, with a strap going from front pastern to hind pastern on each side, have served me very well, and sometimes I call them my portable crush.

They were made for me by Goulburn saddler, Bill Dutaillis* in the late 1970s and since then have been placed under severe pressure by some badly behaved horses. After all this time, some of the buckle holes are getting a bit stretched but the straps are still perfectly serviceable.

Bill made the straps out of a basically treated leather which he called 'CHROME', which has been ideal as it has hardly stretched at all and only very occasionally gets any leather dressing. The pictures should show that Bill placed a buckle in the strap about 40 cms from the end. The end is then wrapped round the pastern and fixed back to the same buckle. This simplifies the design and means the foot does not have to be raised to apply them (unlike some other designs).

The shorter strap is 77 cms from buckle to buckle and the free ends are each 38 to 40 cms. I always place this on the left side as I am right handed and therefore will be standing directly behind the left (nearside) hind leg during an examination.

The longer strap goes on the right side and is 91 cms from buckle to buckle with each free end again about 40 cms. Each strap is 3 cms wide.

For some years I thought that if I had the short strap only on the left side and stood directly behind that leg I would be quite safe. However, after I wore a hoof print on my left rectus femoris for about 6 months (closely adjacent to some anatomy I rather treasured), I decided to always put on both straps.

The straps fit nearly all horses except for the smallest miniatures or very large footed draught horses.

If the horse is difficult to handle round the back feet I would either use a bit of sedation (much more reliable now than 30 years ago), or occasionally I have had to tie the front foot up to be able to get a strap around the hind leg.

Some horses will struggle in the straps and some will go down so it is essential to USE THEM IN A PADDOCK on softer ground and never on gravel or concrete as injuries will occur. I also try not to put the free end back in the buckle 'keeper' too tightly so it can be undone easily.

These days I even use these straps at foalings to increase safety and have had no problems if the mare goes down as long as I am cautious to avoid the feet when undoing the straps.

THE KNEE HOBBLES also known as 'Dinner Time Hobbles' are also shown in the photos.

They are handy for procedures around the horse`s head such as drenching or dental work and make it much more difficult for the horse to rear or strike with one front foot when wearing the sidelines as well.

They also help to restrict movements as some horses are able to move surprisingly well when just wearing sidelines.

Again the straps are about 3 cms wide. The centre piece is 18 cms long and contains a piece of steel sewn into the leather to keep the knees apart at the correct standing position.

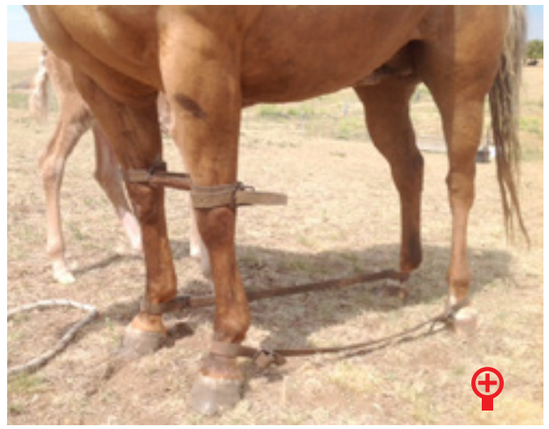
The short piece to the buckle is 12.5 cms long while the long free strap to wrap around the legs is 108 cms.

You will notice that my long strap is wrapped twice around the mare`s leg as my straps are always inclined to slip down below the knees. This is because my straps are made with 2 steel rings for the straps to go through. I have seen other hobbles work much better when the rings are replaced by ‘D s’ which are shaped like a square.

The attached photos show a mare prepared for a post foaling uterine examination. Usually I would not use the knee hobbles as well unless she was very excitable.

The last 2 photos show how the sidelines are buckled back to themselves and how the knee hobbles are threaded onto the legs.

**Dutaillis Goulburn Saddlery, 37 Verner St, Goulburn NSW 2580. T. (02) 4821 2838*



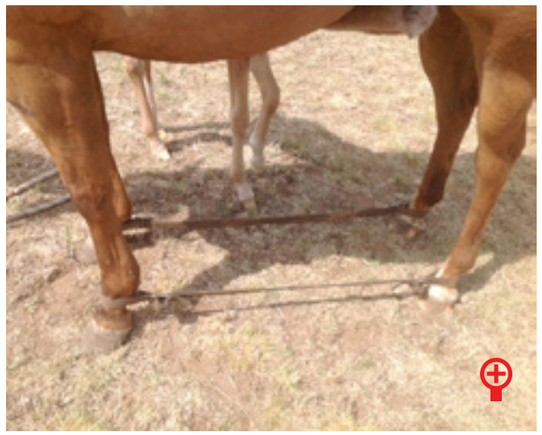


***Figure 1A, 1B, 1C. The paired sidelines, with a strap going from front pastern to hind pastern on each side.***









Note: to get an idea of the scale, the portion of broom handle is 65 cms long. The longer strap goes on the right side and is 91 cms from buckle to buckle with each free end again about 40 cms. Each strap is 3 cms wide.

***Figure 2A & 2B. The shorter strap is 77 cms from buckle to buckle and the free ends are each 38 to 40 cms. I always place this on the left side as I am right handed and therefore will be standing directly behind the left (nearside) hind leg during an examination.***

***Figure 3A & 3B. The longer strap goes on the right side and is 91 cms from buckle to buckle with each free end again about 40 cms. Each strap is 3 cms wide.***

## NOTE FROM HUGH WHITE

This excellent C&T from Nick Scott on horse restraint will strike a chord in the hearts of every older vet. I am sure there are many vets in mixed practice who are still confronted by the need to conduct an internal examination on a horse where there are inadequate facilities. Thirty to forty years ago, workplace health and safety was regarded as a common-sense matter, but this did not stop many of us from placing our lives at risk by doing internal exams on horses around stable doors or gates, in horse floats or in cattle yards or races. Over the years, I personally know colleagues who suffered life-threatening injuries including ruptured livers and spleens when conducting these procedures, and others who have received severe head injuries. While OH&S guidelines may advise ’ideal’ workplace facilities, vets will still be presented with horses on hobby farms or commercial farms where there are inadequate facilities. Nick has described restraints which may be viewed as old-fashioned by some, but in the absence of ideal facilities, could save a life.

## FURTHER COMMENT FROM DAVID JOHNSON, PACIFIC VETCARE, COFFS HARBOUR

This is a great article by Nick, but my concern is that the equipment is pretty difficult and specialised to use unless used by someone with competent horse-handling skills. (A bit like describing how to put on a saddle correctly – sounds easy but actually difficult to do properly unless you know what you’re doing.) In an ideal world, each practice should have specific policies and procedures on handling horses; what equipment, sedation, handlers and when and where rectal examinations of horses can be performed. For example in our practice the policy is no rectal exam can be performed unless the horse is in an approved crush.

## REPLY TO DAVID JOHNSON FROM NICK SCOTT

I would concur with David that without these straps I would be unwilling to perform any examination [not just rectals] to the caudal end of a horse unless it is in a proper crush.

However I would take issue that my straps could only be used by someone with ‘competent horse handling skills.’ I would submit that we should have or study handling skills before trying to examine or treat ANY species.

For example you can receive some nasty injuries from stroppy Chihuahuas or Rottweilers without proper skills and I know from my work with wildlife you must be aware of the widely different handling methods you need for macropods, possums, koalas, parrots, raptors and water birds etc.

The difficulty is that these days a large proportion of mixed rural practices have such a large caseload of small animals that many of our new graduates are not getting the chance to learn the skills in handling large animals which they need to operate safely a nd effectively.

# LEG WOUNDS IN HORSES

**C&T NO. 5467**

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**Go to the eBook version of this issue to read 5 other C&Ts about wound management in horses including C&T No. 5168. Proud Flesh.**

- **Honey in wound management,** C&T No. 4313
- **Management of a forelimb wound in a mare,** C&T **No. 4618**
- **Large flesh wounds,** C&T no. 4663
- **Proud flesh**, C&T No. 5168, Mar 2011, Issue 262
- **Wound Management in the horse** , C&T No. 5169, Sept 2011, Issue 264. reply to Proud Flesh (C&T No. 5168, Mar 2011, Issue 262)

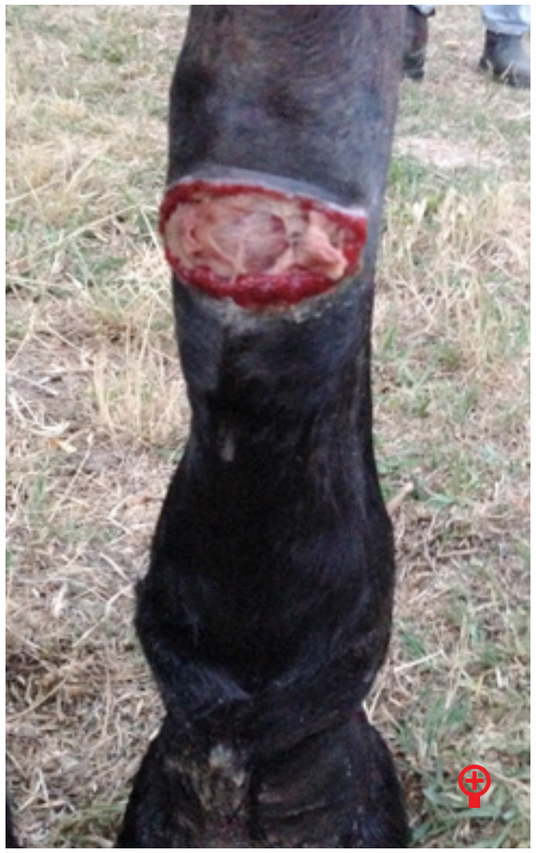


***Figure 1. The wound in late November, soon after injury, with the initial infection controlled.***

Lilian Wong and Jason Andrew wrote an excellent C&T No. 5168 Proud Flesh which refers to an *AVJ* article by Andrew Dart et ali. I certainly do not intend to try and refute any of their recommendations.

The only comment I would like to make is that I find in a general practice situation, successful treatment of these large wounds depends very much on whether the owners have the necessary time, dedication, horsemanship skills and finances to devote to the several months of treatment and bandaging that some of these wounds require.

Secondly, the temperament and co-operation of the horse in tolerating these treatments can make a huge difference to the treatment regime and the outcome.

Many times, once the wound has a reasonable granulation bed, I have advised to just cover the wound with limestone powder (microfined limestone, not the slaked lime) and clean all the dried scabs off once or twice a week.

This can give quite a reasonable result but of course then the wound is at the mercy of various other 'advisors' who want to put weird and wonderful potions on the wound at least daily and irritate it and cause more damage.

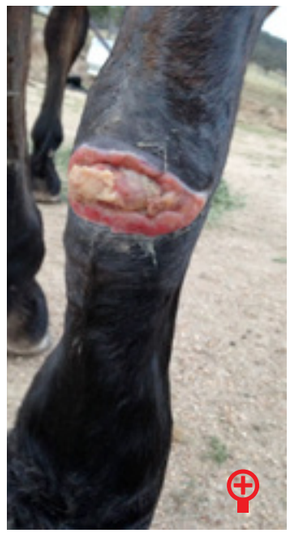


***Figure 2. Wound on 16 December 2013 showing the protruding proud flesh.***

However, one of the most frustrating wounds to treat is when the flexor tendon sheath below the carpus or hock is damaged, sometimes by quite a small wound. Often this wound may not even be apparent at the initial examination.

There is usually no actual damage to the tendon but the rupture of the sheath will cause a massive outpouring of sheath fluid which looks like copious synovial fluid. Exuberant granulation tissue masses around the wound but it will not seal under a bandage and every time the wound







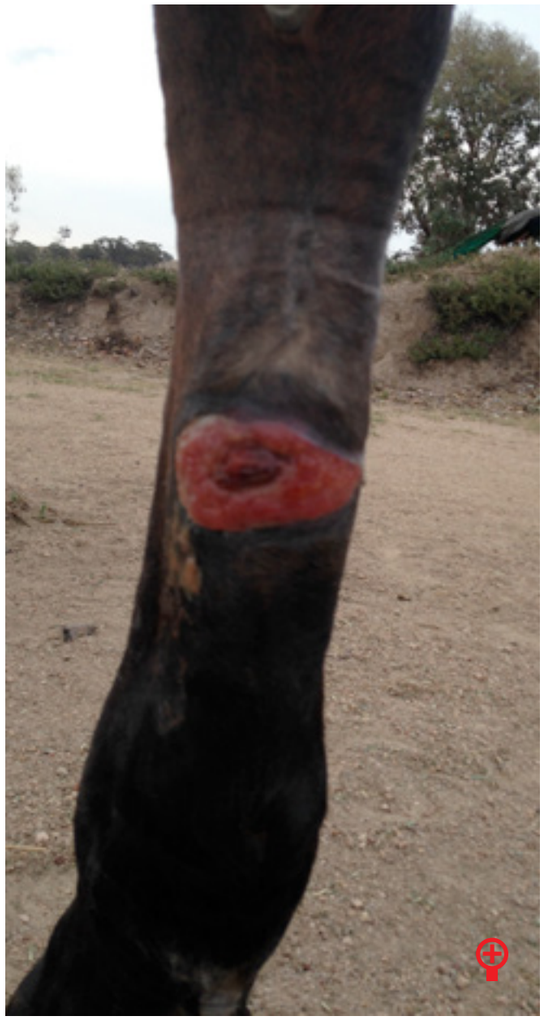


***Figure 3. In late December 2013, after the splints had been applied for over a week.***

is exposed you will see a large gelatinous clot of serous fluid which I feel is pathognomonic. Of course, the tendon sheath will be susceptible to penetrating infection which could spread right down into the hoof so you must keep the wound covered and give high doses of systemic antibiotics.

Once I am sure that infection is controlled, I have found firm pressure applied to the wound will gradually allow the granulation tissue to spread in and fill the defect in the tendon sheath. Those of us who only do mixed horse practice often do not have the confidence to apply a full leg cast, particularly when the horse is quite a distance from the clinic, making supervision difficult. In the past, I have fashioned a 'half leg cast' out of a product like Hexcelite or Vetlite or Askina cast. Once that cast sets, I then get the owners to redress every 2 or 3 days with an appropriate ointment then a strip of cotton wool and gauze roll or Combine dressing on the wound. Then the cast is applied over this and then strapped onto the leg with Elastoplast.

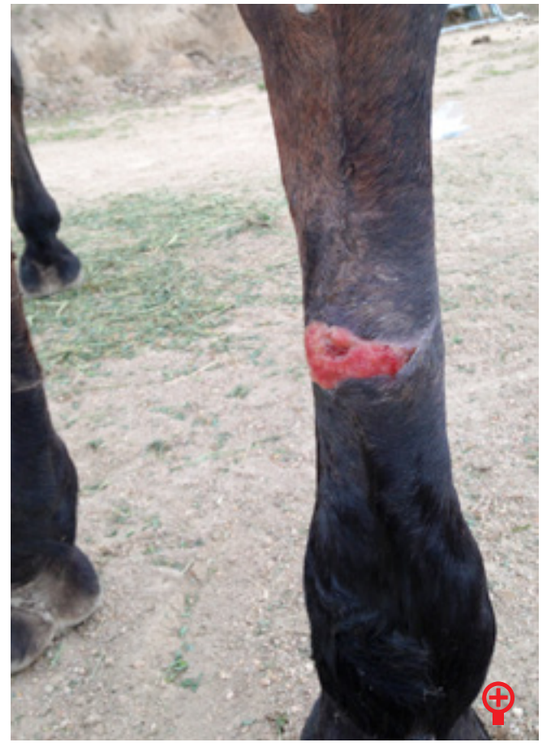


***Figure 4. The wound on 7 January 2014.***

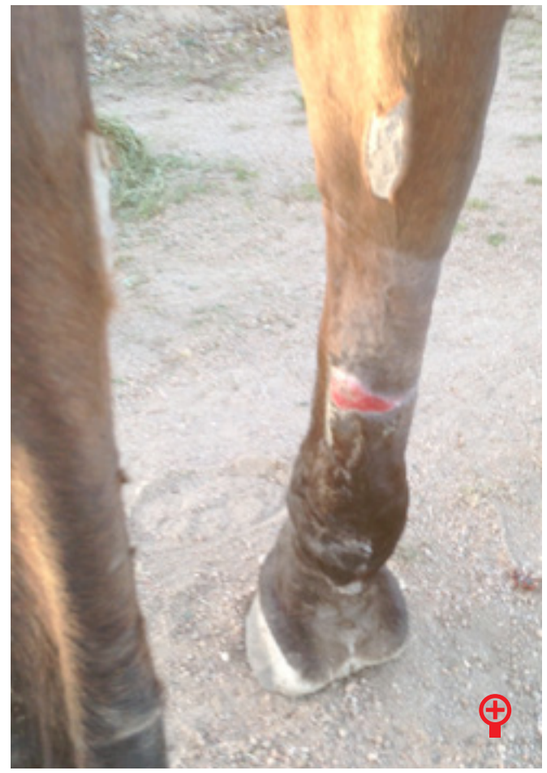


***Figure 5. The wound on 26 January 2014.***

Recently, I had a case with one of these wounds; the horse was 28kms from town and considerable costs had already been incurred with antibiotics, bandages, revisits etc. On my visit just before Christmas, in desperation I gave them 2 pieces of PVC pipe which I had saved for calf splints. I advised the owners to tape those together and strap over the wound as a stop-gap measure until I could get out with some casting material.

The RESULTS WERE SO GOOD that we didn't ever get to make the cast up and you hopefully can see from the attached pictures that the wound healed very quickly under the splint and bandages, once the tendon wound sealed.

However, I must say that a huge factor in the successful treatment was that these owners were particularly dedicated in following my advice in changing bandages, cleaning the wound and giving antibiotics etc. Also, the horse was an excellent patient and tolerated injections and treatments very well.

