THE UNIVERSITY OF SYDNEY
Centre for Veterinary Education
Professional Development Leaders

C&T

CONTROL AND THERAPY SERIES

March 2012 ISSUE 266
Australia's Leading Veterinary Forum

Feature Article

Management of chronic canine hypophosphataemia

Centre for Veterinary Education
Professional Development Leaders

C&T
CONTROL AND THERAPY SERIES

The Centre for Veterinary Education (CVE)
T. (02) 9351 7979
F. (02) 9351 7968
E. cve.publications@sydney.edu.au
www.cve.edu.au
Level 2, Vet Science Conference Centre,
B22, Regimental Crescent, The University of Sydney, NSW 2006.

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PUBLISHER
The Centre for Veterinary Education (CVE)
Director
Hugh White BVSc MVSc MACVSc

EDITOR
Elisabeth Churchward
T. 9351 7979
E. cve.publications@sydney.edu.au
Veterinary Editors
Hugh White
Richard Malik

ADVERTISING ENQUIRIES
Patricia Swift
T. 9351 7979
E. pswift@sydney.edu.au

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COVER IMAGE
Jenna O'Grady Donley pictured with her final year mentor and friend, Robert Johnson – see page 6.

Welcome to the first edition of C&T for 2012. You will have noticed that our front cover shows Jenna O'Grady Donley with her mentor Robert Johnson, who has written a lovely tribute to Jenna on page 6. The accidental death of one so young and talented always comes as a shock.

The CVE held two events in February, with a very successful cattle workshop at the Camden campus of the University of Sydney early in the month and the Feline Conference at the Sydney campus two weeks later. The cattle workshop was the first of its kind conducted by the CVE, with an intensive 4 day program designed by Ian Lean to suit both beef and dairy cattle vets, who were drawn from all states of Australia and from as far away as Kununurra and New Zealand. John House and Alison Gunn, from the Livestock Services Unit at Camden, were critical to the success of the workshop as they arranged the logistics of teaching 34 veterinarians of varying skill levels the practical and didactic components of the workshop.

The Feline Conference was well attended and the feedback from participants was very positive. The two key speakers were enthusiastically received as were all the Australian based supporting presenters. Dr Gary Norsworthy from San Antonio in Texas gave both informative and practical lectures which had masses of useful take-home messages for practitioners. Professor Jane Sykes from UC Davis (an ex-pat formerly from Melbourne) gave a series of fascinating lectures, with the latest information on infectious diseases, adverse drug reactions and bacterial resistance.

Our next major conference will be held offshore at Phuket in Thailand. This conference will feature 4 days of endocrinology with David Church and Tom Graves the main presenters, who will be supported by Jill Maddison. This will be a fantastic conference, so book early and plan your holiday around this event.

As usual there will be many workshops and seminars held around the country this year, as well as TimeOnLine courses and Webinars. Many are advertised in this edition of C&T or can be found on the CVE website. There will be something for everyone and as usual our emphasis is on providing high quality education with practical information of immediate use to all of our customers.

There have been a number of recent awards honouring people associated with the CVE.

Dr Steven Holloway was awarded the 2011 T G Hungerford Award at the Feline Conference Dinner; Dr Graeme Allan has been awarded a Doctor In Veterinary Science (DVSc) by the University of Sydney for his thesis entitled 'Radiological studies of disease in companion and zoo animals'; Prof Boyd Jones was awarded the WSAVA International Award for Service to the Profession and Dr Doug Bryden AM, a former Director of the CVE, was recently awarded a Companion of the University, at Charles Sturt University. We offer our congratulations to each of these eminent members of the veterinary profession and long-time supporters of the CVE.

Hugh White BVSc MVSc MACVSc
DIRECTOR

Valentine Charlton Bequest – Equipment purchases in 2011

Figure 1. Rachel Quek, Jin Ah Hwang and Sanaa Zaki putting the donated equipment to use at the Sydney University Veterinary Teaching Hospital.

In April 1993 the University of Sydney was informed that the Post Graduate Foundation in Veterinary Science – now the CVE – was a significant beneficiary of a bequest from Valentine Eunice Margaret Victoria Charlton. The primary objective of this bequest is to provide for ongoing research and education in feline medicine and welfare with a particular emphasis on feline respiratory diseases.

As trustees of the bequest the PGF aims to ensure the future longevity and perpetuity of the fund by careful investment and preservation of the capital base. The PGF will also ensure that all expenditure of the income or requests for funding uphold the express wishes of the late Valentine Charlton.

In 2011 interest from the Valentine Charlton Bequest was used to fund

- a Cardell MAX – 12HDi+lo-flow Multi-Parameter Monitor with Invasive Blood Pressure Monitoring for use in the Sydney University Veterinary Teaching Hospital, Camperdown; and
- an Olympus Digital Camera with associated software for use in the Veterinary Pathology area of the university.

While this equipment will be used to improve the health and wellbeing of animals in the hospital, they will also be used to develop learning objects to be used not only in the Faculty but also in courses run by the CVE.

CVE ANNUAL REPORT YE 2011

The Annual Report is available at
www.cve.edu.au/reports

CVE 2012 SHORT COURSES

With a wide range of conferences, workshops and online courses, you can confidently choose the CVE to provide you with the professional development you seek to become a better practitioner and ensure the continuing success of your practice.

To register your interest or for further information, including prices and programs, visit **www.cve.edu.au/calendar** or email **cve.events@sydney.edu.au** or call (02) 9351 7979.

CONFERENCES & SEMINARS

2012

16 Mar	**Small Animal Problem Solving & Clinical Decision Making** Kersti Seksel, Jill Maddison (UK), Richard Malik, Darren Merrett, Andrea Harvey (UK), Graeme Allan and Robin Stanley	Sydney
18 Mar	**Canine Internal Medicine** Steve Holloway	Hobart
15 Apr	**From Nose to Tail: A Review of Surgical Techniques in the Dog** Pete Laverty	Adelaide
17 Apr	**Ruminant Nutrition** Paul Cusack	Benalla, VIC
29 Apr	**Wound Management & Reconstruction** Arthur House	Brisbane
24 Jun	**Canine Internal Medicine** Steve Holloway	Canberra
8 July	**Anaesthesia** Sanaa Zaki & Gabrielle Musk	Perth
10-13 Sept	**Small Animal Endocrinology** David Church (UK) & Thomas Graves (USA)	Thailand
21 Oct	**From Nose to Tail: A Review of Surgical Techniques in the Dog** Pete Laverty	Adelaide
21 Oct	**Canine Internal Medicine** Steve Holloway	Perth
17 Nov	**Wound Management & Reconstruction** Arthur House	Melbourne

WORKSHOPS

The following workshops will be available in 2012. Please refer to the CVE website for registration details.