To summarise my clinical notes, I first visited 'Ned' on 13.11.13; he had been freed from a fence entanglement 3 days before. The off hind leg was now severely swollen and lame with the flexor tendons actually exposed and seeping about half-way between the fetlock and tarsus. Luckily, there seemed to be good warmth in the lower leg so it seemed that the wire had not damaged the major blood vessels.

Ned is a big horse (estimated weight 695 kgs) so the wounds were cleaned as much as possible and poulticed for 2 days then bandaged with Flamazine, cotton wool and gauze roll, and Elastoplast. Initially, the owner and her very efficient family changed the dressings daily then every second day etc as the infection slowly improved.

On the day I gave him 48 mLs of Gentam (100mg per mL) i/v and prescribed 50 mLs of Propercillin be given i/m TWICE daily. Tetanus prophylaxis was also given.

By the 15/11 they reported a big improvement so the twice daily penicillin was given till the 16th, then 50 mLs was given once daily until the 25/11.

When I revisited on 22/11/13 he had improved and was only just lame at the walk. Pieces of skin were now sloughing from the wire encirclement at the front of the leg. The tendon sheath was pouring fluid but it all looked clear so I was very hopeful that the penicillin was controlling the infection.

From the 25/11 I advised to keep bandaging but to now give Benacillin 50 mLs once every 48 hours. I felt it was essential to keep up some antibiotic cover while the tendon sheath was still open and discharging.

They continued with this, giving me regular phone updates until I revisited on the 16/12/13. The lameness was going well but the wound was still leaking copious fluid and had not really closed in at all.

As we were flat out with the pre-Christmas rush, I could not decide when I would be able to revisit to make a half cast so I supplied the owners with the splint and explained how to place it over the cotton wool and gauze then strap it onto the leg with Elastoplast.

The owners reported good improvement with this regime and when I re-examined the leg on 7/1/14 the wound had shrunk significantly with just a small amount of tendon discharge coming from the medial side, so they started placing the splint more on that side rather than directly at the back of the leg. After that, I suggested it should be safe to leave the dressing on for 3 days as the discharges onto the dressing were much less. I advised to continue with Benacillin every third day till all discharge had stopped.

Please note the PVC splints I used were made from 90 mm storm water pipe. I also try to keep some emergency splints of 150mm sewer grade pipe which is thicker and more suitable for splints on adult animals. The annoying thing about making these splints is that when they are split down the middle the resulting semicircle is too narrow to fit on the leg. One must split the pipe into 'thirds' to allow the splint to be flat enough to be strapped onto the leg.

The final photos show the splints on their own, then taped together; they each were 18.5 cms long by 8 cms wide.

Unfortunately we don`t have any pictures of the leg when Ned first presented on 13/11/13. Fig 1 was after a week or 10 days, the initial infection is settling down well but you can see proud flesh forming around the edges while the gap in the middle where the tendon is discharging is actually larger than at the initial visit.

***Figure 6A & B. The PVC splints were made from 90 mm storm water pipe.***

# ANSWER TO WHAT'S YOUR DIAGNOSIS? (C&T NO. 5436, DEC 2014 FROM NATALIE MACNAB)

**C&T NO. 5471**

**Dr. Carolyn O'Brien**
BVSc(Hons) MVetClinStud FANZCVS

Registered Specialist in
Feline Medicine
Melbourne Cat Referrals

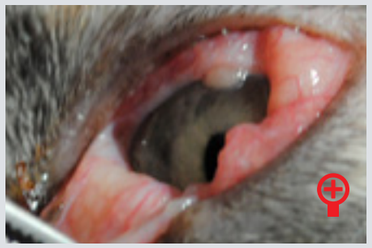


***Figure 1. Swollen conjunctiva lateral canthus. Note discrete paler colour mass upper eyelid which appeared lymphoid in nature.***

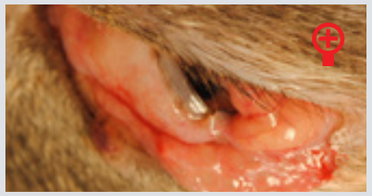


***Figure 2. Swollen conjunctiva lower eyelid near third eyelid.***

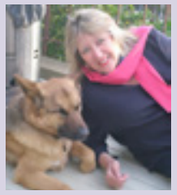
This cat was diagnosed with a mycobacterial infection of the conjunctiva by histopathology (and acid-fast staining). The causative agent was identified via PCR as the novel species provisionally named *Mycobacterium* sp. 'Tarwin' that causes disease in cats typically geographically located in the eastern suburbs of Melbourne, the Mornington Peninsula and the western part of Gippsland, Victoria. (Fyfe, J. A., et al. Molecular characterization of a novel fastidious mycobacterium causing lepromatous lesions of the skin, subcutis, cornea, and conjunctiva of cats living in Victoria, Australia. *J Clin Micro* 2008;46: 618-626.)

Lesions caused by *Mycobacterium* sp. 'Tarwin' are mostly found on the head (including the eyelids, conjunctiva and/or cornea, muzzle/lips, gingiva) and front limbs. This species has not been shown to cause widespread cutaneous or systemic disease.

Definitive treatment guidelines for *Mycobacterium* sp. 'Tarwin' and indeed the other fastidious mycobacteria that cause feline leprosy are yet to be established, because the antibiotic susceptibility of these organisms is largely unknown due to the fact that they are unculturable via current mycobacteriological methods. Clarithromycin combined with rifampicin (with or without clofazamine), ideally with surgical resection of lesions, appears to be the most efficacious treatment regimen. As with other mycobacterial infections, it is recommended that medical therapy be continued for at least 1-2 months past resolution of clinical signs or following resection of all visible lesions.

***Note:** Carolyn is one of our tutors for our Distance Education Feline Medicine course. Registrations are open for 2016 so enrol now at the discounted Early Bird rate. See:* www.cve.edu.au

# INTERESTED IN BEHAVIOURAL MEDICINE?



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## PETS ON PROZAC

CVE's educators, Kersti Seksel, Jacqui Ley and Pauleen Bennett contributed to the 'Pets on Prozac' article which featured in *The Good* Weekend on 21 March 2015. If you missed it, read it in our eBook and view the excellent video featuring interviews with a pet owner and Kersti.

**Read the article**

Watch the interview with Kersti Seksel in our ebook or visit: www.smh.com.au/good-weekend/pets-on-prozac-20150320-13t0yu.html



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**www.cve.edu.au/distanceeducation**

# FROM THE ISFM FORUM – FELINE-MEDICINE FIP & STEM CELL THERAPY

**C&T NO. 5469**

Rachel Payne

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***The CVE & ISFM collaborate in running the DE Feline Medicine program.***
***Early Bird registrations for 2016 now open –***
***See: www.cve.edu.au/defelinemedicine***

## QUESTION

We have a 4-month-old kitten with FIP (actually our head vet's kitten) and have read some articles discussing using mesenchymal stem cells for FIP. We do stem cells here and I'm wondering if anyone had any experience in using stem cells in these types of cases? It is the wet form. IV injection or intraperitoneal as well?

Any input would be very much appreciated.

## REPLIES

### Reply No. 1

**Richard Malik, CVE**

Stem cell therapy is very interesting – I think there is promising early evidence that it is helpful for degenerative joint disease – where the cells set up show as anti-inflammatory cytokine factories. This makes sense, and there is increasing evidence for it. There is a paper by Dow group for its use in renal disease, and another in Quimby's in the *JSAP* concerning cardiomyopathy in dogs where it was not helpful.

But why in FIP? There needs to be either EVIDENCE or at least a conceptual reason for trying it.

### Reply No. 2

**Samantha Taylor**

Samantha Taylor
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European Veterinary Specialist in Internal Medicine
RCVS Recognised Specialist in Feline Medicine
International Cat Care/FAB Distance Learning Coordinator

Rachel – I am interested in what/how you do stem cells in your practice? Agree with Richard that I am not familiar with this treatment in FIP but would be very interested to know what you do use it for and if you have a lab that provides the cells?

### Response from Rachel

Thanks for your input, Sam.

We have in-house stem cell therapy set up (have had it since the beginning of 2012) and have so far done 13 dogs (no cats, but this is the next step!).

We have had huge success with stem cell therapy in dogs for degenerative joint disease. We have to choose our candidates very carefully and they are often those that have exhausted other routes of treatment.

The clients that have taken the leap with us with stem cells (as it is new for us, too!) have been very happy with the results. I was a bit of a skeptic as well, but after seeing the response these dogs have had to it (nearly all of the clients expressing that their dogs are 'puppies again'), makes me a firm believer.

It is pretty expensive but, for the right client and the right dog, such a good investment.

We have had a couple of potential renal failure cats as candidate; however, have not performed stem cell therapy on one as of yet.

My boss had stem cell therapy on his knee and I think this personal experience has made him even more in favour of it.









# DELIBERATE BEFORE YOU MEDICATE (DBYM) – PART 2

**C&T NO. 5470**

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**DELIBERATE BEFORE YOU MEDICATE – PART 2**
1 2 3 4
(C&T No. 5428, Dec 2014 Issue 277)

Many thanks for the lovely letters and emails and phone calls from C&T readers after my first 'Deliberate Before You Medicate' C&T article. I seemed to have touched a nerve whereby practitioners out there are quietly wondering to themselves and concerned about what they are being told to do but are too busy or shy to challenge the *status quo* openly on these issues. So, I will keep stirring the pot a bit more for those of us at the coalface of general practice who end up being the ones left to apply the evidence and face the consequences. Hence, I submit more thoughts re **Evidence Based Medicine** (EBM) and **Practitioner Based Evidence**. As vets, we have enquiring minds, but so often now we get swamped with so much 'targeted' information that we don't get time to sit down and question that what we are told is evidence-based is actually evidence-based.

First, let's look at **tramadol.**

*What evidence was there to start using this in DOGS?*
(Cats and Humans are a different story.)

Very little at the time, it would appear, as there is still very little on this subject in the literature and no historical timeline to back up its use, which did exist for other, older analgesics subsequently abandoned in its favour.

Vets embraced it because of the perceived lack of side effects i.e. gastric ulceration. But is that true? Perhaps if used alone but not if you combine it with NSAIDs, whereas tramadol increases ulceration risk by 28%. Yet recommendations are that tramadol in dogs probably should not be used alone (*cf* below) but combined with an NSAID – which brings us back to a heightened risk of gastrointestinal tract ulceration than if we didn't use the Tramadol at all, so why bother to dispense it? A case series in humans identified that patients prone to gastrointestinal (GI) adverse effects of NSAIDs had a higher risk of GI perforation caused by tramadol administered alone. The mechanism of action is thought to be serotonin-enhanced gastric acid secretion through vagal stimulation. The advice is to add in a proton pump inhibitor (PPI)! My view on PPIs in our pets was dealt with in part 1 of DBYM. The use of a PPI in our pets in this instance, in my mind, would be a case of polypharmacy gone mad simply because a vet thought it would be EBM and a good thing to use tramadol in a dog.

What other concerns could there be? For starters, it lowers the seizure threshold for one, so caution is advised for at-risk dogs.

**What about drug interactions? Be really careful using tramadol combined with drugs likes Clonicalm® (clomipramine hydrochloride). Reconcile- (Fluoxetine hydrochloride) Plavix®clopidrogel that you don't induce distressing serotonin syndrome. Also, take care with Ondansetron?**

What about analgesic efficacy? Tramadol is a centrally-acting analogue of codeine (more on codeine later) with 2 modes of action. Tramadol and the O-d metabolite have a higher affinity for Mu and Delta receptors than Kappa opioid receptors and also inhibit norepinephrine and serotonin uptake in CNS.

*VCNA Small Anim Pract.* 2013 Sep;43(5):1109-25.
*Pharmacokinetic studies in dogs have shown that dogs do not produce ODM as a substantial metabolite after tramadol administration; however, they do produce DDM.[1]Therefore dogs are not expected to have substantial opioid effects after tramadol administration. Plasma concentrations of tramadol after administration of 10 mg/kg by mouth to dogs were slightly less than the plasma concentrations achieved in humans administered 100 mg single doses, but the concentration of ODM was 10 times less in dogs compared with humans.* ***The elimination half-life of tramadol in dogs is more rapid (1.1 hours) compared with humans (5.6 hours****). The production of DDM, which has an elimination half-life of 3.6 hours in dogs, may produce some opioid effects in dogs. Repeated doses of tramadol either decreased drug absorption or enhanced presystemic metabolism of tramadol in dogs, in which a 60% to 70% decrease in tramadol plasma concentrations resulted after just 8 days of treatment (20 mg/kg by mouth).*

In humans, tramadol can trigger spectacular orthostatic or positional hypotension. Does this occur in dogs? Again, no-one I knew using it had blood pressure machines on the patient. Is the MI metabolite the cause and hence postural or standing hypotension not an issue in dogs? Again, no-one I have asked can answer this. Is analgesia misread where the dog simply cannot remaining standing so lies 'calmly' up? As an esteemed colleague wondered aloud to me: Is this similar to how we once duped ourselves that ACP worked in thunderstorm phobia when all that happened was the poor dog lay there paralysed and terrified? Is the post-op tramadol dog not moving because as soon as it attempts to stand its blood pressure crashes so it lies there supposedly pain-free but, in fact, in pain and in distress? If you use this drug, you should be monitoring blood pressure in these patients not just under general anaesthetic but when the animal is awake and in recovery.

Recent papers using tramadol post tibial plateau levelling osteopathy versus Firocoxib versus combination showed the tramadol cohort were more likely to require rescue

analgesia that the other groups. At the 3 day follow-up, the recommendation was not to bother with tramadol alone or in combination – just use the NSAID!

One study found it effective in the setting of cancer but the drug was given in combination with other analgesics so sole efficacy was not determined by Fior et al.

Other studies suggest it's best not to use it alone and when you do use it then its needs to be given often – around 4mg/kg tid.

Personally, I can't see the point other than deluding ourselves and the owners of our canine patients that we are giving effective safe analgesia when, to my mind, the evidence is not yet there; there are, however, several real concerns but no real historical timeline as yet.

Yet, why does everyone I spoke to thus far who uses this drug not know the answers to these basic questions when using such a supposedly 'evidence-based' analgesic? I initially get derisory looks from others when I declare I don't use tramadol as if somehow I am a bad vet not embracing and practicing good medicine, evidence-based medicine. Their derision quickly changes to concern and self-doubt when I raise my concerns regarding the investigative due-process vets need to apply as a default process to any new medication/procedure so as ensure a 360 view of any concept, good or bad.

Overseas, the drug has now been changed to an equivalent of S8 due to its highly addictive properties – not something I want to start home-dispensing for chronic pain if the opportunity for human self-abuse is so high.

*The feline vets have done a globally remarkable job in the last 15 years emphasising that Cats are not shrunken Dogs . It's now the turn of the canine vets to step up to the plate and emphasise that Dogs are not oversized Cats.*

Moving on to **Codeine**.

Not all opioids are equal to all pain targets.

In people, codeine is metabolised to morphine. As many vets know only too well from their own migraines – not all opioids are equal. When a migraine escapes so that codeine or morphine doesn't hold the pain, pethidine will do it superbly. Equally, codeine is not the best analgesic for intervertebral disc disease (IVDD) in humans – NSAIDs and oxycodone (Vicodin) are much more effective but again, need to be part of a multi-discipline therapy, never just depending solely on drug therapy.

Given all that, why then is codeine given to dogs with IVDD? Is it an effective analgesic in these cases? Is it fair to give a dog with disc disease drug-induced constipation? Where is the evidence for its use?

The evidence that is available suggests that much higher doses, up around the 60mg mark, need to be used. At that dose you will get constipation and, if so, in an IVDD case the use of such a drug is cruel!

I have some of the most loyal clients who came in desperation because of the non-responding IVVD pain in their dogs – all on codeine. Clients know about codeine so, again, when it doesn't work, things must be bad!

So when I stop the codeine and implement other strategies and their pets get to be ambulatory and pain-free again, those clients think I am a miracle worker. Which I am not, just someone who fits the analgesic to the patient and the case every single time; no protocols, no recipe medicine, but targeted medicine, often old-fashioned practice-based evidence, but mostly with no less evidence that what claims to be evidence-based medicine.

So, before we 'throw the baby out with the bath water' and discard historically proven approaches in the face of Evidence-Based Medicine protocols, let's make sure the latter actually has acceptable evidence other than sounds-good modern-feel sound thoughts behind the approach.

**FURTHER COMMENT ON MY C&T NO. 5410**

## Questions for Clopidrogel Users

I noticed the 'Further comment on my C&T NO. 5410' in Issue 277 Dec 2014 from Jim Euclid (expanding on his C&T 5410 in September 2014) stating he uses the drug twice a week at 10-20mg/kg.

Equally the drug has been used overseas for some years now but at 18.75mg/kg doses daily.

Jim compares it to aspirin, hence the 72hr interval. However, clopidrogel acts at a different point in the clotting cascade, acting as an inhibitor of adenosine diphosphate receptor (P2Y12) on platelets whereas aspirin is a cox inhibitor, reducing production of thromboxane -A2(TXA2) which is required for platelet aggregation, ideally at a dose that doesn't change prostacyclin concentrations. One cannot extrapolate the t½ of one drug acting in one pathway and presume another drug in another pathway has the same t½, especially in cats. Aspirin itself has a t½ of approximately 2hrs in humans, 4hrs in dogs yet closer to 72hrs in cats.

So what is the t½ clopidrogel in cats? t would appear no one knows!

Without knowing the true feline pharmacokinetics of this drug, it seems Jim is just as entitled to give his drug twice a week with minimal hassle and cost and probably better compliance that those who equally can validate daily administration, based on the initial trials. (I had colleagues overseas track down some of the original workers on clopidrogel and even they don't know the half-life of the drug in cats).

Evidence is now needed on what the t½ lives and bioactivity actually are for this drug in cats. This would make a great research project for students as cats and owners would benefit greatly from appropriate evidence-based dosing regimes.