Bone Plating in the Dog	**24 or 25 March**	Dubbo, NSW
Hip & Stifle in the Dog	**21 or 22 April**	Sydney, NSW
Emergency Workshop	**5 or 6 May**	Adelaide, SA
Canine Rehabilitation Introductory Workshop	**20-21 July**	Sydney, NSW
Canine Rehabilitation ICU Masterclass*	**22 July**	Sydney, NSW

* Prior learning will be required to attend this workshop.

TIMEONLINE COURSES

TimeOnline courses are delivered wholly online, giving you the flexibility to study when and where you wish and complete your course at your own pace. Listed dates for all short courses are subject to change. Please refer to the Events page of the CVE website, **www.cve.edu.au**, for the latest updates, full programs, prices, etc.

19 Mar - 15 Apr	**Wildlife (Undergrads ONLY)** David Blyde
30 Apr - 27 May	**Animal Welfare** Pauleen Bennett
21 May - 17 Jun	**Avian** Alex Rosenwax
2 Jul - 29 Jul	**Rabbits & Rodents** David Vella
9 Jul - 5 Aug	**Pain Management** Gabrielle Musk and Sanaa Zaki
23 Jul - 19 Aug	**Treating Burns (Undergrads ONLY)** Anne Fowler
24 Sept - 21 Oct	**Treating Burns (Undergrads ONLY)** Anne Fowler

TimeOnline

For information on 2012 courses visit:
www.cve.edu.au/timeonline
Or email: **cve.timeonline@sydney.edu.au**

CVE WEBINARS

Looking for a quick educational pick-me-up?

Watch out for the CVE Webinars in 2012. One hour of education with the convenience of doing it from your own desk.

Whether Veterinary Issues or Practice Management, there will be something each month to interest you.

Watch for these symbols to see what is available.

Terms and Conditions and Policies of the CVE can be accessed through the CVE website.

Authors' views are not necessarily those of the CVE

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AWARDS TO CVE DE TUTORS

The WSAVA International Award for Service to the Profession presented to Prof Boyd Jones Nov 2011

Boyd Jones BVSc FACVSc DECVIM-Ca MRCVS (center) with past and current WSAVA Presidents.

Boyd, well known to CVE members as our DE Tutor for 'Internal Medicine: Keys to Understanding', is pictured above receiving his award from John Holt, a former President of WSAVA, at last November's World Congress in Korea.

This Award is based on exemplary service by a veterinarian who has fostered and enhanced the exchange of scientific and professional ideas throughout the world. The recipient will be chosen on the basis of service to local, state, national and international organisations that have catalysed scientific meetings, exchange of information and international goodwill, for the benefit of the profession worldwide.

Prof Boyd Jones graduated from Massey University, worked in mixed practice then taught at the University of Melbourne. He returned to Massey, became Head of the Small Animal Hospital and undertook sabbaticals in Britain and at the University of Florida. He was involved with local and international veterinary organisations and participated in continuing education. He is a Fellow of the Australian College, Diplomate of the European College and an RCVS Specialist in Snall Animal Medicine. He is a former President of the Australian College, Chairman of The Veterinary Council of New Zealand, a board member of The Veterinary Council of Ireland and Vice President of The European Association for Evaluation of Veterinary Establishments (EAEVE). He was Professor in Small Animal Clinical Studies at University College Dublin, and Dean of the Faculty from 2002-2007. He returned to New Zealand as Professor of Companion Animal Medicine at Massey University. He has participated in distance education learning and continuing education including WSAVA Congresses. Prof Jones is an editorial board member and has acted as a referee for clinical journals. He has been an examiner for University graduate degrees and for specialist College qualifications. In 2008 he was the Chair of the scientific committee for the 33rd WSAVA Congress in Ireland.

Throughout his career Prof Jones has contributed as a referral clinician, for advice on and investigation of cases from practitioners. He has published 170 refereed papers and book chapters and interests include service and working dogs and veterinary education, as a Director of Veterinary Education International.

(Excerpt from WSAVA-FASAVA World Congress Programbook)

STOP PRESS *** STOP PRESS!

Dr Graeme Allan awarded DVSc

Graeme Allan (second from left) teaching at Cootamundra in 1983.

We were also informed, just before this issue went to press, that Graeme – co-tutor of our Diagnostic Imaging Distance Education program with Robert Nicoll – has been awarded a DVSc for clinical research, thus confirming his status as Australia's foremost leader in veterinary diagnostic imaging.

This is particularly significant as we understand that this is the first time a vet has been so honoured. Watch this space for the full story in a future issue…

CONGRATULATIONS FROM THE CVE STAFF, COUNCIL AND COMMUNITY

We offer our heartfelt congratulations to both Boyd and Graeme on their well-deserved recognition. The staff and council at the CVE are very proud of our long-term association with veterinarians/educators of this calibre and these Awards have only confirmed what all our Distance Education Participants who were lucky enough to have enrolled in their courses have always known – learning under Boyd and Graeme's tutelage has always been a true privilege.

Note: Both Graeme and Boyd are the recipients of the T G Hungerford Award (in 1993 and 2009 respectively), the highest award the CVE/PGF can confer and which recognises excellence in continuing veterinary education. The T G Hungerford Award was instituted by the Council of the Post Graduate Foundation in Veterinary Science on the retirement of Dr T G Hungerford OBE who was the first Director of the Foundation. The award was in recognition of his enormous contribution to the veterinary profession and to the Australian community and was first awarded in 1987.

2011 T G Hungerford Award – Oration

We are delighted to announce that Steve Holloway is the recipient of the 2011 T G Hungerford Award - see page 6.

Our June issue will feature Richard Malik's oration which was delivered at the T G Hungerford Award Dinner held at The Refectory, University of Sydney on Thursday 16 February 2012.

Watch this space!

Dr Douglas Bryden AM - Companion of Charles Sturt University

Former CVE Director, Dr Douglas Bryden AM, has been made a Companion of Charles Sturt University in recognition of his contribution as a Consultant to the University assisting with the development of the Veterinary program. The program was established to address the declining participation of veterinarians in rural practice, rural communities and the livestock industries and has been an outstanding success.

We will follow up this story in our June 2012 Issue 267, but in the meantime sincere congratulations to Doug from the CVE/PGF community, who benefitted enormously under his Directorship and governance.

Thank you to all contributors

… and more C&T articles and Perspectives needed

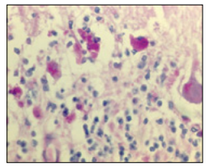
Thanks to every author who contributed articles or comments to the *Control & Therapy Series* (C&T). Without your generosity the Series would cease to exist.

If you have treated a Large Animal, or Reptile, or any Wildlife lately, please write up the case and send it in. We aim to keep the Series broad and interesting.

C&T Series goes live!

Members/Readers of the soft copy version will be delighted to see that the March 2012 issue is in *e-book* format, allowing for a range of interesting features to be incorporated into the body of the PDF, such as the linking of **audio and video** with static print articles. **Look for this symbol ‹e-book› and 'roll over' it with your mouse.**

Georgina Child and Amy Lam's article 'Increased incidence of an inherited neurodegenerative disease (NCL or CL) in Border Collies' is our inaugural e-article and incorporates a video of 'Clover' and an enlarged slide image of NCL. (Courtesy of Peter Windsor & Gauthami Kondagari from OLIVER, copyright The University of Sydney)



Other features include the enlargement of Xrays and the ability to 'roll over' an article to view additional pertinent material omitted from the print version due to space constraints.

This is a wonderful advance for the Series and we encourage our contributors to embrace this opportunity by taking accompanying videos for their C&T articles and supplying Xrays and other visuals whenever possible.

PRINT copy recipients are invited to go to our website www.cve.edu.au/candtebook to view our e-book version.

Winners of Best Article in this Issue

Major Prize

Entitling the recipient to one year's free membership of the CVE

- **Virginia Grice:** Management of chronic canine hypophosphataemia

CVE Publication Prize Winners

- **Martin Whitehead:** Multi-focal osteomyelitis in a Bearded Dragon
- **Nick Lloyd:** Proliferative and necrotising otitis externa in a young cat
- **Dave Goodwin:** 'Seaver's Slide' saves the day!
- **Natalie Burke:** Flea-related anaemic crisis in a young kitten
- **Nathalie Dowgray:** *Isospora* causing diarrhoea and weight loss in hand-reared kittens

Co-Winners of Best Pictures

Entitling the recipients to a free DVD from the CVE's Vetbookshop

- **Eamonn Lim:** Cladosporium and posaconazole
- **Amy Lingard:** What's YOUR diagnosis?

Winner of Best Video

Entitling the recipient to a free DVD from the CVE's Vetbookshop

Georgina Child & Amy Lam: Increased incidence of an inherited Neurodegenerative disease (NCL or CL) in Border Collies

Contact

For further information on the *C&T Series* contact Lis Churchward, CVE Editor **cve.publications@sydney.edu.au** or (02) 9351-7979.

The C&T and Perspective Series is the brainchild of Dr Tom Hungerford, first Director of the PGF (1968-1987), who wanted a forum for uncensored and unedited material. Tom wanted to get the clinicians writing.

'…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.'

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Tribute to Jenna O'Grady Donley

By Robert Johnson – Jenna's final year mentor and friend

Jenna Donley from the University of Sydney BVSc graduating class of 2011 passed away in early December as the result of an accident in Borneo. Jenna was not only a brilliant student but a most kind and caring person. She had a great future in the veterinary profession, particularly in the fields of rural mixed practice and wildlife and zoo medicine. Her Honours thesis on renal disease in captive non-domestic felids was awarded one of the highest marks ever in the University of Sydney Veterinary Faculty. A trust has been set up by the University of Sydney to ensure that the work that Jenna started will go on. She was awarded the University Medal for her academic efforts, which was collected posthumously by her very courageous mother.

Jenna's passion for zoo and wildlife medicine led her to complete clinical rotations at Taronga zoo and Adelaide zoo. In addition, Jenna poured her energy and enthusiasm into her fifth year research project on characterising renal disease in non-domestic felids. She was successful in winning the Morris Animal Foundation Student Scholarship for her honours project, competing against student researchers from around the world and was due to present this work in Orlando Florida in March 2012. Jenna worked closely with her supervisors Jacqui Norris, Richard Malik and Joanna White on this project, as well as the generous and dedicated staff at Taronga (Sydney) and Taronga Western Plains Zoo, where the project was based. The Morris Animal Foundation has now given Jacqui permission to present Jenna's work on her behalf. Jacqui and her team will continue to present these research findings to conferences locally and internationally to give greater awareness of the urgent need to move forward in providing evidence based solutions to a remarkably common group of diseases in some of our most endangered animal species.

As her final year mentor I was well aware of Jenna's focus and commitment to being a zoo veterinarian. She did however realise that it was very worthwhile to gain initial experience in general practice, especially rural mixed. We also discussed the benefit of various postgraduate study paths in zoo medicine and related fields. Jenna wished to continue her research interests as well as gain valuable practice experience. I soon realised that she was the sort of person that when given advice would act upon it, so it had better be good! Our contact throughout the year was by email, SMS or face-to-face meetings. Jenna also spent a 4 week rotation at Taronga Wildlife Hospital. Throughout the year Jenna managed to complete her Honours thesis, study for her final year exams and achieve a wide variety of clinical experience. She also made time for her much loved family and her life partner Matt. She will be sadly missed but her memory and her devotion to the welfare of captive and wild animals will endure.

For information regarding how to make a gift in memory of Jenna O'Grady Donley, you can download the Gift Form at: ***sydney.edu.au/supportsydney/how/memorial_gifts***

CVE Clinical Competency AWARDS FOR 2011

Each year we take great pleasure in inviting each Australian and New Zealand Faculty of Veterinary Science to contact us with the name for a recipient of the Centre for Veterinary Education Clinical Competency Award. This prize of $1,000 worth of CVE publications and/or other CVE products (Courses etc) is offered to the graduating student who has been recognised by the Faculty as being the most competent in clinical skills over the clinical portion of his or her undergraduate years. We are delighted to award the prize to the following graduates:-

Charles Sturt University	**Rhys Duncan & Kate Burnheim**
Murdoch University	**James Haberfield**
University of Melbourne	**Elise Harding**
University of Queensland	**Julia Dowsett**
University of Sydney	**Penelope Brown**

Note: The Massey University recipient will be announced in our June 2012 issue.