Leaving the dosage questions aside: When do we actually prescribe the drug? The original basis was of use only at the low dose and only as a preventative. The criteria were not '*the presence of a murmur but rather a history of previous or on-going thromboembolic disease, evidence of severe left atrial enlargement, the presence of atrial fibrillation (which is rare in cats), or echocardiographic evidence of spontaneous echo-contrast in the left atrial cavity (a.k.a. 'smoke' or 'snow'), all of which reflect stasis of blood flow and are therefore risk factors for thrombus formation.'* One can also find some data about this at: **www.vet.cornell.edu/news/FatCatStudy.cfm**

Should we give clopidrogel with aspirin? Not instead of, OR only give clopidrogel? Or is there now a suggestion from the FATCAT study that some cardiologist suspected that aspirin does not prevent the atrial clots in cats? So, if you want to prevent atrial clots do you use Plavix® (clopidrogel) and forget the aspirin totally?

## Other clopidrogel facts

Drug interactions: The drug does have some significant drug interactions with the PPI like Losec, Nexium etc so one needs to be prescribing 2nd gen PPIs instead so as not to inhibit the actions of clopidrogel.

I personally need to be provided with much more evidence about the how, when and why to use this drug than is currently the situation.

## Stilboestrol® for Canine Urinary Incontinence

Hold onto your hats on this one whilst I heretically explore the 'facts' on this drug.

Ah, how I do love the myths – oops, sorry, the 'facts' about this drug. Either this is the most toxic drug on the planet according to what we have been told about it or it is, in fact, one of the safest…

Why?

First, let's all acknowledge the elephant in the room. This drug has been, and continues to be, used effectively and affordably for decades in millions of cases of urinary incontinence, right up to the present day.

This drug is LICENCED for use in Australia for oral use in small animals so we are not using it off-label or out of species when used in dogs. We are allowed to use it.

Allegedly, this drug can cause bone marrow suppression. It does – but you have to give it every day! Yes, it's a powerful hormone and we do need to respect it in every aspect, from handling to when and to what patient it is dispensed. But – has any practitioner ever seen bone marrow suppression with this drug when used for canine incontinence? And, if so, did that adverse drug reaction occur using the 5mg high doses or with the 1mg daily x 3 days then every 3rd day until condition ceases regime?

I ask because when the very big push came about 15-20yrs ago for 'Good vets' to use synthetic, expensive, hormone analogues (around the time of the new drugs' launches), I canvassed several international vet forums. Yet – NOT ONE VET has ever seen the issue! I followed up this year with another survey – same results. The only time an adverse drug reaction issue was seen was in 2 cases where 20x oral dose was given repeatedly by a human medic or an off-label mis-mating use of injection was not only given but repeated! Otherwise, no adverse drug reactions.

Lappin 1989 and Barsanti 1983 recommended it as the drug of choice for incontinence in dogs as 0.1-1mg/kg for 3-5 days and as required thereafter.

So, why the scare mongering? The 'practice based evidence' suggests Stilboestrol® used wisely at low doses must be one of THE safest drugs on our shelves but we are 'told' the opposite and told to use more expensive alternatives. Yes these alternatives carry their own risks – Pseudofed and Propalin both have hypertension concerns. So Why are we lambasted for using Stilboestrol®?

What hard, cold, power statistics does anyone who pushes the anti-Stilboestrol® warning have, that shows this drug to be so dangerous as to be avoided; especially when the stats for other drugs are much worse but don't have the same bad press.

Stephen Page did a superb job (no surprises there) in reviewing this topic for the AVA in *AVJ* 1991. Page's conclusions* need to be taught to every vet student as a given from the clinical front-line experience of practitioner-based evidence validates his statements close to a quarter of a century later.

I quote : '*DES has certain advantages in being orally bioavailable with a short half-life***. *Short courses administered outside the luteal phase have not been associated with adverse side effects.'***

Given that 99% of the incontinence we see is in desexed females, then we need to recalibrate the amount of angst we self-inflict when dispensing this medication.

Incontinence will lead to euthanasia of a family pet in far greater numbers than the statistical risk of an adverse drug reaction from Stilboestrol®.

All my clients are given the 4 options for incontinence control; all explained, success rates and risks explored, daily costings outlined and then the client chooses what they can afford and wish to use. About 90% choose Stilboestrol®, about 9% choose the highly effective but costly Propalin and the remaining 1% pick a selection of other meds/surgery options/ benign neglect. In 30 years, I can't think of another drug that has given me less trouble – yet using it makes me a 'Bad Vet'.

## PPIs Proton pump inhibitors continued

My views on these are expressed in first part of my DBYM article, so I have been now asked what I do use. That would be cautious low doses of Ranitidine (Zantac) which, despite the need for care in renal cases, will however get many renal uraemic patients eating again. It would appear to target the uraemic gastritis and nausea superbly and brings quick and great relief to the dog and cat. You do need to check blood pressure and also do an ocular check as glaucoma at high, long doses has been recorded. Also, I'm finding it superb for the canine reflux/gagging drinking water cases that are controlled cheaply on just this drug for years. Dose changes between species, and in rabbits you need to use a higher dose.

| | |
|---|---|
| Rabbits | 4-6 mg/kg bid-tid |
| Guinea pigs | 5 mg/kg bid |
| Dogs | 2 mg/kg bid-qid |
| Cats | 3.5 mg/kg bid |

## Activyl® and Bravecto® single packs

Let's end on a positive note.

The definition of good business practice is to find and exploit a niche good or service that the opposition isn't catering for, and provide it.

MSD seems to have embraced this theory whilst listening to what we, as front-line vets, need and they produce their products in single packs. *Many vets seem to be unaware that our right to prescribe and our privilege to dispense does not cover the off-label use of S5s – i.e. you can't sell any S5 Comfortis etc singly out of their proper packaging.* Whilst some might think they will never be caught doing so – the reprehensible, unethical action of splitting an Advantix pack may lead to the suffering and death of a cat against which you don't have a legal leg to stand on. That said, it is also so

frustrating for front desk staff to spend valuable time advising a walk-in client on the correct flea control only for that person to walk back out without a purchase as they 'only want one' and 'the vet/pet shop down the road' will split the pack for them. Since Activyl® has come on the market in single packs, we have been able to successfully complete every enquiry at our front desk. So, whilst Bayer's Advantage range remains my preferred flea product, Activyl® has filled a void in our anti-flea service. I am equally pleased to hear MSD's Bravecto® tick product will also be in a single, non-scored, one animal single dose packing thus eliminating stress and lost time at front desk. Thank you MSD for listening to what vets want BEFORE you apply for registration sizes and dose regimes from thyroid medication to parasitic control.

*But, best of all practitioners, use the best piece of equipment you own - **Your own Voice**, which follows this article here. Clayton blood testings will be covered in Part 3 DBYM.*

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**ADDITIONAL REFERENCES**


***Note: I'd like to acknowledge and thank James Dunne MVB CertSAS MRCVS, Ark Vets Knocknacarra, Unit 3 Millers Hall, Western Distributor Road, Galway Republic of Ireland T. 00353-91-510131 www.arkvetsgalway.com for generously collating these references for me to support my C&T article.***



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# INVITED COMMENTARY COURTESY OF:


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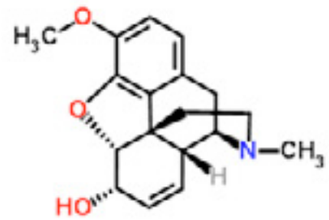
## TRAMADOL NOTES

Tramadol

2-[(Dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol

*Stars indicate chiral carbons*



Codeine

(5α,6α)-3-Methoxy-17-methyl-7,8-didehydro-4,5-epoxymorphinan-6-ol

### HISTORY

Tramadol, a centrally acting analgesic of the aminocyclohexanol class with opioid-like effects, was first synthesised in 1962 (at Grunenthal in Germany) (Buschmann 2013) and is a racemic mixture of the 2 enantiomers, (+)-tramadol and (-)-tramadol. Structurally, as presented in the figure, tramadol and a typical opiate codeine, are very different – yet some structural features are shared and may be important in determining mode of action. In 2013, tramadol was unexpectedly found in the root bark of an African medicinal plant with a history of use for pain relief (Boumendjel et al 2013). However, this surprising finding may have been due to plant uptake of tramadol present as a contaminant of surrounding soil (Kusari et al 2014). Tramadol is used in humans for the relief of moderate to severe pain. There are no preparations of tramadol specifically registered for use in veterinary species though tramadol is finding increasing use in dogs, cats, horses, birds, reptiles and zoo, exotic and wildlife species.

### MODE OF ACTION

Tramadol is unusual amongst analgesic agents in having a multimodal pharmacological mode of action (MOA) – while it has a weak affinity for the μ opioid receptor (6,000 fold less than the affinity of morphine), there is clear evidence of an important non-opioid MOA based on studies demonstrating (i) lack of naloxone reversibility; (ii) lack of significant naloxone-induced withdrawal; (iii) production of mydriasis (rather than miosis); and (iv) attenuation of its antinociceptive or analgesic effect by serotonin or adrenergic antagonists (Grond and Sablotzki 2004).

Of all the tramadol metabolites (and there are many) the O-desmethyl metabolite (M1) has the highest affinity for the μ receptor but this is still much less than that of morphine.

Tramadol inhibits the neuronal reuptake of noradrenaline and serotonin (5-hydroxytryptamine, 5-HT). These monoamine neurotransmitters are involved in the antinociceptive effects of descending inhibitory pathways in the central nervous system. The α2-adrenoceptor antagonist yohimbine and the serotonin antagonist ritanserin block the antinociceptive effects of tramadol, but not those of morphine.

Importantly it has been bound that each of the isomers of tramadol have distinct actions. For example. (+)-tramadol has a 2- fold higher affinity for the μ opioid receptor than the racemate.

### DOG STUDIES – PHARMACOKINETICS

The pharmacokinetics (PK) of oral, IV, rectal and epidural tramadol in dogs has been studied (Giorgi et al 2009; Lebkowska-Wieruszewska et al 2009; Carlo et al 2010; Giorgi et al 2011; Giorgi et al 2009; Lintz et al 1981; Saccomanni et al 2010; Wu et al 2001; Buhari et al 2013; Giorgi et al 2009; KuKanich and Papich 2004; Sousa et al 2008; Vettorato et al 2010; McMillan et al 2008) including studies looking at the effect of surgery on tramadol PK and the effect of co-administration of grapefruit juice. The metabolism of tramadol in dogs is quantitatively different to many other species including humans and little M1 is evident. If tramadol is nonetheless effective this may depend on the non-opioid MOA.

### DOG STUDIES – EFFECTIVENESS

A number of studies have found the use of tramadol either alone or in combination with other agents to be effective in alleviating a variety of painful conditions or lowering anaesthetic MAC when administered to dogs by oral, IM, IV, SC or epidural (Albuquerque et al 2013; Almeida et al 2009; Almeida et al 2010; Borges et al 2008; Buhari et al 2012; Caldeira et al 2006; Canuta et al 2012; Carareto et al 2008; Cardoso et al 2014; Cardozo et al 2014; Carlo et al 2009; Choi et al 2011; Clark et al 2011; Costa et al 2014; Evangelista et al 2014; Fajardo et al 2012; Flor et al 2013; Guedes et al 2002; Guedes et al 2005; Gupta et al 2009; Halder and Bose 2000; Itami et al 2013; Kongara et al 2009; Kongara et al 2012; Kongara et al 2013; Kukanich and Papich 2011; Lopez et al 2012; Lu et al 2014; Mahidol et al 2015; Malek et al 2012; Martins et al 2010; Mastrocinque and Fantoni 2001; Mastrocinque et al 2003; Mastrocinque et al 2012; Melanie and Portela 2007; Mondal et al 2005; Mondal et al 2006; Morgaz et al 2013; Nam et al 2013; Natalini et al 2007; Natalini et al 2007; Neves et al 2012; Paolozzi et al 2011; Sandoval et al 2010; Santos et al 2013; Seddighi et al 2009; Silva et al 2008; Stanescu et al 2013; Teixeira et al 2013; Verdier et al 2013; Yazbek and Fantoni 2005; Zulch et al 2012). However, not all studies demonstrated acceptable levels of pain relief (Davila et al 2013; Delgado et al 2014; Kogel et al 2014; Kongara et al 2010).

### DOG STUDIES – SAFETY

The safety of tramadol in the dog and situations where care needs to be taken or situations where use should be avoided have been demonstrated by a number of investigators. For example, no adverse haematological and biochemical effects observed after short term IM treatment of dogs with tramadol at 1 and 5 mpk q24h for 5 days (Akhtardanesh et al 2014). No adverse effects on innate immunity development following exposure to tramadol (Axiak-Bechtel et al 2015). Tramadol appeared safe in dogs undergoing surgery under pentobarbitone anesthesia (Buhari et al 2012). Alert to potential interactions of tramadol and selective serotonin reuptake inhibitor (SSRI) exposure (Fitzgerald and Bronstein 2013). Tramadol did not adversely affect the gastric barrier function in dogs (Hill et al 2014). No adverse effects on the cardiovascular system in dogs anesthetized with sevoflurane (Itami et al 2011). Seizurogenic potential of tramadol highlighted (Kim et al 2011). Tramadol use associated with potentially beneficial increased respiratory volume and rate in anesthetised dogs (Osterloh et al 1978).

### CONCLUSION AND RECOMMENDATONS

The C&T article by Aine has raised an extremely important point applicable to many drugs that have not been systematically tested for use in animals, especially those drugs with significant PK differences compared with the species for which the drug is primarily indicated – in this case humans. The literature describing the use of tramadol in dogs is growing and suggests that there are circumstances where tramadol could be used safely and effectively. But which circumstances are these and how does the clinician determine the balance of benefits and risks? Certainly there are situations where tramadol should not be used or if used must be done with great caution and vigilance. In the end, the growing literature needs to be critically appraised and those situations where it can contribute positively to canine health and welfare clearly described. A review of tramadol would make an excellent Cochrane-type review – but who is going to perform this important task?

**Note:** Stephen has provided a comprehensive reference list which, due to space constraints, is available in the eBook.

# INVITED COMMENTARY COURTESY OF:

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***Tanya Stephens*** *BVSc MANZCVS (Animal Welfare) is a small animal practitioner based in Sydney. She has an active interest in veterinary ethics and evidence-based treatment, and her publications on these topics include 'Veterinary Ethics' in Peter Bowden (ed), Applied Ethics: Strengthening Ethical Practices (Tilde University Press, 2012), 'Needless Treatment of Pets', Australasian Science, July/August 2014, and numerous presentations (including at the AVA Conferences in 2013 and 2014).*

## COMMENT ON TRAMADOL USE

I am a small animal practitioner with my own practice with a particular interest in veterinary ethics and Evidence Based Veterinary Medicine (EBVM).

When I came across Tramadol being used on dogs some years ago, I did what I have always done, I went searching for information. I undertook a literature search and found no evidence for its effectiveness in dogs. I haven't quite understood why it became popular with such scant evidence. It goes without saying that Tramadol has never been used at my practice.

A recent study, (Holford, S. et al (2014) 'Parent-Metabolite Pharmacokinetic Models for Tramadol - Tests of Assumptions and Predictions', *J Pharmacol Clin Toxicol* 2(1):1023) concludes 'There are substantial differences between species in the pharmacokinetics of Tramadol and it's primary metabolite.....M1 exposure in the goat, donkey and cat was comparable to humans, which indicates it is likely to be an effective analgesic at typically used doses in these species but not in dogs or horses'.

The use of any therapy shown to be ineffective is not in keeping with the scientific basis and expectations of the veterinary profession and there are animal welfare and ethical implications for such usage. It is of particular concern that an animal in pain would be given an ineffective therapy. It is really not good enough for a clinician to rely upon

someone's opinion that Tramadol is OK for dogs. If evidence based medicine is replaced by 'opinion based medicine', we lose credibility as veterinary scientists and any legitimate claim to be the primary source of information and views on animal health and welfare.

Which brings me to the important topic of EBVM. EBVM is the use of best relevant evidence in conjunction with clinical expertise, to make the best possible decision about a veterinary patient. The use of EBM has already led to better outcomes for human health.

The use of EBVM, similarly, has the potential to significantly improve animal health and welfare. Any initiative that makes clinical decision making easier and more robust will have the added benefit of improving the veterinarian's health and welfare!

It is unfortunate that some of the information that is available to vets is inaccurate. For example, the WSAVA Guidelines on Pain (2014) lists Tramadol for pain relief in dogs and a section of the Guidelines relate to the use of 'metaphysical effects' for pain relief!!! These guidelines would have benefitted from a good dose of EBVM.

There is today a vast amount of veterinary scientific literature. And it's growing. The busy practitioner would find it difficult to trawl through and assess this information to determine the 'best' therapy, which is why EBVM resources are so important.

For the practitioner there are some excellent EBVM resources available and the Royal College of Veterinary Surgeons is at the forefront with the RCVS Knowledge EBVM Network. The EBVM Toolkit from RCVS Knowledge is designed to help busy practitioners answer a clinical question with the best available evidence. www.knowledge.rcvs.org.uk/evidence-based-veterinary-medicine/ebvm-toolkit/

## VETS WORLDWIDE ARE INVITED TO BE PART OF THE EBVM NETWORK.

Please go to the eBook version to read the list of other EBVM resources provided.

These resources, enable clinicians to easily access systematic reviews without needing to undertake their own. I really like BestBets for vets and check it often for the latest reviews as these are regularly updated.

Skeptvet which is produced by the US based EBVM Association has a wealth of information and you can join the EBVMA to keep up to date and join in discussions. This group is very much practitioner focused.

Always keep in mind, of course, 'clinical expertise' in EBVM decision making and don't forget the client, the important third party in ethical decision making, and the one who pays the bills!

For more resources of interest, non veterinary organisations promoting EBM include the UK based group Sense about Science and the Australian group Friends of Science in

Medicine, which has over 1000 members including Gustav Nossal and Peter Doherty.