2011 T G Hungerford Award

The 2011 TG Hungerford Award was presented to **Dr Steven Holloway** at the Annual Dinner on 16th February 2012.

Steven graduated from the University of Sydney in 1983 and worked for two years in private practice in Sydney followed by a two-year medical internship at the University of Melbourne, after which he was awarded an MVS and obtained membership of the ACVSc (Feline Medicine). He then undertook an internal medicine residency at the University of Florida, followed by two years as a clinical instructor at the University of Florida. In 1990 he became a Diplomate of the ACVIM (SAM). Steven returned to Australia in 1994 studying equine herpesvirus infections with Professor Michael Studdert and was awarded a PhD from the University of Melbourne in 1998. He lectured at the University of Sydney in 1998-1999 and was a Senior Lecturer and Associate Professor of Small Animal Medicine at the University of Melbourne 1999-2009. Steven is currently a registered specialist in small animal medicine and works at Advanced Vetcare in Melbourne.

With his outstanding contribution in the arena of veterinary education, the Centre for Veterinary Education Council is honoured to present Steven Holloway with the 2011 T G Hungerford Award.

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Sudden deaths of cattle due to arsenic poisoning

C&T No. 5200

Peter Launders
Cowra Veterinary Centre
102 Darling Street
Cowra NSW 2794
T. 02 6341 3113
E: cowravet@bigpond.com

Clinical scenario

Further to Adrian Bryant's article and Peter Windsor's comment (C&T No. 4975 from March 2009) ‹e-book›, I have also experienced cattle dying suddenly due to ingestion of arsenic. This case report goes through the diagnostic process that led me (finally) to a definitive diagnosis of arsenic toxicity.

On the day after Boxing Day 2009 I received a call from a local producer as a number of steers on agistment at his property had died suddenly. A mob of 100 2-year-old Angus steers had arrived 10 days previously from the Hunter Valley. Ten steers were dead by the time I arrived at the property. Clinical signs displayed before the deaths included mania or aggression, convulsions, ataxia and recumbency. Death occurred within hours of the development of clinical signs. The steers had been vaccinated against clostridial diseases ('5-in-1') 6 to 9 months earlier; were on native pasture, with no lush green feed and few weeds and had been receiving no supplementary feed or lick blocks. There were no old cars, dumps or rubbish in the paddock, and no previous incidents of sudden death on the property. The remainder of the mob in Orange was unaffected.

A number of the dead animals were located in or close to a dam in the paddock. One steer was in lateral recumbency but unable to get up. The steer had mild abdominal bloating on its left side with a dark brown-greenish scour present nearby, but no signs of bubbles or grain in the faeces. Rectal examination revealed a small amount of blood but no faeces. Mucous membranes were dark purple with some excess salivation. Heart rate (120bpm), respiratory rate (40bpm) and temperature (39.7°C) were all elevated. The producer mentioned that some cattle had access to triticale grain (by getting through the fence into a neighbouring property and getting access to a grain silo) so lactic acidosis (grain poisoning) was considered a possibility. The recumbent steer was treated with intravenous Vitamin B1 and intravenous dexamethasone but was dead when rechecked an hour or so later.

A necropsy examination was performed on a freshly dead steer that was lying in right lateral recumbency with mild bloating of the abdomen. The blood was of normal colour and clotted normally. The kidneys appeared congested but the liver, spleen, heart and lungs all appeared grossly normal. The rumen and reticulum also appeared normal and very full of dry grassy feed (consistent with intestinal stasis). There was no grain in the rumen or in the nearby faeces. The mucosal lining of the omasum and abomasum was grossly inflamed and ulcerated (consistent with nitrate-nitrite toxicity or enterotoxaemia). The inflammation and erythema continued down through the small intestine and large intestine.

Numerous samples were taken for laboratory analysis: jugular blood, aqueous humour, kidney, spleen, liver; urine, small intestine, small intestine contents, large intestine, mesenteric lymph node, omasum, abomasum and impression smears of small and large intestine. In-house testing of the urine showed the presence of glucose, consistent with enterotoxaemia.

The tentative diagnosis was enterotoxaemia, possibly triggered by the change in diet from the Hunter Valley property to the agistment property. Enterotoxaemia is caused by a clostridial organism that is normally present in cattle. Disease and death occurs when the number of organisms multiplies and the epsilon toxins produced enter the bloodstream and cause extensive damage to the animal's blood vessels. Clinical signs of enterotoxaemia typically include mania, inco-ordination, convulsions, intestinal stasis and death.

Though the steers were vaccinated against clostridial diseases, vaccination may be required on a more frequent basis to prevent enterotoxaemia in certain (ill-defined) conditions. However, a number of pathological features expected to be seen with enterotoxaemia were not present at necropsy (e.g. small intestinal contents not creamy/yellow; no pulmonary oedema/congestion). The producer was advised to move the remaining steers to another paddock and vaccinate them with '5-in-1' (even though the vaccine is not immediately protective).

Diagnostic possibilities

Differential diagnoses at this stage included nitrate-nitrite toxicity (cloudy weather; but blood not brown), lactic acidosis (but no grain in rumen), lead poisoning (but no known access and unusual to see large numbers of cattle affected), unknown toxicosis (possibly from treatment of the grain), cyanobacteria (algal bloom in dam water), pneumonia (due to travel stress but lungs grossly normal), botulism (but tongues not protruding and no flaccid paralysis) and anthrax (but soils acidic and blood clotting). Arsenic toxicity had not been considered.

Two days after the initial visit, a second necropsy was performed on a steer that had died overnight, bringing total losses to 16 head, though no new clinical cases developed following the change of paddock. Gross appearance on necropsy was similar to the first necropsy with the following differences: the omasum/abomasum/intestines were less inflamed, rumen contents were more fluid, there was fluid present in the pericardial sac, the liver was pale (possibly necropsy autolysis), the rumen lining was sloughing (possibly normal necropsy change), there was a quantity of dirt/sand present in the abomasum and the lungs were congested and purple (agonal changes).