# INVITED COMMENTARY COURTESY OF:

**Richard L'Estrange**
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I would like to thank the CVE for very kindly inviting me to comment on C&T # 5470, submitted by Dr Aine Seavers.

I commend Dr Seavers for encouraging veterinary practitioners to constantly question the dogmas and trends that appear from time to time in veterinary practice and to do their own research and investigation of the literature. In my practice at least (when I had one), the use of tramadol was borne out of the frustration of 'what else can we do?' for arthritic dogs in particular whose pain was either not well controlled on NSAIDs +/- other modalities, or who could not receive NSAIDs for some reason. It seemed a sensible idea to try this non-controlled human opioid which could be given orally and there seemed at the time to be no reason why it would not be both safe and effective. Decision-making regarding the use of pharmaceuticals should centre on efficacy and safety in the target species. Whilst cats are not small dogs, it might equally be said that dogs are not small humans and may not even be large rats or mice.

I cannot for one minute claim to be an expert on tramadol, but from my reading on the topic I have the following concerns:

The drug is currently unregistered but available for use in dogs and cats in Australia under APVMA permit 14727. This permit mentions a number of contraindications, precautions and side-effects that practitioners should be aware of.

Some basic assumptions surrounding the use of tramadol in the dog derive from rat, mouse or human studies.

The metabolism of tramadol is complex and there is significant pharmacokinetic variation between individuals or possibly breeds which may explain the variable clinical results anecdotally observed in dogs.

Conclusions drawn from efficacy studies in dogs may be confounded by the use of concurrent analgesics.

There needs to be more work done regarding the safety of concurrent NSAIDs and tramadol in my opinion. There are papers involving rats, humans and dogs that give cause for concern.

There is a spectrum of adverse events reported to be associated with the use of tramadol in the human literature that gives cause for concern regarding the safe prescribing of the drug by veterinarians.

With these issues in mind I support Aine in encouraging practitioners to look critically at the use of tramadol in dogs and to examine the evidence themselves before deciding upon its continued use within their practices.

(The author is an employee of Zoetis Australia Pty Ltd however the opinions expressed within the above text are the private opinions of the author and not the opinions of Zoetis)



# ANSWER TO **WHAT'S YOUR RADIOLOGICAL DIAGNOSIS?**

## (C&T NO. 5463 MAR 2015)

**C&T NO. 5471**

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**Background history for the case:**

'Billy' was a 12yo entire male Dachshund, presented for work up of an inspiratory wheeze, coughing and a dental procedure. Routine bloods were run, revealing a mild increase in ALKP = 220, with no other abnormalities on the CBC/biochem. Thoracic radiographs where also performed revealing a diffuse radio-opaque change to the liver.

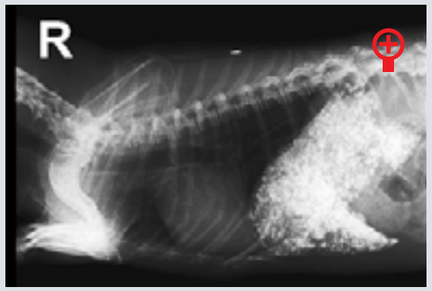


***Figure 1. Right Lateral thoracic radiograph***

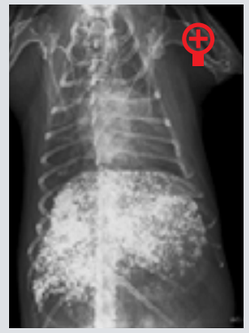

***Figure 2. DV thoracic radiograph***

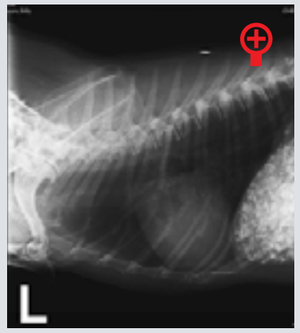


***Figure 3. Left Lateral thoracic radiograph***

## DIAGNOSIS:

**Provided by an imaging specialist:**

Idiopathic hepatobiliary mineralisation – almost always an incidental finding and unrelated to the reason for presentation. Wedge biopsy would be required to characterise the location of mineralisation better; however, in most cases like this, dogs are well and further investigation is unwarranted.

# OROFACIAL PAIN SYNDROME IN A 7-WEEK-OLD KITTEN

**C&T NO. 5472**

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On 4 December 2013, a 7-week-old female DSH rescue kitten (in care) came in with a history of furiously pawing at her face for 24 hours. She had been vaccinated with an unknown vaccine (F3) by the head carer 1 week prior. At this point, she had moist erythematous skin on either side of her face and evidence of self trauma. There was ulceration of her tongue suspicious for Calicivirus infection. There was no history of access to any caustic substance. No fleas were seen. She was started on doxycycline paste approximately 8 mg once a day (1/3 notch) and an E-collar placed.

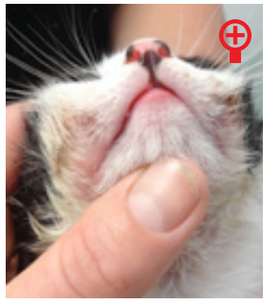

***Figure 1a & 1b. On day of first presentation.***

The next day she came back in as was much worse; she'd been furiously ripping at the E-collar then furiously clawing at her face overnight which was extremely distressing for all to see.

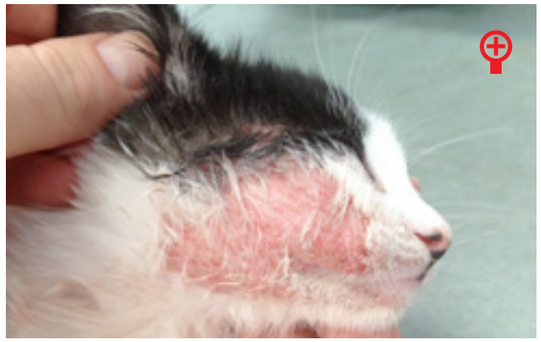

***Figure 2 . Day 2-The day after starting doxycycline only.***

A presumptive diagnosis of orofacial pain syndrome associated with Calicivirus was made.

I elected to crush a 30mg phenobarbitone tablet between 2 teaspoons and then poured the powder in to a 3mL syringe and mixed with 1 mL of water to give (after shaking) a suspension of roughly 3mg/0.1mL. I gave 0.1mL to start and asked the carer to wait while I considered options.

Adding in famvir 1/4 tablet once a day was easy but I was a little uncertain about dosing with opiates with such a little kitten. I discussed the case with Andrea Harvey at SASH and we decided that buprenorphine 0.05mL (20ug/kg) would be good so the one mL ampoule was drawn up in to 20 x 0.3mL 100iu/mL insulin syringes. 5 units in each. I showed the carer how to break off the needle, check that the end felt smooth and then to squirt the contents into the side of the mouth.

The final regime for medication was:-

- famciclovir 125mg 1/4 tablet once a day 8 days
- doxycycline 100mg/g paste 1/3 notch (approx 80mg ) once a day 2 weeks
- buprenorphine 20ug/kg twice a day 10 days
- phenobarbitone 3mg twice a day 10 days

Thankfully this combination worked really well and one week later the kitten was MUCH improved and there was no relapse as the medications were dispensed.



***Figure 3. The 300ug buprenorphine ampoule divided in to 20 0.3mL 100u/mL insulin syringes.***

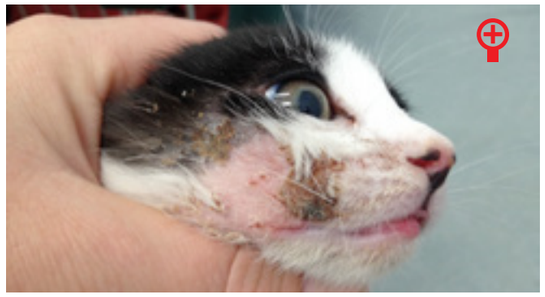

***Figure 4. Skin healing well and kitten comfortable and happy. The hair fully regrew.***

*Acknowledgement: Thank you Andrea (Harvey) for your phone consultation with regards to this case.*

# TWO CASES OF FELINE LEUKAEMIA VIRUS INFECTION IN A REGIONAL CITY – OR WERE THEY?

**C&T NO. 5473**

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**This article describes 2 unrelated cases of FeLV-like disease which initially tested positive for FeLV but subsequently, on further work up, were determined to be FeLV negative. They are a powerful reminder of the need for confirmatory testing whenever FeLV infection is suspected.**

## CASE 1 (Marshall Thornton):

'Skittles' was a 3-year-old male neutered DSH. He presented with a 4-day history of weakness, lethargy and inappetence. The owner works for a local private zoo, and regularly has snakes, reptiles, birds, and marsupials under care at home. Skittles had been an indoor only cat for about 6 months; however, prior to this, with another owner, he had been allowed outdoor access and had a history of fighting. He was the only cat in the house.

On physical examination, Skittles was depressed, had white mucous membranes with indiscernible capillary refill, was 8-10% dehydrated, and was slightly hypothermic (rectal temperature 37.6°C). Abdominal palpation was unremarkable except for a painful right kidney on palpation.

In-clinic laboratory testing revealed:-

- Urinalysis of a cystocentesis sample was fairly unremarkable ('large' leukocytes, although significance of this finding using a dipstick was questionable)
- Mild pre-renal azotaemia
- Mild hyperglycaemia
- Mild hyperbilirubinaemia
- Severe anaemia 0.07 L/L

Blood was collected and sent to Vetnostics for haematology and feline retroviral testing.

I had a cat with severe anaemia of unknown aetiology – no history or physical findings suggestive of trauma or haemorrhage, and no access to rodenticides or venomous snakes. The severe anaemia and hyperbilirubinaemia made me think of haemolysis and especially haemotropic *Mycoplasma sp*.

While waiting for results from Vetnostics, I started treating the life-threatening anaemia with a fresh blood transfusion. A friend of the owner supplied a healthy 4.5kg cat to be the blood donor. I used a 60mL syringe containing 6mL of citrate phosphate dextrose anticoagulant which I took from a 450mL blood collection bag. I collected 45mL of blood from the donor cat's jugular vein under light sedation with alfaxalone (Alfaxan CD®, Jurox). The blood was transferred to a freshly emptied 100mL 0.9% NaCl bag. Skittles was transfused at 25mL/hr using a Nikki infusion pump via a catheter in his left cephalic vein. I also administered 1.25mg dexamethasone SC (Dexapent®, Ilium, 0.25mL) and 25mg enrofloxacin SC (Enrotril®, Ilium, 0.5mL).

The following morning I received the following report from Vetnostics:-

- FeLV antigen POSITIVE (serology, ViraCHEK, Synbiotics Corporation).

## Comments (Dr K Todhunter):

'There is a severe non–regenerative anaemia with large numbers of erythroid precursors including blasts in the peripheral blood strongly suggestive of Acute Erythroid Leukaemia. Some aspects of the haematology fit including the mild thrombocytopaenia, neutropaenia, and mild lymphocytosis along with the age (3 yrs). There has been a loose association of this condition with FeLV but not in every case. These cats often have enlarged spleens with normal sized lymph nodes.'

Skittles was much brighter the following day but was discharged with a grave prognosis. Further work-up of his painful right kidney, including ultrosonographic imaging, was declined by the owner.

Skittles was well at home for a few days; however, he deteriorated quickly and 8 days later was euthanased.

## CASE 2 (Marshall Thornton):

'Tibbles' was a 4½-year-old male neutered DSH. Coincidently, Tibbles had been adopted from the same local pet store as Skittles, however several years apart. Tibbles presented with a recent history of weight loss, lethargy, reduced appetite and aggression. Tibbles was an indoor-only cat and the only cat in the house.

On physical examination, Tibbles had pale pink mucous membranes, delayed capillary refill (4 seconds), tachycardia (HR 200) with an intermittent mitral murmur and pyrexia (rectal temperature 40.5°C).

At the top of the differential list at this point in time was a cardiomyopathy or bacterial endocarditis. Offered a complete work-up, the owners declined and instead requested an antibiotic trial for Tibbles. Cefovecin 40mg SC (Convenia®, Zoetis, 0.5mL) was given.

Six days later Tibbles represented due to a lack of improvement.

At this point in time, the owners consented to a blood profile and blood was collected under light sedation using medetomidine (Domitor®, Zoetis, with atipamazole reversal). Tibbles was found to be severely anaemic with a PCV of 0.09 L/L.

I received the following report from Vetnostics:-

- *FeLV antigen POSITIVE (serology, ViraCHEK, Synbiotics Corporation)*

## Blood film (Dr Doug Hayward):

'Initial assessment is suggestive for the presence of erythroleukaemia given the identified rubriblasts and increased nucleated real blood cells despite marked non–regenerative anaemia. Further considerations, however, include IMHA and/or haemotropic *Mycoplasma* infection given further findings. Initially, therapy for possible IMHA and *Mycoplasma* infection along with close monitoring of the FBC is worth considering.'

Following discussion with the owners, euthanasia was elected based on the poor prognosis for Tibbles.

Around the time that these cases presented to me, I became aware of a research group at the University of Sydney developing a real-time polymerase chain reaction (PCR) for the diagnosis of FeLV. I sent fresh blood samples from both Skittles and Tibbles to Mark Westman and Jacqui Norris. Unfortunately, because the PCR was still being developed I did not receive results for Skittles and Tibbles until a few weeks later, after both had already been euthanased. When the results came through I was surprised to find that both cats tested negative for FeLV on PCR.

## FeLV Testing – What and Why (Mark Westman)

All in-clinic FeLV test kits detect viral antigen in blood, whether whole blood, plasma or serum. The target of these test kits is the viral capsid protein p27. These tests are highly sensitive, detecting close to 100% of viraemic cats. However, there are 2 main issues associated with these tests:-

1. The low prevalence of FeLV in Australia (<2%) results in a low positive predictive value (PPV) for the test kits **– thus false positive results occur as frequently as true positive results.**
2. Approximately 60% of cats exposed to FeLV will become regressively infected, meaning they are not viraemic but are still infected with the virus. The only way to detect regressive infections is by using PCR to look for proviral material (DNA copies of the virus inserted into the host genome) in circulating leukocytes.

The significance of regressive FeLV infections on feline health is still largely unknown.

***Figure 1. Note. Skittles the cat looks very 'flat' and lethargic (Case 1).***

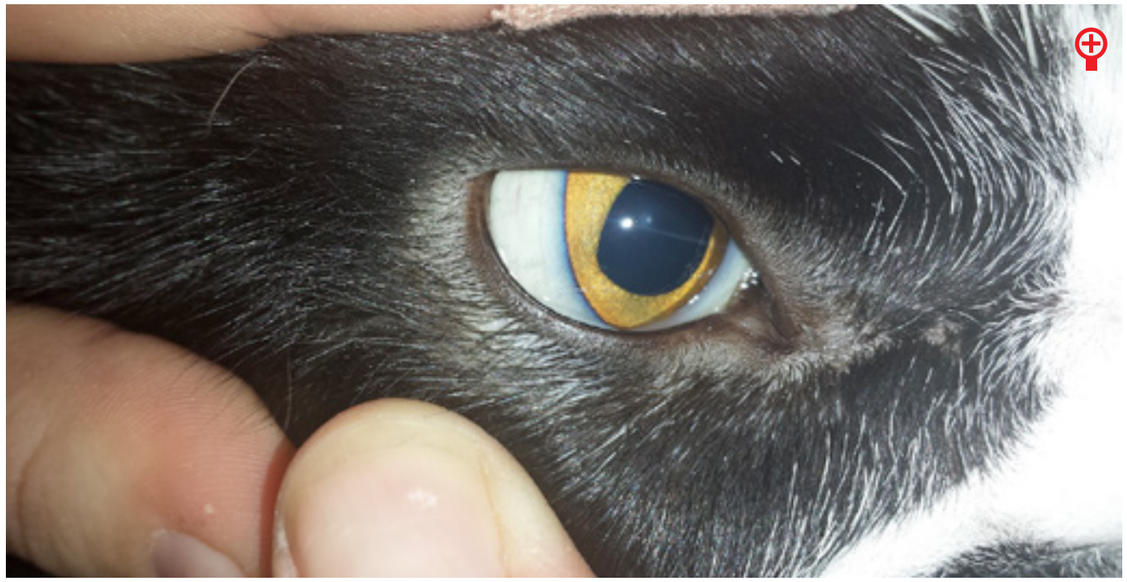

*Figure 2. Note scleral blood vessels are not obvious (Case 1).*

| FeLV +ve (in-clinic testing) | FeLV –ve (in-clinic testing) |
|---|---|
| Could be false +ve due to low PPV of test | Could be false –ve due to regressive FeLV infection |

For ALL cases where FeLV is suspected, confirmatory testing should be mandatory. Immunofluorescence assay (IFA) testing was the historical 'gold standard' for FeLV antigen testing, and will confirm if a positive p27 in-clinic test is a true positive. However, IFA testing will not detect regressive FeLV infections, as it only screens for viraemic cats. PCR testing detects both progressive and regressive FeLV infections, and is highly sensitive and highly specific.

**(Marshall Thornton)** Although knowing that both Skittles and Tibbles were actually FeLV negative most likely would not have changed the outcome for either case, it may have influenced the owner's decision to euthanase before pursuing further diagnostic work up. For example, in Tibble's case, it may have resulted in the owner consenting to PCR testing for *Mycoplasma sp*., or at least a treatment trial with an antibiotic effective against *Mycoplasma sp*. (e.g. doxycycline), before electing euthanasia. I will be certainly recommending FeLV PCR testing for all cases of suspected FeLV infection from now on.

*Mark is currently conducting research into the prevalence of FeLV in Australian cats and and may be able to help out with free FeLV PCR testing in certain cases. He is also recruiting FeLV positive cats for a treatment trial using a HIV antiviral medication. If you are interested please email Mark or phone him on 0409 761 951.*

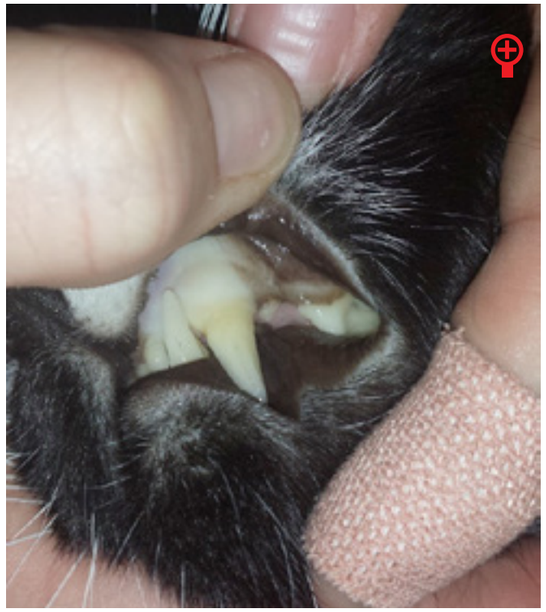

*Figure 3. Note very pale gums, reflecting severe anaemia (Case 1).*

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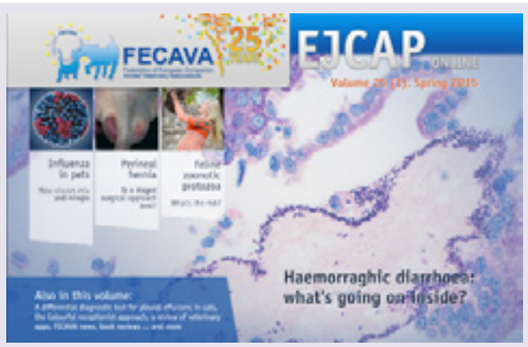








# A CASE OF UNKNOWN HYPOPHOSPHATAEMIA

**C&T NO. 5474**

**Emma Billing**
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'Lacy', a nearly 13-year-old fat Cattle Dog Cross neutered male presented to the clinic for a couple of episodes of being wobbly and falling over in the last 24hrs. The episodes were not related to exercise or eating, but did appear to happen after a period of rest when the dog tried to rise and get moving again. Appetite normal and demeanour normal between episodes. Lacy's on ½ a Previcox® tablet 227mg daily.

Physical examination showed moderate degenerative joint disease in the hips and elbows with suboptimal flexion and pain on extension of these joints. Stifles were both thickened but had good range of motion. There was some mild spinal pain, especially around the lumbosacral region. Lacy is a very nervous dog who has been on daily Valium for some time (prescribed by a previous vet) for persistent anxiety. HR was 120 and RR panting, but it was difficult to ascertain what was 'nerves' and what was pathological. Chest auscultated well and clear but femoral pulses were reduced and the femoral pulse felt weaker than I would have expected in that sized dog. Mucous membranes were pale pink (maybe slightly icteric with a bit of imagination?) with a 2s capillary refill. Abdominal palpation was difficult due to the dog being overweight, and also guarding. Temperature was normal. Stools normal, no vomiting.

I originally thought it may have been a decompensating dilated cardiomyopathy, so lateral and ventrodorsal radiographs were taken, but showed a normal cardiac silhouette and a mild bronchial pattern in the lungs attributable to age. Next step, in the absence of any other bright ideas, was bloods. EDTA and Clot tubes sent to Vetnostics for a Body Function profile.

Blood results are as follows (abnormals only):-

- Hb 92 (115 – 180)
- RCC 3.8 (5-8)
- Hct 0.27 (0.37 – 0.55)
- Urea 10.2 (2.5-9.0)
- Phos 0.4 (0.8-2)
- Ca 2.57

Now the only other time I have seen a crazy low phosphate was in a severely ketoacidotic cat. Low phosphate can cause muscular weakness, so was likely the cause of the 'wobbly' episodes, and can also affect the heart muscle reducing cardiac output. The slightly increased urea may be attributable to this. It can also cause haemolysis, though the serum at the time of collection was clear. It was a bit alarming and the owner was called immediately and requested to come in and start oral CoPhos 2 mLs EOD. Sue Foster (love that vet) from Vetnostics has a special interest in hypoP cases and kindly spoke with us at length about possibilities and further testing. A fractional electrolyte excretion of the kidneys was recommended as KraMar treats back in 2009 were found to cause a proximal tubular nephropathy which was fatal. A thorough diet history was also recommended.

Two days later Lacy returned and bloods and urine were taken for fractional excretion of electrolytes – which came back normal. So not kidneys then… it was recommended that we retest the P levels in the bloods in 10 days.

Diet consisted of Dog Pro pellets (a small handful daily), bones, porridge and yoghurt (with currants and coconut), and occasional fruit and bird seed/chook food (presumably if the dog broke into the chookyard). It was recommended to cease the currants and any fruits from the grape family, and to instigate a diet based more on red meat.

Ten days later, repeat bloods showed a Phos of 1.06, so normal, although the owner mentioned that Lacy is still weak at times, though not as bad, but does seem to have spells where the gums go pale. PCV had increased to 30 and the serum was clear as well. The owner was not interested in pursuing any heart workup past X-rays, so it will remain a mystery as to why Lacy went hypophosphataemic, or whether there is a heart component here as well. However, the treatment appears to be working and we will continue to follow Lacy closely.

### Follow-up:

Routine bloods were taken on 16.12.14 to follow up how Lacy was going on the CoPhos paste every second day. The owner reported that Lacy was well, and that the dietary management to a more meaty diet was agreeing with her.

Results showed Phos 1.19 (0.8-2.0) and other parameters normal. PCV was 40.

However, in early March (4th) his owner reported that Lacy had been having more episodes of 'weakness' and had been found unconscious the previous afternoon. Bloods were taken for a full body function this time, and abnormal results were as follows:-

- Hb 97 (115-180)
- RCC 4.0 (5-8)
- Hct 0.29 (0.37-0.55)
- Phos 0.71 (0.8-2.0)

The Ca was WNL at 2.42 (2-2.8) and the retic count was 1.1% abs 44, so not so regenerative, sadly.

So Lacy was transfused the next week at the owner's request, with 1 bag of greyhound blood. It was tolerated well and she was moved to daily CoPhos paste and had clinically been managing well.

Repeat bloods on the 14.4.15 showed similar findings:-

- Hb 98
- RCC 3.8
- Hct 0.27
- Urea 10.2 and
- Phos 0.4! Again….

So Lacy was moved to daily CoPhos 2mLs and bloods taken a week later where…

- All was WNL! Phos 1.06.

So, it would appear Lacy either is a poor absorber of Phosphate dietarily, or is losing it from somewhere we can't find… either way, a high Phosphate diet and the addition of CoPhos supplement seems to be enough to hold him for now. Also, the anaemia seems to be holding for now… so not sure if the low Phosphate is causing the anaemia, or he has a secondary issue? A bit of a conundrum poor Lacy, but it's great that he has responded so well to supplementation and dietary management.

# LOCALISED TICK PARALYSIS IN A GOLDEN RETRIEVER; A LESSON IN FOLLOWING ONE'S OWN ADVICE

**C&T NO. 5475**

**Heather Shortridge**
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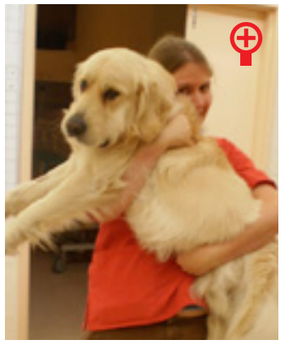

***The author pictured with 'Pickle'.***

Several years ago, I took my then 22-month-old male entire Golden Retriever 'Pickle' to the coast for a long weekend. Based in Armidale we didn't normally have to worry about ticks, but the day before our trip to the coast I applied a dose of Frontline Plus® (Fipronil and S-Methoprene) to Pickle.

We had a good weekend at the coast in September and returned to our normal habits in Armidale.

About 3½ weeks after our trip to the coast I noticed that Pickle's lower jowls were sagging, revealing the inside of his gums. Pickle was subjected to a bit of a poking and prodding of his gums but I couldn't really determine what the issue was.

Several days later I happened to be patting Pickle under his chin and found a large paralysis tick (approx 1cm long) there!

I removed the tick and Pickle's jowls returned to their normal position over the next few days.

It seems that Pickle had a localised case of tick paralysis. This may be seen commonly by those who work in areas with lots of paralysis tick cases, but having worked in mostly non-tick environments it came as a surprise to me.

By the time I removed the tick, it must have been there for 4 weeks, during which time Pickle had been eating normally, and being subjected to regular vigorous exercise.

The tick itself may have been slowed in its activity by the dose of Frontline® before it latched on, but it was very engorged by the time we removed it.

Anecdotally, my colleagues in Armidale had always said that tick paralysis could take up to 6 weeks to develop because of our cold climate, although it was September when Pickle got his tick.

Two main points I took from this case are:

1. Look for a tick in cases of strange local paralysis
2. Follow my own advice and do a thorough tick search on returning from a tick area

Additionally, this was a good reminder that just because an animal has not been in a tick area for a while, it doesn't mean a tick is not implicated in any problems which develop.

Fortunately, Pickle had no complications from his tick and we have now moved to Canberra so we are again living in a low risk area!

***Figures 1&2.*** *Ixodes holocyclus* ***paralysis tick in water and showing scale by centimetres (courtesy of Dr Anne Fawcett)***

eBOOK

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| | |
|---|---|
| | Reply to Tick paralysis in the cat C&T Nos. 5148 & 5149, Issue 264, Sept 2011 **C&T No. 5193** Frank Gaschk |
| | Round Table Discussion – Part 1 Replies to Tick Paralysis in the cat C&T No. 5193, Dec 2011, issue 264 **C&T No. 5251** |
| | Round Table Discussion - Part 2 **Perspective 93** Replies to Tick Paralysis in the cat<br>C&T No. 5193 by Frank Gaschk, Dec 2011, Issue 264<br>*Multiple Authors: Rob Webster, Kath Briscoe, Fiona E. Campbell & Rick Atwell* |

The following has just been published in ***Veterinary Medicine: Research and Reports:***

**DIAGNOSIS prevention and management of canine hip dysplasia a review**

Authors: Schachner ER, Lopez MJ







# USE THE MOST VALUABLE PIECE OF EQUIPMENT YOU HAVE – YOUR OWN MOUTH

**C&T NO. 5476**

**Aine Seavers**
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**Internet post:** I would greatly appreciate your collective thoughts – these owners are getting irate and I need to call them back this morning!

The patient's an 8-month-old female Cockapoo with 3 month duration pruritus; she scratches her trunk primarily, but appears to leave her feet alone. She has had no other health issues. The main outward manifestation of the problem is crusting around the eye margins, and nares, and most recently lip folds.

I looked at skin scrapes and tapes from the dogs face, paws and trunks and saw masses of neutrophils and bacteria, but no parasites. My initial treatment; started her on Advocate® anyway just in case and... *(the C&T reader can now fill in with whatever else they would normally prescribe.)*

## Reply from Aine Seavers

In THIS situation with THOSE clients in THAT state of mind; Do nothing else until first the client makes an appointment to see you WITHOUT the dog!

Explain to them that you are **GOoD but not GOD** and that extra 'o' makes a huge difference.

Medics (Vets and Drs ) are educators. Owners, once educated, facilitate the healing, not the vet nor the doctor, as we can't control how the animal lives, what its needs are etc. Only the owner can do that.

You have not given this dog its problem, nor sold them this dog, but you will try to partner with them to help them now figure out the next step.

You cannot perform major all-encompassing diagnostic work-ups in your head – nor, equally, send off for extensive testing at an actual laboratory but at no charge to them. Diagnostics cost money and, together, you can work out what they can afford to have done.

There is a strong likelihood that this dog has inherited allergic diseases or sensitivities **that may never be Cured only Controlled**; exactly the same situation as in people, despite all the bells and whistles and unlimited funds that can be thrown at human allergic skin cases or asthma cases.

Explain that money spent up-front now can save them a fortune over the course of this pet's illness and by being fully informed early on as to what exactly is going on with the pet, then they can better control, and be less frustrated by, the skin condition as they will understand special medicated bath needs, contacts, flare-ups and allergen peaks. So, refer this client.

A client of mine once likened her dog's atopy to 'skin asthma' and that is a good hook to help people understand that even the best, most stable asthmatic will have flare-ups and so, too, will an atopic dog, depending on external factors.

I tend to find there are not so many difficult skin cases ***per se*** that need referring, rather difficult clients who often return from specialists with the same medication and regimes you yourself would prescribe for another similar case owned by someone else. That is a Specialist's true forte – the extra ability to handle/educate an owner, as much as handle a disease.

So use the most valuable piece of equipment you have – your own mouth. Open it and start informing and educating your client. Your stress levels and those of your staff will reduce and you will neutralise your client's frustration/irate moods as you have pre-empted their complaints and addressed their anxiety.

It is not nice to see one's pet itch all day long especially for no reason, so give them information and reasons. Otherwise, distressed owners will fill the communication gap with their own narrative and it will not be a narrative flattering to you, nor helpful to the poor pet.

# SOLUTION:

## Radiographic findings:

1. *There is irregular bone proliferation on the ventral aspect of vertebral bodies of L6 and L7 extending across the intervertebral disc space at this level, as well as on the caudoventral margin of L5.*
2. *The margins of the end plates of the vertebral bodies appear within normal limits.*

## Conclusion

Osteoproliferative change on the caudal lumbar vertebral bodies - suspect reactive periostitis associated with metastatic spread from lower urogenital tract or perianal/perineal neoplasm.

## Comments & Follow-Up:

The reactive change is unusual in that it is primarily associated with the ventral aspect of the vertebral bodies AND the vertebral endplates are smooth and very normal. This is in contrast with vertebral disorders that it is commonly mistaken to be:

- Spondylosis deformans (see Figure 2 solution), which is typically associated with the ventral aspects of the vertebral endplates, the bone proliferation is smooth and well defined. In advanced stages it can bridge the vertebra completely
- Discospondylitis (see Figure 3 solution)- this is infection associated with the intervertebral disc extending into the adjacent vertebral endplates. The endplates are irregular with a mix of lucencies and opacities indicative of the lysis and proliferation of bone associated with the reaction to the presence of infection. In this case example the intervertebral disc space has collapsed.

The change evident on the vertebrae in this patient is more typical of a reactive change that occurs with metastatic neoplasia (typically carcinoma) along the fascial planes and adjacent periosteum of the vertebrae when tumours are present in the lower urogenital tract or in the perineal region. In some cases the reaction can also extend along the sacrum, pelvis and even the proximal femurs.

Based upon the radiographic features and despite the dog being a castrate, I would recommend careful evaluation of the lower urogenital tract and perineal region for a mass effect. Further diagnostic tests to consider include rectal palpation to evaluate the caudal pelvic canal for evidence of urethral or prostatic mass, rectal mass or anal gland nodule/mass. Ultrasound examination of the kidneys, ureters, urinary bladder, regional lymph nodes (para-aortic/sublumbar lymphocentres) and prostate should also be performed. Ultrasound-guided aspirate of the region adjacent to the reactive change could be undertaken also for definitive determination of the underlying aetiology of the reactive change if no other (primary) lesion is identified, although in my experience the primary lesion is usually found, so direct aspirate from the soft issue adjacent to the reactive change in the vertebrae is rarely required. The prognosis is obviously dependent upon the underlying aetiology of the reactive change, hence the requirement for further ultrasound evaluation.

## Outcome:

This dog was found to have prostatic carcinoma.







# CVE DIAGNOSTIC IMAGING – **WHAT'S YOUR DIAGNOSIS?**

**C&T NO. 5478**

**Signalment:** 8 years old male neutered Setter

**History & Clinical Findings:** initially presented for a one week sudden onset history of hindlimb weakness and episodic yelping. On physical examination the dog had mild lumbar pain which responded to corticosteroid treatment initially, but after two weeks, pain returned and seemed worse.

- **What radiographic changes/abnormalities are evident in the two views provided?**
- **What is your diagnosis?**
- **What would you do next?**

**Robert Nicoll** *BSc (Vet) BVSc DACVR*
*Prior to specialising in diagnostic imaging, Dr Robert Nicoll worked in mixed veterinary practice in Bathurst, NSW for several years. After undertaking his residency training at the University of Wisconsin, Madison, USA, he returned to Australia. With Graeme Allan he formed Veterinary Imaging Associates and more recently, their teleradiology practice Online-Vets.com, providing an international diagnostic service. Since 1998, Robert has been an associate tutor with Graeme in the Diagnostic Imaging Distance Education course and has worked with Graeme on developing a special digital radiography stream for those who have made or are looking to make the leap into filmless radiography.*

Fig 1 –Lateral lumbar spine

## DIAGNOSTIC IMAGING

*The CVE is keen to encourage our Members/Readers to embrace the eBook version of the quarterly C&T, as it's a great complement to the print version and allows the inclusion of multi-media. To encourage reading of our C&T eBook, Robert and Graeme, tutors for the CVE's highly regarded Diagnostic Imaging DE program, will be supplying a Question each quarter, with the Answer available only in the complementary eBook version.*

**SOLUTION** 1 2

PERSPECTIVE 116

# IMAGING AND THE VOMITING PATIENT – SHOULD I BOTHER WITH XR ANYMORE?

**Zoe Lenard**

BSVc(Hons) FANZCVS(Radiology)

*Zoe is also the Tutor for the CVE's Distance Education Abdominal Imaging program*

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In human medicine, the reliance on abdominal radiography has waned. Abdominal radiography as a first-line test is recommended following clinical examination in only a few scenarios: suspected small intestinal obstruction, and perforation (although with the latter, the thorax is radiographed with the abdomen included on the edge of the field, so just the 'top' of the abdomen around the liver and diaphragm is assessed).[1] Reasons for this are two-fold: firstly, abdominal radiography lacks sensitivity/specificity in many tests (i.e. other tests are better) and secondly there is a trend away from unnecessary radiation exposure.[2] Alternative tests include ultrasound (but realistically, in people usefulness is limited by how 'fat' humans are) CT (which poses a higher radiation dose) and sophisticated blood analysis.