Numerous samples were again taken for laboratory analysis: jugular blood, aqueous humour, kidney, liver, small intestine, small intestine contents, impression smears of small and large intestine, lungs, pericardial fluid, rumen fluid and dam water. Field measurement of rumen fluid showed a pH of 7-8, which is not consistent with lactic acidosis (where an acidic pH is expected), but the reliability of this measurement is questionable as it was done more than an hour after death.

The case was discussed with the pathologists at Eliza Macarthur Agricultural Institute (EMAI), the District Veterinarian from the Livestock Health & Pest Authority (LHPA) and veterinarians with extensive experience with cattle deaths to come up with a list of likely differentials and a diagnostic plan to investigate these differential diagnoses.

The diagnostic plan was dependent on the laboratory results with further tests being requested as the most likely differentials were ruled out:

- **Enterotoxaemia** (*Clostridium perfringens*) – organisms identified on intestinal smears but **negative** for epsilon toxin
- **Cyanobacteria (blue-green algal bloom) – negative** in dam water
- **Nitrate-nitrite toxicity – negative** in aqueous humour fluid dipstick test
- **Histopathology** results:
  - o Liver – severe peracute multifocal necrotizing hepatitis
  - o Kidney – severe hyperacute medullary tubular necrosis

Based on the histopathology results, the EMAI pathologist was leaning towards a **bacterial or viral infection** in the liver and kidneys

- The pathologist attributed the erythema of the omasum and abomasum to congestion from a shock organ reaction, rather than any pathology.
- After further discussion with colleagues, the pathologist advised that viral infection was unlikely to be the cause. Even though the liver damage appears quite similar to that seen with herpesvirus in horses, herpesvirus in cattle does not typically cause liver damage.

Bacterial culture:

- **Negative** for *Salmonella*
- **Positive** for *Aeromonas sobria* (likely to be an incidental finding as this organism is primarily a pathogen of aquatic species not mammals; interestingly, the liver pathology seen in fish with *Aeromonas sobria* infection is similar to that seen here!)

A couple of other specific diseases were considered but ruled out:

- **Black disease** (*Clostridium novyi*) – possible as liver fluke present in the Hunter Valley; **unlikely** as no inflammatory changes in the liver
- **Lactic acidosis – no supporting evidence** (no grain in rumen/faeces, rumen fluid not acidic, expect to see range of syndromes with some less severely affected, not just all dying suddenly)

A breakthrough!

At this stage, Andrew Thompson from EMAI, a different pathologist who had taken over the case, suggested testing for arsenic and lead toxicity:

- **Lead poisoning – negative** in kidney
- **Arsenic toxicity – positive** in liver (>1mg arsenic/kg) by Reinchs test

Clinical signs of arsenic toxicity include diarrhoea, dehydration, abdominal pain, weakness, convulsions and cardiovascular collapse with rapid onset and progressing quickly to death within hours. On reflection, the abomasal ulceration should perhaps have led us to consider arsenic toxicity earlier. However, the second necropsy did not show this almost pathognomonic sign and it is unusual to see liver necrosis with arsenic toxicity. While the diagnostic process in this case took almost 3 weeks to reach a conclusion, the early actions taken (primarily moving stock to a different paddock) were successful in minimising further stock losses by restricting exposure to the toxin.

Due to the presence of arsenic and the subsequent restrictions on selling or moving the cattle, the local LHPA District Veterinarian took control of the case to identify the source of the arsenic and advise on movement restrictions. A property inspection identified a distinctive 'chemical' smell in a small shed in the initial paddock with evidence that the cattle had licked the floor clean trying to get the arsenic salts, and chewed plastic bags. Soil tests from inside and outside the shed revealed arsenic levels of 2200mg/kg soil and 1400mg/kg soil respectively. The owner was advised not to slaughter any of the cattle for at least 72 days to minimise the risk of any food safety/residue issues. The producer was advised to excavate the area and bury the contaminated soil with the carcasses.

The producer had purchased the property in 1991 and had not used arsenic in that time. He contacted the previous owner who had no recollection of using arsenic since it was taken off the market in 1982. However, he did recall having used arsenic for a sheep plunge dip at some stage. Thus, the arsenic had been present undisturbed in the shed/soil for almost 30 years.

Hopefully, this case reinforces the key points that arsenic persists for a long time in the soil/environment and that it should still be considered as a possible cause of sudden death in cattle. Another key point to take away (and to remind producers) is that the process of investigating and diagnosing the cause of sudden death can be long, frustrating, expensive and often unrewarding as there may be many possible causes which will require serial rounds of laboratory testing to reach a definitive diagnosis.

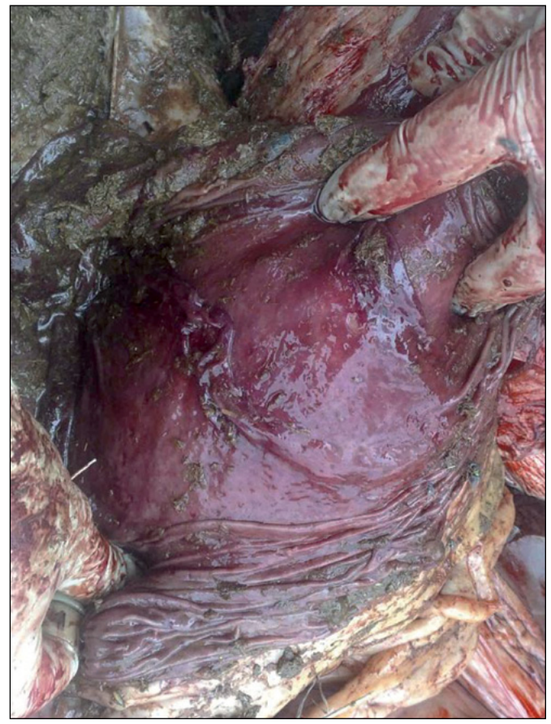

Figure 1. Abomasal erythema and ulceration

Authors' views are not necessarily those of the CVE
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WINNER

Multi-focal osteomyelitis in a Bearded Dragon

C&T No 5201

Martin Whitehead
Chipping Norton Veterinary Hospital
Albion Street, Chipping Norton
Oxfordshire OX7 5BN
United Kingdom
E. martin.whitehead@virgin.net

Martin, generously taking pics for the C&T Series.