The human emergency department of a large human hospital is hardly comparable to modern veterinary practice, because tertiary human facilities have access (often 24 hours a day) to specialist radiologist staff and facilities incorporating XR, CT and US services. The situation remains different in veterinary medicine. Whilst the numbers of equivalent veterinary radiologists/internists has increased access to these services can be limited particularly out of hours.

There is no doubt that abdominal ultrasound is a highly useful modality in veterinary practice, particularly for non-GIT disease like pancreatitis, pyometra and determining the origin/extent of masses. It does require significant operator experience (examples include performing a thorough hepatic assessment or assessment of pancreatitis affecting the left limb or pancreatic body) and high-spec equipment. Finally, it takes years to become competent at the whole-abdomen ultrasound examination given variations in patient species and size. Evaluation of the gastrointestinal tract and the right cranial quadrant of the abdomen (gall bladder fossa, the pyloroduodenal junction, the right limb and body of the pancreas, the proximal duodenum and associated ducts, and possibly the porta hepatitis) is difficult in normal patients, and even more challenging when disease is present in these regions.

The development of focused limited ultrasound examination procedures in human medicine has filtered into veterinary medicine. Devised to provide rapid information early on at the bedside, a *Focussed Assessment with Sonography for Trauma* (FAST) test has been developed for the animal abdomen and thorax. These studies check for developing pockets of free fluid at specific locations in the abdomen and are useful in the case of suspected haemorrhage. Texts outlining the use of these tests in veterinary medicine have been recently published.[1] I believe all GP practitioners with ultrasound should develop a good FAST technique to help them detect fluid pockets and manage their acute abdomen patients, but FAST scans may be of little help in evaluation of vomiting animals.

In veterinary practice, there remains a strong argument for performing abdominal radiography. The information obtained in certain circumstances by plain abdominal radiography can be excellent and very useful for rapidly determining management options. Abdominal radiography is relatively cheap compared to US and CT and more rapidly performed with results in less than 20 minutes. Finally, it can give a rapid global assessment of the state of the abdomen, particularly useful for assessing the retroperitoneal space, edge of the thorax and urinary tract rupture (radiographic contrast study).

So the question for veterinary medicine is, if we are to maximise the benefit radiography in our patients, which cases should have abdominal radiography? Re-phrased: when is it in the best interests of the patient to perform a quick, simple, relatively cheap test possibly with lower sensitivity (radiography) than a more expensive, less available test, possibly with higher sensitivity?

My firm opinion is that the following scenarios warrant immediate abdominal radiography:

1. Any patient where a gastric dilatation/volvulus (GDV) could be present.
2. Severe or protracted vomiting, where there is a suspicion from the signalment or history that a foreign body or intussusception may be causing intestinal obstruction.
3. 'Acute abdomen' scenario resulting in severe abdominal pain or collapse: in this case to exclude obvious pneumoperitoneum (e.g. in hepatic abscessation or intestinal perforation). Small volumes of free gas are difficult to detect with abdominal US, and confirming the site of intestinal perforation may be very difficult. (Figure 1).

This mirrors (coincidentally) the recommendations of the public health system in WA.[1]







With GDV, radiography is diagnostic. With intestinal obstruction, there are well documented objective radiographic criteria that are frequently helpful in determining whether the dog or cat should proceed to exploratory laparotomy (refer to standard texts and see Figure 2). Unfortunately, radiography is not always definitive for the presence of obstruction; in these cases if vomiting persists, repeat the radiographs after 6-12hours of symptomatic treatment to check for progression, or perform ultrasound or exploratory laparotomy if indicated.

Whilst not specifically related to vomiting, abdominal radiography remains the test of choice to accurately localise the site of urinary tract rupture. You may have clues that there is a urinary tract rupture from peritoneal fluid analysis or decreased urine output, but a contrast study (retrograde urethrogram/cystogram for the bladder/urethra, and excretory urogram for the kidney/ureter) is required to determine the site of the rupture.

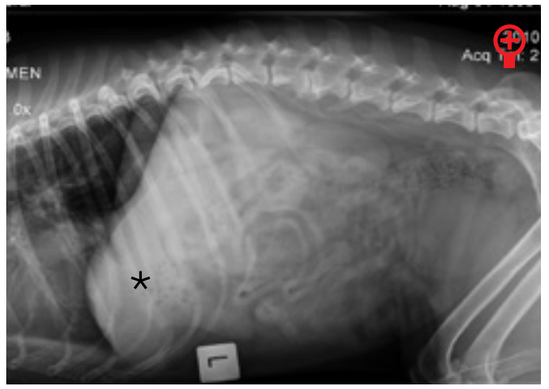

*Figure 1. This aged Staffordshire terrier cross presented collapsed and pyretic with severe abdominal pain. Radiographs showed a focal region of gas bubble formation in the region of the liver, cranial to the stomach (*) consistent with hepatic abscessation. Whilst this lesion would have been detected with ultrasound, radiographs were rapidly obtained providing the diagnosis.*

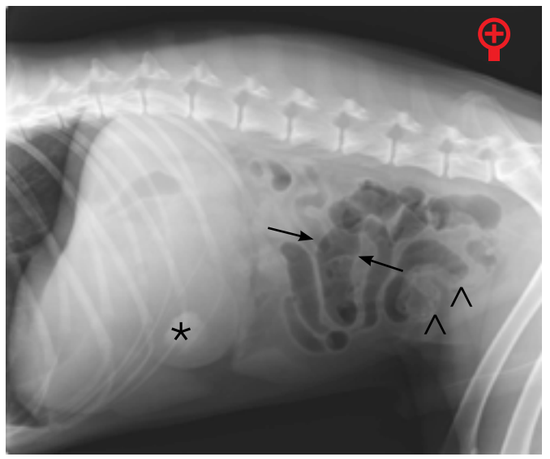

*Figure 2: A young Huskie presented with acute vomiting and severe dehydration. Radiographs showed marked gastric distension: note the rounded pylorus and the small amount of mineral accumulation in the gastric lumen (*). There is significant gas distension of intestines (arrows), and on the VD projection the location of the colon was more obvious, meaning the distension visualised here is small intestinal. Stippled material (arrowheads) was preset in the small intestine in the caudal abdomen. These are signs consistent with gastric outflow obstruction and small intestine obstruction. A small intestinal linear foreign body causing plication and obstruction – with several additional, small, cloth, foreign bodies – was detected at surgery.*

Surely abdominal US is superior to abdominal XR in the vomiting animal? Yes, in the hands of an experienced operator (e.g. a radiologist) *provided* there is not a large volume of gas or ingesta in the gastrointestinal tract. If the patient has recently eaten, has a gas-distended stomach, or has a large volume of firm faeces/gas in the colon, radiography can be a better choice as you may easily miss a lesion with ultrasound, regardless of your skill level. Radiography in these patients still may not give you a definitive answer, but still could provide more useful information than ultrasound (Figure 3).

For vomiting dogs with suspected pancreatitis ultrasound is superior to radiography. For high intestinal obstructions or pyloric outflow obstructions ultrasound can be superior but there is a high degree of operator skill required as the right cranial abdominal quadrant is the most difficult area to scan accurately in dogs (and some cats). Is ultrasound indicated in acute vomiting? Perhaps if vomiting is severe and intractable or other tests suggest pancreatitis. If not, I would considere'aggressive' symptomatic and supportive treatment the best way to spend the client's money, and then gauge response to treatment.

What about the patient with chronic vomiting: does imaging help? Leib et al[4] retrospectively reviewed 89 pet dogs with chronic vomiting and found that in nearly 70% of cases, the diagnosis could have been reached without ultrasound. In only 23% of cases were the results of ultrasound considered vital or beneficial to the diagnosis. If the final diagnosis was intestinal lymphoma or gastric carcinoma, ultrasound was more useful. Of course, generalised evaluation with ultrasound of abdominal viscera is *helpful* to exclude any other causes of chronic vomiting (like food allergy, renal infection or failure) but frequently poorly specific.

Plain radiography will not help with the assessment of intestinal wall thickness (at any location in the gut) and ultrasound is infinitely superior to contrast radiography (barium swallow) for the evaluation of intestinal layering. If you have access to an experienced/quality sonographer there are very few indications for barium swallow in modern medicine. Such studies generally are a waste of client's money. An exception is the low-dose gastrogram, where a small volume (5-15mLs) of liquid barium is administered and the patient rolled, then radiographs (VD, R lateral and possibly L lateral) obtained to see if there is a foreign body (filling defect) in the pylorus. It sounds easier than it really is and, in my experience, is rarely required.

So for the *vomiting* dog or cat, my message is:

- Don't be afraid to radiograph the abdomen for **any** case of vomiting where there is a concern that obstruction may be present.
- Radiography is **always** the best test to rule out a GDV. Because GDV can be catastrophic, radiography should always be considered in susceptible breeds showing vomiting or abdominal discomfort.
- Radiograph an 'acute abdomen' – it may give provide valuable information and you can do it whilst you are waiting for the results of the haematology/biochemistry panel.

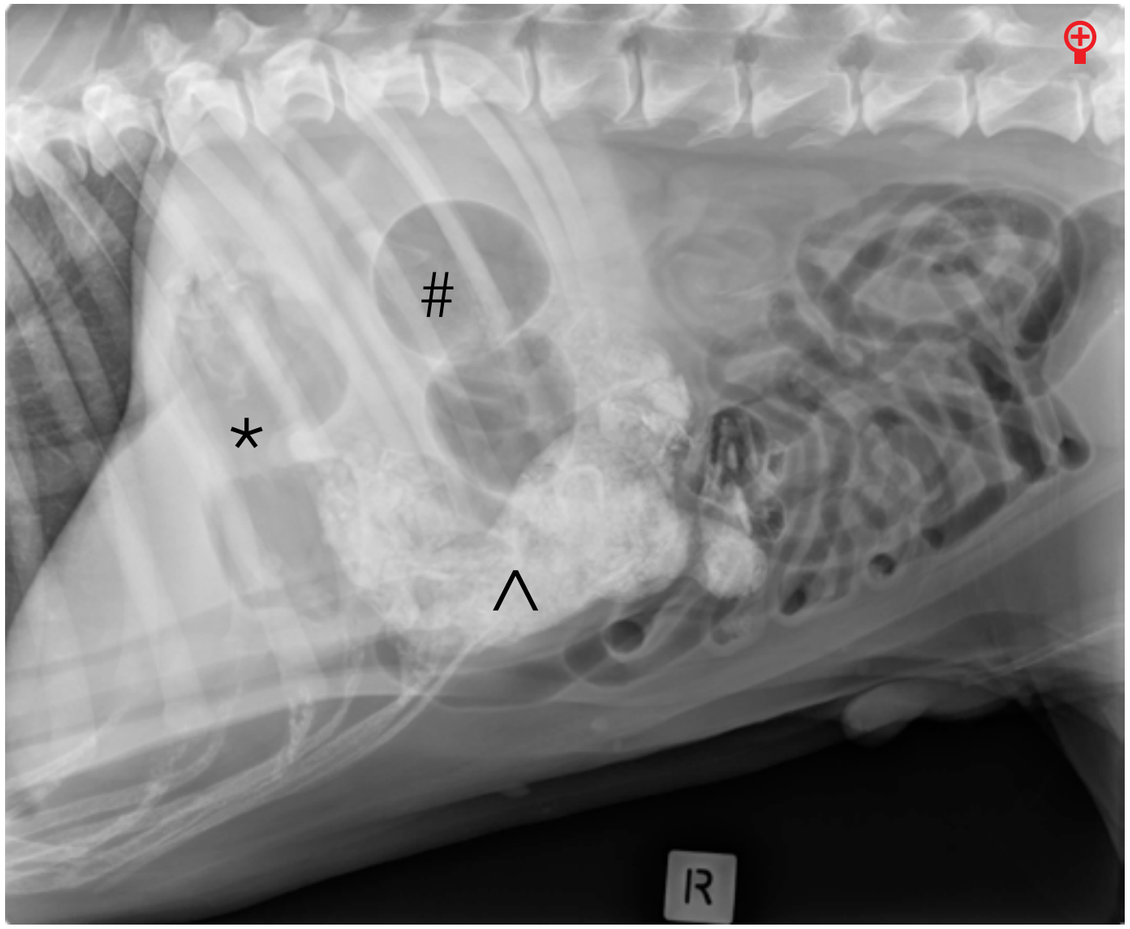


*Figure 3. Diesel, a 9 y.o. Mastiff dog presented for abdominal US with a history of marked weight loss (~30% of body weight over some months), vomiting and inappetance. Definitive conclusions were difficult to make from the ultrasound due to the large amount of shadowing created by intestinal material. A radiographic study (obtained after the ultrasound) showed moderate gas distension of the stomach (*), marked gas distension of the caecum (#) and a mineralised faecolith (concretion of bones) present in the transverse colon (^). In this case, these gas or mineral structures made ultrasound a far less useful tool than ultrasound for evaluation of the cause of vomiting. At surgery a small tumour was found in the colon causing obstruction; this lesion was not detected at radiographs due to the shadowing artifact.*

Once committed to abdominal radiographs, do them properly. Sedation is usually required for a diagnostic study. Butorphanol (or another opioid) +/- low-dose acepromazine is a safe, effective combination.

For a GDV, obtain a single R lateral projection – it is usually diagnostic. For other studies always take 2 orthogonal views.

- R lateral and VD
- Obtain the same lateral each time
- VD always preferable to DV for better quality image

Remember, if in doubt you can get a second opinion usually within a few hours from a tele radiography service. Embrace the digital world!

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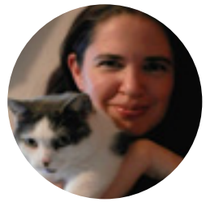
**Personal comment from Richard Malik**: *My own view is GP vets need to change the way they cost out things. Most clinics have digital radiology – so taking radiographs is quick, easy, cheap (low marginal cost) and they are easy to send off for a second opinion. Our ultrasound skills vary, and we are not nearly as good as radiologists. So why not always do both, get the most information we can, but charge it out at a fee most clients can afford. It seems silly to me not to take a radiograph (or two) that will take 5 minutes to do, to complement each and every ultrasound exam.*







**WINNER!**

PERSPECTIVE 117

# FELINE PLASMA CELL PODODERMATITIS – A PATHOLOGIST'S EYE VIEW

**Melanie Dobromylskyj**

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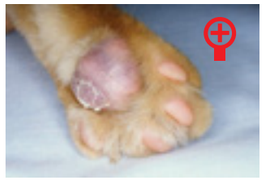
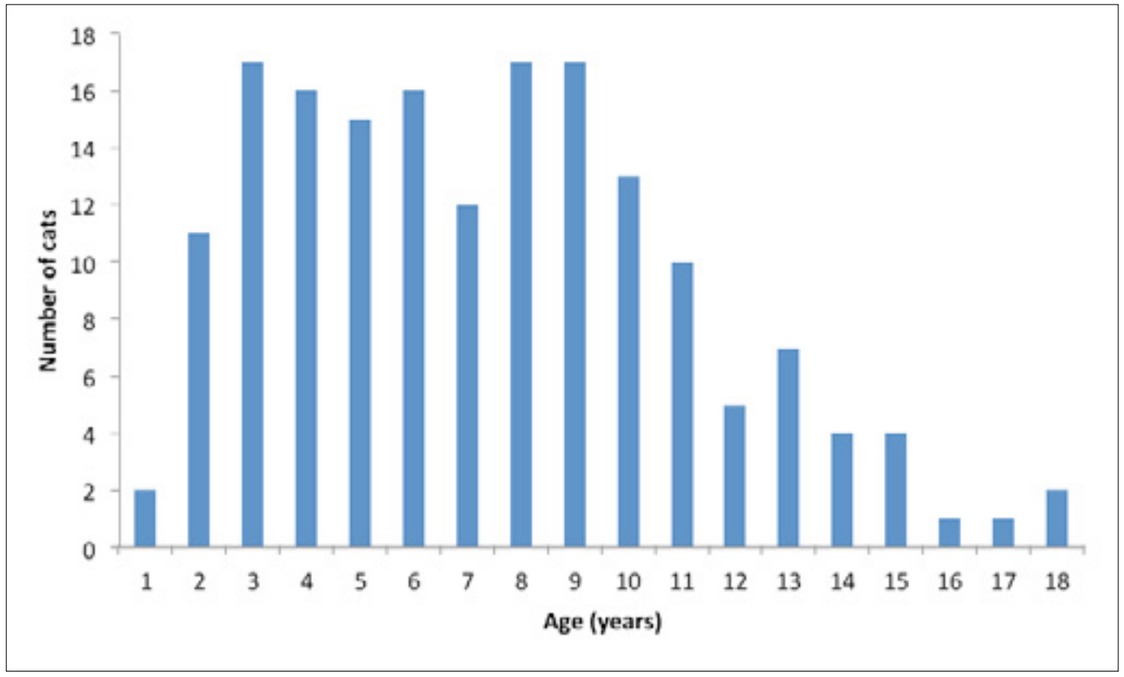
Feline plasma cell pododermatitis is an uncommon but well-recognised condition in cats, which is described in all dermatology and pathology textbooks. Yet the aetiology is poorly understood and a search of the veterinary literature reveals a relative lack of published information on this fascinating feline disease.

Affected cats present with purple, spongy swelling of one or multiple paw pads, typically the metacarpal and/or metatarsal pads, which are often criss-crossed by linear striations giving the pad a characteristic gross appearance. Lesions often then progress to ulceration with secondary superficial bacterial infection, and the presence of pain and associated lameness appears to vary between cases. A classic entry on the histopathology submission form – 'the foot pad has exploded!'