Martin has won a free place at our upcoming *Pet Lizards and Snakes Webinar* – see below for details

Bearded dragons (natives of Australia) are the pet lizard most commonly seen in our UK practice. Inevitably, due both to the incomplete state of veterinary knowledge for reptile species and to financial constraints (they are often children's pets), we often do not reach a definitive diagnosis. Among the most frequent diagnoses made for systemically ill 'beardies' are metabolic bone disease (often with pathological fractures), preovulatory ovarian stasis and osteomyelitis. The 2.5-year-old male beardie pictured was a case of advanced osteomyelitis. The husbandry was appropriate and he was in good body condition, but he presented with multiple limb swellings; both forefeet, right hind foot, left stifle and left hind second toe. Despite having first noticed swollen toes and reduced activity 4 months previously, and further swellings appearing in the meantime, the owner had not sought veterinary attention because the patient had appeared bright otherwise, was eating well and had not lost weight.

The conscious whole-body dorsoventral radiograph (Figure 1) demonstrated multiple areas of bone lysis including both carpi, both tarsi, the left stifle and some toes. A poor prognosis was given and euthanasia recommended but the owner was keen for 'something to be done' so the beardie was briefly anaesthetised (intramuscular medetomidine and ketamine to allow intubation then isofluorane for maintenance) to allow fine-needle aspirates of the swellings around the lytic areas of bone to be taken, after a surgical scrub of the aspiration sites, for cytology, culture and susceptibility. During anaesthesia a Doppler blood pressure device was used to monitor the heart and a lolly stick taped to the head to stabilise the endotracheal tube (Figure 2). A blood sample was also taken and the beardie given meloxicam and enrofloxacin while awaiting the culture results. The blood sample revealed raised uric acid indicating renal failure. The white-cell count was in the normal range. The culture grew only a coagulase-negative *Staphylococcus* – which I judged likely to be a contaminant. As there was, unsurprisingly, a poor response to the analgesia and antibiotics the beardie was euthanased about a week later.

Obviously, if there are multiple sites of osteomyelitis, there may also be multiple undetected sites of soft-tissue infection. I did not get to do a necropsy examination in this case, but the renal failure may well have been secondary to the septicaemia that presumably 'seeded' the multiple sites of osteomyelitis. In most cases in which fine-needle aspirates are taken prior to antibiotic treatment, culture does grow a likely causative pathogen, but a substantial minority yield no growth or a likely contaminant, as in this case.

For beardies and other reptiles with radiographic evidence of osteomyelitis, if the history suggests that the lesions have not been present for too long (how long is 'too long'? – my current cut-off is a few weeks) and I can find only a single lesion on clinical examination and radiography, I recommend treatment and use analgesia and many weeks of systemic antibiotics, preferably on the basis of culture and susceptibility results (usually ceftazidime, enrofloxacin or amikacin) and I have had some good responses. However, if, as in this case, there are multiple lesions that have been present for more than a few weeks I strongly encourage euthanasia on welfare grounds as my success rate with such cases has been very poor even in the absence of identified concurrent illness. However, as in this case, no matter how bleak a prognostic picture we paint, owners sometimes need 'something to be done' before they will consider euthanasia. Often the same owners will have delayed visiting the vet for weeks or months despite their reptile having obvious illness, resulting in the pet being beyond help when we first see it.

Pet Lizards and Snakes Webinar

Robert Johnson BVSc MACVSc (Feline Medicine) CertZooMed BA CMAVA

In this webinar Dr Robert Johnson (pictured with 'Skink') will discuss:

Basic veterinary care of pet lizards and snakes, including:

- Commonly seen species in practice
- Rules and regulations
- Husbandry and handling tips
- History taking – what questions to ask?
- The physical examination
- Simple diagnostics and sampling techniques
- Commonly seen conditions
- How to treat and medicate
- Basics of anaesthesia, surgery

Date: 22nd March @ 2.00 to 3.00 pm
Cost: $40
Venue: At your computer

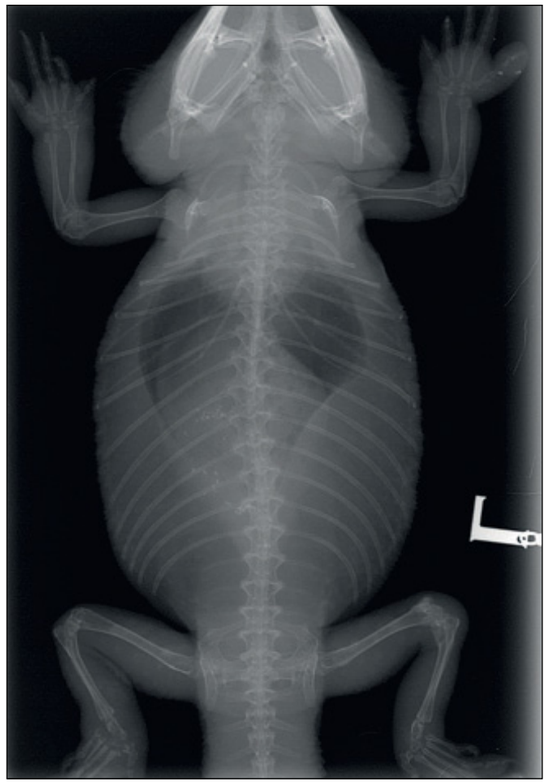

Figure 1. Dorsoventral digital radiograph of the bearded dragon with multi-focal osteomyelitis.

Figure 2. The beardie in question.

Comment courtesy of

Mike Cannon BVSc MACVSc Grad Dip Ed

Mike Cannon, well known to CVE supporters as our DE Avian Tutor, has extensive experience with zoo-keeping and wildlife parks.

Martin has done good work documenting this case. I agree with his diagnostic approach (radiology, aspirate for cytology and C&S, collect blood sample for Full Blood Count and Biochemistry). It is unfortunate that a necropsy examination and histopathology could not be performed as this may have revealed information to rule out some of the more common problems.

The results Martin reported are interesting as there are several aetiologies that may be possible:-

- The lack of growth other than a coagulase-negative Staphylococcus does not rule out organisms that require special staining or culture, such as Mycobacteria or Chlamydia; these have been reported in cases of radiographic lysis in the joints and bones of lizards[1]. Fungi could also be a possibility. As the owner did not allow necropsy and histopathology, we can only guess at the aetiology.