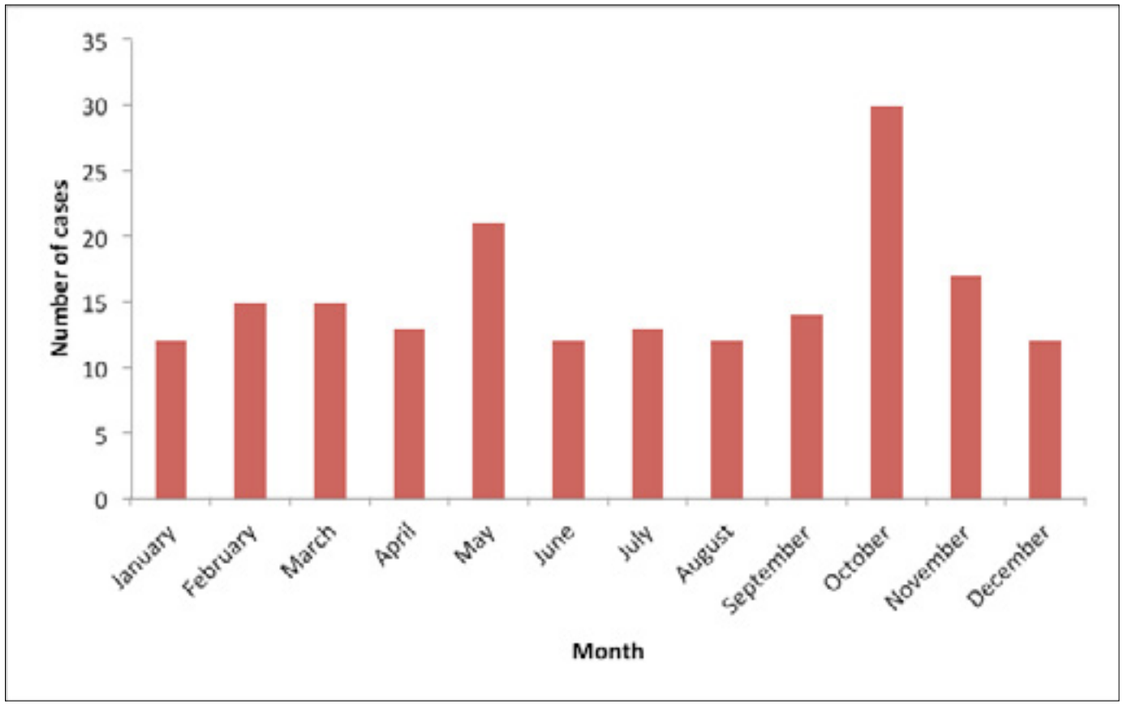
The particular case described here had a brief clinical history of swollen pads affecting all 4 feet, together with involvement of the nose – a finding also occasionally described in the literature. This cat is a female neutered, 8-year-2-month-old Domestic short-hair, and the tissues biopsied were taken from a swollen right fore pad.



The histological appearance of the tissue submitted is entirely typical for this disease, with an intense, predominantly mononuclear inflammatory cell infiltrate expanding the dermis as well as the underlying adipose tissue. The infiltrate is an almost entirely monomorphic population of well-differentiated plasma cells, including Mött cells (Figure 1) – Mött cells are plasma cells that have spherical inclusions within their cytoplasm (called Russell bodies) which correspond to accumulations of immunoglobulins (antibodies). Low numbers of small lymphocytes and neutrophils are




**Graph 1.** ***Age distribution of cats diagnosed with plasma cell pododermatitis, based on 170 cases submitted to the laboratory between 2006 and 2013.***




**Graph 2.** ***Case numbers by month of submission, based on 186 cases submitted to the laboratory between 2006 and 2013.***

admixed in some areas and the overlying epidermis is markedly hyperplastic and segmentally ulcerated. For the reporting pathologist, the diagnosis based on the clinical history, the gross and histological appearances is rather easy in these cases, as nothing else looks like this in a cat. But determining the underlying causes of this disease is apparently far more complex! QUERY: Would you be happy diagnosing a characteristic case with a fine needle aspirate??? Richard

Previous studies have produced a number of interesting but somewhat variable findings including spontaneous regression, apparent seasonality, responses to treatments such as steroids, doxycycline or surgical excision/debulking, together with variable but persistent hypergammaglobulinaemia and concurrent conditions including feline immunodeficiency virus (FIV) infection, feline leukaemia virus (FeLV) infection, glomerulonephritis and plasmacytic stomatitis. Whether plasma cell pododermatitis is a purely immune-mediated condition or whether there is an underlying infectious agent is still a matter for debate – studies searching for various infectious agents within the pad have not yet yielded any conclusive evidence, despite looking for a variety of organisms including *Bartonella*, *Ehrlichia*, *Anaplasma*, *Chylamidia felis*, *Mycoplasma*, *Toxoplasma gondii*, feline herpesvirus type 1 (FHV-1)

For this article, a search was made of the computer-based records held at a large, commercial diagnostic laboratory in the UK, for samples with a diagnosis of 'feline plasma cell pododermatitis'. This search revealed 186 such cases recorded between 2006 and 2013. These cases were primarily from first opinion practices and most were from UK-based practices.

Of the 176 cases for which the cat's gender was recorded on the submission form, 70 were female and 106 were male.

This apparent gender imbalance is also seen in some of the published studies, albeit based on smaller numbers. For example, Guaguere et al. (2004) reported 19 out of 26 cases as male, while Scarampella and Ordeix (2004) had 8 male cats out of ten cases. Bettenay *et al*. (2003) had 11 males out of 15 cases where the gender was recorded. In our 176 cases, this apparent gender imbalance is statistically significant (p=0.0085).*

Age was recorded for 170 of our cases, with a median age of 6 years and a range from 9 months up to 17 years (see Graph 1); there is an apparent tendency for this condition to affect young to middle-aged cats, although there is a huge variation in the ages affected. These findings agree with those in other published studies, including Bettenay *et al*. (2003) where the mean age was 5 years, with a range from 1 to 12.5 years, and Pereira & Faustino (2003) with a mean age 4.7 years and a range from 3 to 7 years. Scarampella & Ordeix (2004) had cases ranging from 6 months to 8 years, and Guaguere *et al*. (2004) from 6 months to 12 years.

For those cats in our records where the breed was noted (180 cases), all bar 11 were domestic short haired, domestic long haired, 'domestic cat' or 'cross-breed' (93.9%). The 11 pedigree cats included 5 Siamese (2.7%), and 1 each (0.6%) of Bengal, Ragdoll, Burmese, British short hair, Persian and Abyssinian. The breed prevalence of the background feline population (based on the cat breeds recorded for over 3,000 fixed tissue specimens submitted to the laboratory over this same time span) is 88.6% non-pedigree (domestic short haired, domestic long haired, 'domestic cat' or 'cross-breed'), with 1.8% Siamese, 1.1% Burmese, 2.2% Persian, 0.7% Ragdoll, 0.3% Abyssinian, 0.2% British short hair and 0.6% Bengal.







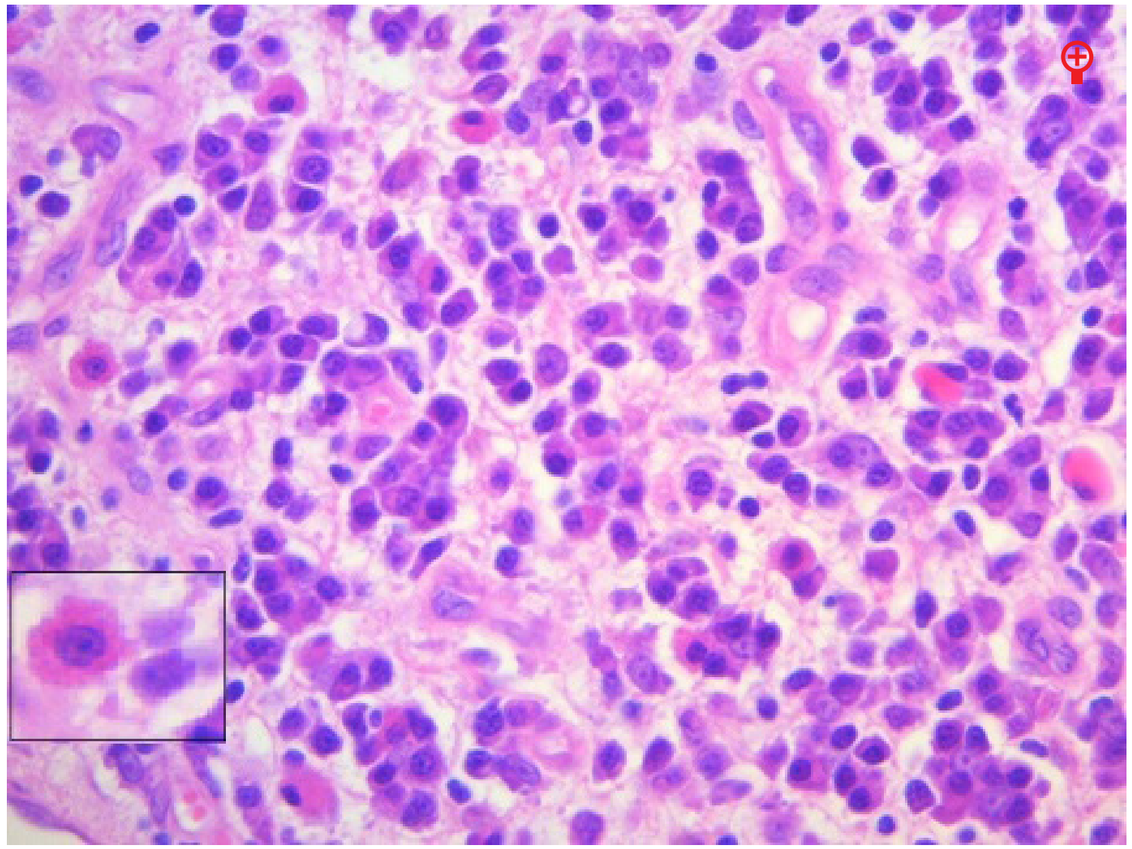


**Figure 1.** ***An intense, predominantly mononuclear inflammatory cell infiltrate composed almost entirely of well-differentiated plasma cells, including Mött cells (see inset).***

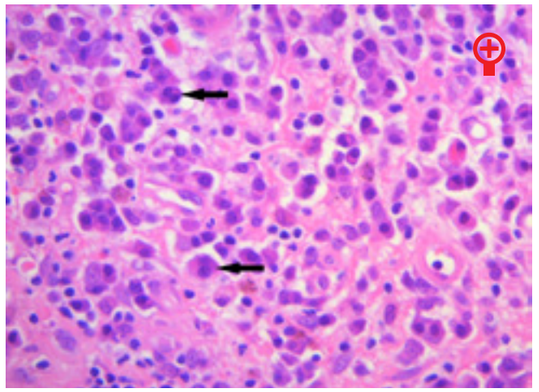
Analysis according to the month the biopsy was submitted to the laboratory did not reveal any apparent seasonal distribution (see Graph 2), although of course the length of time the lesion has been present prior to biopsy may vary considerably between cases and this may obscure any apparent seasonal pattern in this data. One paper (Gruffydd-Jones *et al*. 1980) included a case with recurrence in the summer months, although no other publications have described this.

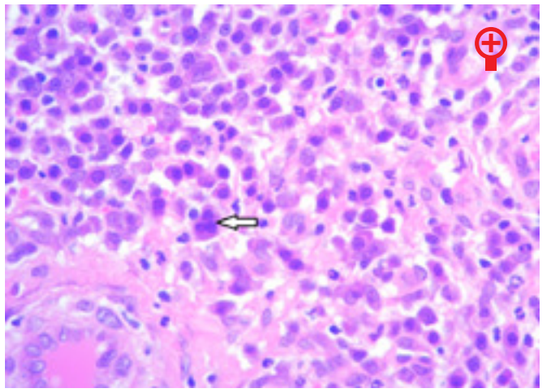
**Editor's Note: When males are over-represented, always think of territorial aggression as a component of the aetiology.*

Sadly, no clinical history or indication of biopsy site(s) was included for 28 of our samples. However, for those with some history provided, 83 cases appeared to have 2, 3 or 4 affected feet, with 24 cases specifying all 4 feet were affected to some degree. Seventy-five cases involved 1 foot only, although it is possible single-foot cases are over-represented in our biopsy population; clinicians would presumably be much more likely to biopsy a case if only single pad was abnormal, due to concern about a possible underlying tumour or bacterial fungal infection, for example. Bettenay *et al*. (2003) reported 6 cats with all 4 feet affected, 1 cat with just hind feet and 2 cats with the forelimb feet affected. Two cases in our cohort had apparent involvement of the nasal planum, as in this present case; such a case is also nicely described by De Man (2003).

In terms of concurrent diseases (biopsies submitted at the same time as those from the feet) 5 cases had plasmacytic stomatitis/gingivitis, and 2 had eosinophilic granuloma type lesions in the oral cavity – since these are both in themselves fairly common conditions within the cat population, this is probably co-incidental.

The potential link with FIV infection is very interesting; although obviously many cats with plasma cell pododermatitis do not have FIV, it is feasible that a disease resulting in altered immune function could also produce errant B-lymphocyte and plasma cell behaviour. In a paper describing 6 experimentally infected cats (Simon *et al*. 1993), 4 had evidence of plasma cell pododermatitis, and in 1 case they performed immunohistochemical staining on the pad tissues and found FIV-immunoreactive cells *in situ*. Scarampella & Ordeix (2004) reported 4 out of 9 cases were FIV-positive, while Guaguere *et al*. (2004) had 16 FIV-positive cats out of 26 cases, together with one FeLV-positive cat. In humans infected with human immunodeficiency virus (HIV), B-lymphocytes show signs of phenotypic and functional alterations, such as polyclonal B-cell activation, loss of B-cell memory and hypergammaglobulinemia; it is interesting to speculate whether FIV produces similar effects in feline B-lymphocytes, leading to accumulation of functionally abnormal plasma cells within tissues such as the pads, as well as the hypergammaglobulinemia described by Scarampella and Ordeix (2004).





**Figures 2 and 3.** ***Bi-nucleated (black arrows) and tri-nucleated plasma cells (white arrow).***

Since doxycycline is both an antibiotic and an immunomodulatory drug, the response of cases to doxycycline therapy could indicate 1 of 2 things (or possibly both) – either there is some bacterial involvement (as yet to be found e.g. bacterial L-form), and/or this is an abnormal immune response involving primarily plasma cells and localised to the foot pad.

**Hypothesis number 1):** this disease could be due at least in part to an infectious agent within the pad or pads. However, does the fairly common involvement of multiple feet imply that infection of 1 pad can trigger the development of disease in the others? Maybe the infection itself is fairly transient, and merely initiates a localised immune response within the pads. Some forms of trauma can have a similar affect, effectively triggering a form of auto-immunity due to exposure of tissue components not normally seen by the immune system and therefore not recognised as 'self'. If the tissue component targeted by this auto-immune attack is found only within the pads (and nose), for example a particular subtype of collagen, then that would explain why the resulting disease affects the pads alone.

**Hypothesis number 2):** this disease could be due at least in part to an infectious agent, but the agent is not present within the pad but elsewhere – such as the gastrointestinal tract. Several diseases in humans are hypothesised to act in this way. The best understood is ankylosing spondylitis, where a link has been demonstrated between a particular MHC gene (HLA-B27), a high starch diet and the presence of *Klebsiella pneumoniae* within the intestinal tract (see Rashid *et al*. 2013 for a fascinating review) producing the disease itself at another anatomical location. Another human example is rheumatoid arthritis, in conjunction with often subclinical infections with *Proteus mirabilis* within the urinary tract (Ebringer and Rashid 2006, 2014). The proposed mechanism in these diseases is 'molecular mimicry' – bacterial antigens which are similar in structure to normal tissue components stimulate production of antibodies which not only target the bacteria but also demonstrate cross-reactivity with self-antigens. This results in auto-immune disease at distant but specific anatomical sites.

**Hypothesis number 3):** this could be a non-infectious, purely immune-mediated disease, possibly targeting self-antigen located specifically within the pads and nose. The plasma cells within these pads are interesting in their own right, in that they appear to be actively dividing *in situ* – as indicated by the presence of mitotic figures and atypical bi-nucleated and multinucleated cells (suggesting nuclear division in the absence of successful cell division). These are features described by Dias Pereira & Faustino (2003) and also noted in the present case (see Figures 2 - 4).

However, plasma cells are supposedly terminally differentiated, non-dividing cells derived from B-cells, so how is this happening? It may be that the dividing cells we see in the sections are actually plasmablasts, a developmental 'half-way house' between a B-lymphocyte and a fully mature plasma cell – plasmablasts are capable of secreting antibodies but can also still divide and act as antigen-presenting cells. Alternatively, it is possible that these are fully mature plasma cells which are capable of self-replication – but this would be rather aberrant behaviour for a plasma cell. Additionally, mature plasma cells are not supposed to have a very long life span (with the exception of some special subtypes), so their presence in such large numbers is even more impressive. In human studies looking at rheumatoid arthritis, bi- and multinucleated plasma cells (and some containing mitotic figures) have been identified within the affected synovial tissues (Perry *et al* 1997). The authors suggest these cells are undergoing cell division and that this is at least partly contributing to their accumulation in such large numbers within the synovium. Whatever the precise underlying mechanism, there is also something abnormal about the plasma cells we see in feline plasma cell pododermatitis.

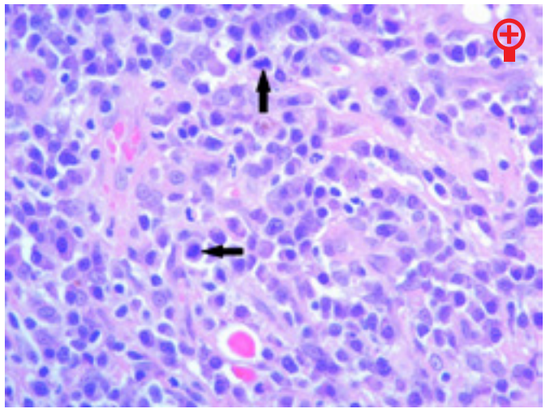
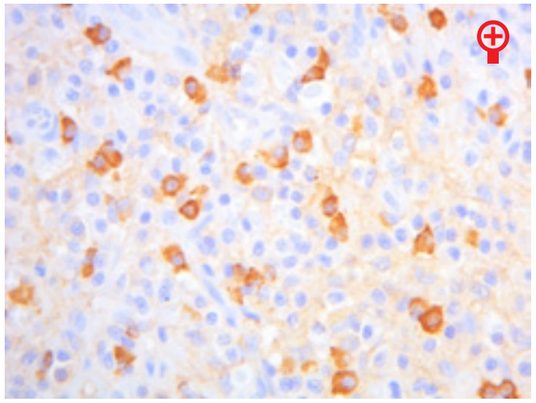


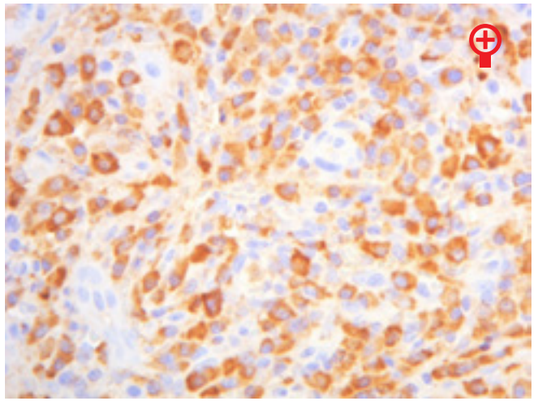
**Figure 4.** ***Mitotic figures within plasma cells (black arrows).***











Figures 5 and 6. Immunohistochemcial staining is positive (golden brown) for kappa (figure 5) and lambda (figure 6) light chains. Note that both types of light chain are present, indicating a non-neoplastic cell population proliferating within the pad.

We know that the plasma cells within these affected pads are not neoplastic, by the use of immunohistochemical stains for the antibodies they produce. Plasma cells can each only produce a single kind of antibody of a single isotype. Furthermore, of the 2 types of light chain that exist as part of an antibody (kappa and lambda chains) each individual plasma cell can only produce 1 type. Therefore a normal (inflammatory) population of plasma cells will contain a roughly equal mixture of cells producing either kappa or lambda light chain, while a neoplastic plasma cell population (derived from a single malignant cell, termed monoclonal) will produce only 1 type, either kappa OR lambda.

One study (Kyriazidou *et al*. 1989) stained tissues from 4 cases of plasma cell pododermatitis and compared them to 2 cases of plasmacytoma (i.e. neoplastic) and other types of plasmacytic inflammatory processes in cats – all of the cases of plasma cell pododermatitis were positive for both kappa and lamba, as was this current case (see Figures 5 and 6).

This same paper also looked at the isotype of antibody being produced (5 isotypes exist in mammals including IgG, IgA, IgM, IgD and IgE – remember each plasma cell will produce a single isotype); for the neoplastic plasma cell populations a single isotype would be expected because the cells are monoclonal, while for inflammatory lesions several isotypes would be typical due to polyclonal expansion of the B-cells and hence plasma cells. The Kyriazidou study looked for IgG, IgA and IgM and found that the 5 other inflammatory lesions produced none, 1, 2 or all 3 of these isotypes. The 4 plasma cell pododermatitis cases were all positive for IgG, with only 1 case demonstrating positive staining for IgA and none for IgM. Although this is only a small number of cases, it would be really interesting to know whether this means a relatively restricted set of B-cells and plasma cells are being expanded within the pads, and whether these represent 'auto-reactive' clones. Several human studies have shown that there is a selection of 'dominant' B-cell and plasma cell clones within the synovium of rheumatoid arthritis patients for example, and that these clones are often auto-reactive (Steele *et al*. 2011; Doorenspleet *et al*. 2014). Studies of this type depend on isolation of individual cells within the synovium and sequencing of variable regions of their B-cell receptor, but it might be interesting to see if PARR (PCR for Antigen Receptor Rearrangement) testing of these pads affected with plasma cell pododermatitis indicated a relatively oligoclonal (few clones) or truly polyclonal (many clones) cell population. An oligoclonal expansion of plasma cells might well suggest an auto-immune pathogenesis for this fascinating disease, although whether and what other triggers are potentially involved would still remain an important question...

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PERSPECTIVE 118

# WOULD YOU MISS A DIAGNOSIS OF JOHNE'S DISEASE IN A GOAT HERD?

**Dr Sandra Baxendell**

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While dairy goats generally get the bovine strain of Johne's disease (also called paratuberculosis,)[1] they often do not show the typical signs that are observed in cattle i.e. watery diarrhoea, dehydration and thickened, corrugated intestines. In goats, the main clinical sign of Johne's disease is just wasting. As most veterinarians know, goats with very poor body condition can be due to a variety of causes, most often gastro-intestinal parasites. Also, Johne's disease in goats (and sheep) can occur in younger animals; that is the case with cattle i.e. as early as 12 months[2]. Often, the stress of first kidding can initiate Johne's disease but it can also trigger Caprine Arthritis Encephalitis (CAE) which is also a cause of wasting in goats. A recent study of Johne's disease in goats in Saudi Arabia found that the only consistent clinical sign was 'weight loss despite apparently normal food intake'.[3]

One complication is that goats with Johne's disease, and therefore in poor condition, are more prone to other diseases such as pneumonia, parasitic gastro-enteritis, and digestive disorders. Thomas (1983)[4] reported 2 years of necropsies of 67 goats from a large UK goat herd in the first 2 years of Johne's disease control, which are summarised in the Table below:

| Diagnosis | No. of goats affected | Percentage (%) |
|---|---|---|
| Johne's disease | 19 | 28 |
| Johne's + another disease | 8 | 12 |
| Pneumonia | 8 | 12 |
| Digestive disorders e.g. entero-toxaemia, acidosis, bloat | 8 | 12 |
| Parasitic gastro-enteritis | 6 | 8 |
| Gut torsion | 3 | 4 |
| Miscellaneous | 10 | 16 |
| No diagnosis | 5 | 8 |

Goats with Johne's disease which would have eventually died of this condition can die first of another condition. A survey of deaths in 13 goat herds (10 dairy and 3 meat herds) in Quebec, Canada between 2009/10, found that 29 goats of the 152 necropsied had Johne's disease, but only 16 of these actually died of Johne's disease.[5]

In a study of goat herds in Norway, PCR tests were performed on bulk milk samples. It was found that 3.3% of herds which had previous Johne's disease cases had positive PCRs, but for herds with no history of Johne's disease there was a 9.1% positive rate for PCRs.[6] This higher level in supposedly 'normal' herds indicated that the diagnosis of Johne's disease had been missed in these latter herds.

Clinical signs reported in goats with Johne's disease include:-

- Loss of body weight
- Poor, dry coat
- Emaciation despite access to plentiful feed
- Muscle wasting, rather than fat loss[7]

And, less often, there are the following clinical signs and gross signs on post-mortem examination.

- Apathy
- Dehydration
- Clumping of faeces
- Enlarged ileo-caecal lymph node
- Enlarged mesenteric lymph nodes
- Caseous nodules in mesenteric lymph nodes
- Thickened caudal ileum

A study in a large US goat herd with a high incidence of Johne's disease [8] found the following gross signs during 120 post-mortems on infected goats:-

- Thickened ileo-caecal valve and ileum (49/120)
- Corrugated ileum (34/120)
- Inflamed ileum (12/120)
- Haemorrhagic ileum (4/120)
- Abscessed ileum (1/120)
- Changes in ileo-caecal or mesenteric lymph nodes (45/120)
- These lymph nodes 3 times normal size or larger (33/120)
- These lymph nodes are oedematous (6 /120)
- These lymph nodes are large and haemorrhagic (1 /120)
- These lymph nodes are large and mineralized (1 /120)
- These lymph nodes are hyperaemic (1 /120)

However, a large number of goats with positive diagnostic tests for Johne's disease had no gross signs at all on necropsy.

Also, there is 1 report of a goat with nervous signs from a hepatic encephalopathy in a goat with Johne's disease.[9] This 3-year-old dairy goat had lost weight and become weak in the previous 2 weeks before being presented for veterinary examination. This doe also had depression, posterior weakness, fine head tremors, and intermittent trembling of the head and neck. The goat's blood ammonia levels were extremely high and on post-mortem the liver showed fatty infiltration. This liver disease, due to the goat's inappetence and wasting because of the Johne's disease, caused the neurological signs. Most vets would not include Johne's disease on a differential diagnoses list for neurological diseases.

Prevention of the introduction of Johne's disease is by ensuring that all new introductions of goats are from herds that are accredited tested negative of Johne's disease. Such herds are in a searchable database on the internet (www.edis.animalhealthaustralia.com.au/public.php?page=mapsearch&aha_program=3 ). However, as at 28/5/15 there were only 24 Australian goat herds in the goat Johne's disease market assurance program. In countries without such a scheme, the only option is to close their herd and only introduce new genetics by artificial breeding.[10] These closed herds must also ensure no cattle, deer or alpacas or their products (manure, milk) are introduced.

Control of Johne's disease in an already infected herd is very difficult but would involve improving general hygiene and separation of kids at birth. General hygiene includes using fenceline feeders or keyhole feeders so that there is no faecal contamination of the goats' feed. It has also been suggested that *Mycobacterium avium* subspecies *paratuberculosis (*Map) bacteria can survive for many weeks in biofilms in livestock waterers[11] and this has led to a US Department of Agriculture recommendation to chlorinate drinking water or add 3 tablespoons of chlorine bleach to 100 gallons of livestock trough water every week combined with only using galvanized metal or stainless steel water troughs. Separate boots for kid rearing areas and adult goats is also desirable, as is frequent cleaning of manure for composting for 12 months. Monthly weighing of goats to pick up cases of Johne's disease has been used overseas, where access to other diagnostic tests has been too difficult or too expensive. As wild rabbits have been shown to have the Johne's disease organism, rabbit control should be part of any control program.[12][13]

The Goat Milk Producers Federation of the UK have a Code of Best Practice for controlling Johne's disease and this involves annual or more frequent testing of all replacement does, never feeding bulk unpasteurised milk, rearing kids in isolation from adult goats for the first 6 months, vaccination of all young kids, necropsies of all wasting goats and routine PCR testing of bulk milk samples.[14] Norway have taken a different approach and have eliminated Johne's disease, Caprine Arthritis Encephalitis (CAE) and Caseous Lymphadenitis (CLA) from herds by snatch-birthing kids, rearing separately on cows' colostrum and milk replacer and then replacing the original adult herd after thorough disinfection of the barns and milking areas.[15]

Pasteurization times and temperature treatments for colostrum that kill the CAE virus (i.e. 1 hour at 56 degrees F) does not necessarily kill *Mycobacterium avium* subspecies *paratuberculosis (Map)* bacteria. The temperature needed may be higher i.e. 135 degrees F for 30 minutes with stirring.[16] It has been shown that cows' colostrum pasteurized to kill the Johne's disease bacteria will coagulate but this can be overcome by adding water and using a blender and the resultant colostrum is still useful for feeding to calves.[17]

A key component to stopping the spread of Johne's disease in Australian goats is the national kid rearing plan, (www.animalhealthaustralia.com.au/national/kid/rearing/plan ) with its recommendation to never feed bulk milk to kids and to rear kids on milk replacer or pasteurised bulk milk. The importance of this recommendation is demonstrated by the trial results reported by Storset et al (2001).[18] In this trial, 7 goats were given suspensions of *Mycobacterium avium subspecies paratuberculosis* in milk replacer 3 times a week between 5-8 weeks of age for a period of 9 weeks. All these goats developed a cell mediated immune response to Johne's disease, compared to none of the 6 controls, although 2 animals did not develop significant antibody levels. These 7 kids were then observed for 2 years. Two goats started faecal shedding at 12 months and another 2 by 2 years of age. When the goats were necropsied at the end of the trial, 5 of the 7 goats had lesions and the bacteria in the intestines and/or the mesenteric lymph nodes. However, 2 animals had no detectable lesions in the distal ilium and colon on necropsy. Admittedly 2 years is a short period for incubating Johne's disease, as often clinical signs do not appear for some years. However, this research shows that subclinical infections i.e. carriers, can easily be missed.

This is backed up by the findings of Thomas (1983),[19] who tabulated the age of faecal shedders in a large UK goat herd in the 3 years following diagnosis and initiation of control. His results are shown in the table below:-

| Age (years) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Total No. of shedders | 0 | 18 | 14 | 14 | 14 | 4 | 3 | 4 | 0 |
| No. of goats in this age group | 149 | 154 | 83 | 61 | 50 | 35 | 27 | 12 | 9 |
| % of shedders in this age group | 0 | 12 | 17 | 23 | 28 | 11 | 11 | 33 | 0 |

Frequent testing of all adult goats is needed to remove any faecal shedders as quickly as possible. Faecal culture has a specificity of almost 100% but the test takes several weeks (8-10) for the bacteria to grow and this time can be even longer in goats (10-12 weeks). Sensitivity is low in the early stages of infection but approaches 100% in the advanced clinical stage. Research has shown that positive culture results were found in 69% of goats with diffuse lesions and from 44.4% of those with focal lesions found on necropsy.[20] Research completed by Eamens et al (2007) showed that the faecal culture tests on pooled faecal samples could be used for goats and that the recommended dilution was 1 in 25 and a time frame for culture of 10 weeks. This dilution detected 13 out of 16 positive (3 with the sheep strain and 13 with the bovine strain) goats. This dilution was best for reducing costs without a large drop

in sensitivity. Two low shedders were not detected except by individual culture.

Faecal smears stained with Zeihl-Neelsen can give a rapid result, but have low sensitivity and specificity. It has been suggested that faecal smears can only be used in advanced clinical cases as an interim diagnosis.[21] False positives can occur if the environment is heavily contaminated by faeces from heavy shedders.[22] There is also a skin test with an intradermal injection of johnin, similar to the tuberculin test, but this test has only very limited value.[23]

Initially, Compliment-Fixation or CF Tests were used in goats and this was the test used when Johne's disease was first reported in Australian goats.[24] Then Agar Gel Immuno-Diffusion or AGID tests were developed as the diagnostic test for goats e.g. when 331 goats were tested in Western Australia as part of the surveillance for proof of freedom from Johne's disease.[25] ELISA tests were developed and these have better sensitivity and specificity in cattle than other earlier serological tests. Research in the USA with dairy goats compared ELISA tests using sera and individual milk samples and found that the sensitivity was 64% compared with 48% respectively to faecal cultures. However, a RIRDC study compared the AGID and ELISA tests and found the ELISA detected more cases of Johne's disease in goats.[26] ELISA tests are the serological tests mentioned in the Goat Market Assurance Program or MAP (**www.animalhealthaustralia.com.au/wp-content/uploads/2011/04/GoatMAP-manual.pdf**). Also mentioned in this MAP is the PCR test, which is a DNA based test and which is now widely used in cattle. A recent study looked at using ultrasonography to detect enlarged mesenteric lymph nodes (94%) and/or thickened intestinal walls (80%).[27]

There is no test that identifies the goats that are in the early stage of incubating Johne's disease. Goats with Johne's disease can be classified into four stages as summarized in the table below:[28]

| Stage | Clinical signs | Positive Blood Test Result | Shedding in Faeces |
|---|---|---|---|
| Early incubation/ silent infection | None | None –although may pick up a cellular immune response by interferon gamma assay | No |
| Subclinical | none | Possible | Yes but low numbers |
| Clinical | Weight loss | Yes | Yes- high numbers |
| Advanced | Emaciation, dehydration, clumped faeces, intermittent diarrhoea | Yes | Yes- extremely high numbers |

The number of identified goat herds with Johne's disease and reported by Animal Health Australia reports is very low and this could be due to the Caprine Arthritis Encephalitis (CAE) control program that involved snatch birthing kids and raising in isolation on milk replacers. **However, goats can become infected with Johne's disease from both cattle and, to a lesser extent, sheep with the disease. All veterinarians dealing with dairy goats in states such as Victoria and Tasmania, where Johne's disease is prevalent, should keep Johne's disease on their list of differential diagnoses where there is loss of body condition in adult goats. Don't just think gastro-intestinal parasites. Remember also that the sheep strain, while less likely to infect goats, is also less likely to develop severe clinical signs, sero-conversion and shedding.** If doing a necropsy, vets should take the advice of Thomas (1983)[30] i.e. that smears of ileum and mesenteric lymph nodes that are the stained with Ziehl –Neelsen stain should be examined 'in all post mortem examinations of goats'. The Australian New Zealand Sub-Committee on Animal Health Laboratory Standards recommends that the following samples be taken for both culture and histopathology for diagnosing Johne's disease:-[31]

- Entire ileocaecal valve
- Ileocaecal lymph nodes
- Ileal (caudal jejunal) lymph nodes
- Two (10 cm) pieces of ileum (one proximal and one distal (terminal))
- One (10cm) piece of proximal colon
- One (10cm) piece of caecum (for histopathology only)

If your goat clients need more information or convincing of the need to necropsy wasting goats, I would recommend they look at this PowerPoint and audio combination about the devastation that Johne's disease caused in a Saanen goat herd in Chile over many years without any diagnosis. See: **www.johnes.org/presentations/Diagnosis/Maine-DVMs-Cases.m4v**

Only when an accurate diagnosis is obtained can a goat owner initiate the correct control program and start on the way to recovery. A vaccination program can then be started which will delay clinical signs and shedding, although it won't prevent cases of Johne's disease.

**References:** Due to space constraints, the comprehensive list of reference can be accessed in the eBook version of this issue.

## INTERESTING LINKS

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**www.campbellpet.com/products/Handling-and-Restraint/EZ-Nabber**

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