- As the Uric Acid (UA) levels were raised, this would support profound renal damage, but UA only rises when there is severe renal damage. A better indicator of renal disease is the Calcium:Phosphorus ratio. In a normal reptile, the ratio is >1, while in a case of renal disease this falls to < 1. This is often the first biochemistry change seen in renal disease. Hyperkalaemia may also be a sign of acute renal disease. Were any of these changes present? Unfortunately, renal disease has to be approaching a severe status before any biochemical signs are detected in the blood. Reptiles are quite hardy and do not ▶

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show clinical signs until well into the disease process, so early stage renal disease is usually undetected.

- Metabolic Bone Disease – particularly Renal or Nutritional Secondary Hyperparathyroidism. It is difficult to be certain when examining the radiograph but there may be generalised demineralisation of the skeleton. As well, there may be facial structure changes (a more rounded and shortened face) that would be typical of Metabolic Bone Disease – the angle of the image makes this difficult to assess fully – Martin, were these present?

    - It is also possible that this beardie also had Renal Secondary Hyperparathyroidism (RSHP) – a result of chronic renal failure, rather than the more common Nutritional Secondary Hyperparathyroidism (NSHP). Although NSHP cannot be completely ruled out – the fact that the beardie was on a good diet when Martin queried the owner does not mean that this has always been the case. It may be useful to discuss this case with the owner to use a more detailed history: of sunlight exposure, actual dietary components provided and the amounts the beardie ate; Is the beardie by itself in the enclosure or is it sharing with another lizard (this is always a nightmare – one eventually misses out on vital heating and dietary requirements); temperature and light regimes – use questions such as these to explore all aspects of the diet and husbandry more thoroughly, to find any facts that may shed light on this case. In my experience, owners are often blissfully unaware of husbandry problems, as they feel they have everything 'as best as it can be'.

This is an interesting case and we all struggle with clients that delay in presenting their animal and then do not allow us to do a thorough diagnostic work up and follow the case to a full resolution. I have seen cases similar to this, as have other reptile veterinarians in Australia and overseas, and in many cases the aetiology is not exposed. I congratulate Martin for documenting a case such as this to spread the word and to add to our knowledge. In many syndromes we see in reptiles, formal studies have not been done to document the actual changes and so we still have much to learn.

Reference

G Soldati; Z H Lu; L Vaughan; A Polkinghorne; D R Zimmermann; J B Huder; A Pospischil. Detection of mycobacteria and chlamydiae in granulomatous inflammation of reptiles: a retrospective study. *Vet Pathol*. July 2004;41(4):388-97.

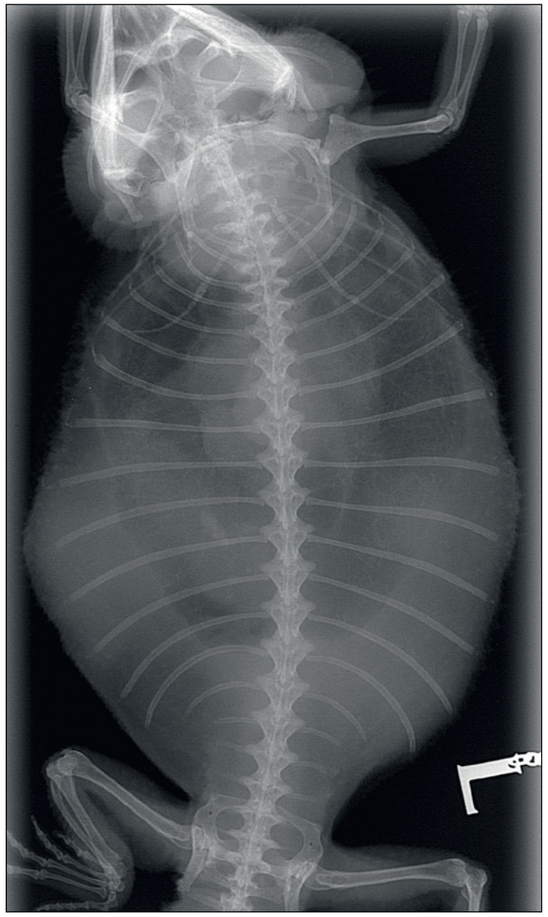
Reply from Martin to Mike Cannon's comments

The blood indicators of renal failure in this case were 'textbook'; raised uric acid and phosphorus with a very low Ca:P ratio of 0.38, indicating severe renal failure, as Mike explains. I did not measure potassium. The renal failure may have been caused by the infection that produced the osteomyelitis, may have been a pre-existing factor perhaps predisposing to infection, or may have been incidental to the osteomyelitis. Beardies presenting with renal failure severe enough to substantially increase serum uric acid have usually lost a lot of weight over a few weeks, are inappetant and obviously underweight. As this animal was in good condition and reportedly had been eating well for months after the first signs of osteomyelitis, my guess is that in this case renal failure began after the osteomyelitis.

Mike wonders whether this case, as well as having osteomyelitis, has generalised radiographic demineralisation of the skeleton, which would be consistent with metabolic bone disease (MBD). I think it probably does, although as I explain below I am not sure how abnormal that is for a UK beardie. Judgment here is subjective and, although in many cases demineralisation is blatantly present or absent, in many other cases I cannot be sure if there is significant demineralisation or not. I try to judge these radiographs before looking at blood results to avoid those influencing my interpretation, and I usually take at least 2 exposures with slightly different kV and mA settings, which I then compare to my store of radiographs of previous beardie cases that I decided did or did not have MBD. Judgment of 'borderline' cases is to some extent influenced by the kV and mA settings (that is why I take exposures at different settings) and by size and body condition (amount of soft tissue). There are beardies with better-mineralised skeletons than the above case, but among all those beardies that our practice radiographs, the above case does not at all stand out as having poor skeletal mineralisation. Figure 1 shows our 'best ever' mineralised beardie skeleton (a big 6 y.o. beardie that was lethargic and inappetant and that had cystic abdominal masses consistent with neoplasia). To us, this radiograph really stands out as we see very few cases with radiographic bone density approaching this. The animals we radiograph are all ill or injured, but our radiographs of adult beardies with apparently good husbandry and without blood-biochemical indicators or specific signs of MBD (as opposed to non-specific signs such as lethargy and inappetance which may be related to other illness and/or MBD), show a wide range of radiographic skeletal mineralisation. Some animals with no specific signs of MBD have very deficient skeletal mineralisation – much worse than the above osteomyelitis case – and we confidently diagnose those as having MBD. But what is the lower limit of the 'normal' range of radiographic mineralisation? Do all but the most radiographically mineralised have MBD? If so, then – despite our diagnosing clinical MBD very frequently – almost every adult beardie without clinical MBD that our practice has radiographed had 'subclinical' MBD. Or, was the skeletal mineralisation of many of them just 'normal' for the UK (which is perhaps the same thing)? Until we know better, we treat them as if they have subclinical MBD and so, in addition to any other care, we review husbandry and increase the UV and calcium supply. In the osteomyelitis case above, as already noted, total calcium was a little low and phosphorus raised, consistent with renal failure – but changes with MBD could be similar! I did not think the face was rounded.

As Mike says, MBD can be secondary to renal failure (renal secondary hyperparathyroidism) but in captive reptiles it is more usually secondary to husbandry issues – inappropriate diet (nutritional secondary hyperparathyroidism) and/or insufficient UV light. The important part of the UV spectrum for vitamin D3 production is UV(B) and there is much discussion concerning the amount of UV(B) needed, the best type of UV source to use, and how far it should be from the reptile. And it varies with species, of course! MBD secondary to husbandry issues is probably the most common diagnosis for systemically ill beardies as well as for several other lizard species (young veiled chameleons seem particularly sensitive) and tortoises.

Mike is right to emphasise history taking for reptiles – we have longer consults (20 minutes) for reptiles than for dogs and cats for that reason. This beardie was kept on its own and the husbandry was good. However, 'good' husbandry in the UK is still a different thing to being in their natural environment under the Australian sun. Beardies in the UK typically live in a vivarium indoors and, as UV does not pass through glass,



they are never or almost never exposed to any natural UV light (and compared to Australia the UK is UV deficient in any case!). These days most, but still not all, keepers know that a UV source is needed, but many such lights do not provide as much UV as does the sun. Even indoors in the UK beardies need supplemental heat. Pet beardies are usually fed mixed salad/vegetables along with crickets and mealworms and sometimes locusts and waxworms. This is likely to be a restricted diet compared to their diet in the wild. Crickets, mealworms, locusts and waxworms are recommended by pet shops not because they are an ideal food, but because they are easy to grow and supply – beardies can live on them but they are not optimal. In particular, the calcium content of crickets and mealworms is low and the Ca:P ratio is very poor. A calcium and vitamin D3 supplement, either sprinkled on the food or by 'gut loading' the crickets, helps, and I recommend varying the diet by feeding bugs and earthworms from the garden (safe in the UK providing pesticides are not used, but in some other countries there are bugs which are poisonous to beardies, such as fireflies in the USA) and pinky mice. However, in the UK, in beardies, some other lizard species and tortoises it is still relatively common to see advanced MBD in the absence of renal failure even when husbandry appears to be good and, as noted above, I suspect that at least in beardies subclinical MBD is extremely frequent. These species are just not evolved to live in captive conditions in the UK.

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Christmas comes late!

C&T No. 5202

Ellie Atkinson – 2011 CVE DE Feline Participant
Castle Veterinary Clinic
Unit 3, Poundbury Business Centre
Poundbury, Dorset DT1 3WA, UK
E. ellieatkinsonvet@hotmail.co.uk

A 1 year old DSH cat (aptly named 'Twinkle') presented with an acute history of gagging, retching and pawing at his mouth after diving into a box of tinsel to play. An unusual foreign body (FB) was found– see picture above. It was wedged across the hard palate like a bone in a dog and poor kitty was unable to clear it as the points of the star had wedged in the caudal mouth (luckily for kitty... as otherwise this may have ended up a gastric FB!) I managed to grab it with forceps. I can safely say this is the first time my diagnosis has been 'Star in the mouth'! And I thought cats were so much more intelligent than the lesser species…

WINNER OF BEST VIDEO!

Increased incidence of an inherited neurodegenerative disease (NCL or CL) in Border Collies

C&T No. 5203

Georgina Child BVSc DACVIM (Neurology) [1, 2]
Amy Lam BVSc MACVSc[1]
[1] Small Animal Specialist Hospital
Richardson Pl, North Ryde NSW 2113
[2] University Veterinary Teaching Hospital, Sydney
65 Parramatta Rd, Camperdown NSW 2006
Contact Georgina Child
T. (02) 9889 0289 (SASH) or georginachild@gmail.com

Veterinarians that have Border Collie breeders as their clients should be aware of this disease and recommend DNA testing for all breeding dogs (males and females) prior to breeding.

Recently we have seen or been notified of 6 Border Collies that have been tested as affected or are showing typical clinical sigs of NCL. These dogs were bred by various non-registered breeders and from locations throughout NSW and QLD. **Neuronal Ceroid Lipofuscinosis (NCL) or CL** is inherited as an autosomal recessive disorder with affected dogs having 2 copies of the abnormal gene. It causes progressive neurologic deterioration from approx 16 months of age and invariably results in euthanasia by 2½ years of age. It is a devastating and untreatable disease and awareness of this disease by veterinary practitioners is important – to recommend genetic testing of all Border Collies prior to breeding in an attempt to reduce the incidence of this disease and to recognise the clinical features of the disease to prevent unnecessary investigations in dogs presenting with the typical signalment and neurologic abnormalities seen in this disease.

Neuronal Ceroid Lipofuscinosis (NCL) or CL has been recognised in Australian Border Collies since the 1980s. With breedline analysis and careful breeding the disease was all but eliminated in the 'show' Border Collie population. However, awareness of this disease is poor amongst the breeders of non-registered and 'working type' Border Collies. In the1990s scientists from the University of NSW, including the late Prof Alan Wilton, and the University of Melbourne identified the genetic mutation responsible and published their findings on the genetic defect in Border Collies – an autosomal recessive non-sense mutation – CLN5 gene. This research was supported by the Border Collie Clubs. A DNA test for this mutation has been developed and is commercially available.

Clinical signs

Border Collies with CL typically present with progressive neurological signs with an onset of 15-18 months of age. Affected dogs are typically presented with one or more of the following clinical signs – perceived visual disturbances; hyperaesthesia; startling easily; mild generalised ataxia (clumsy); abnormal behaviour including pacing, head swaying, disorientation, loss of previous training, 'fly catching' and possibly seizures. Seizures are seen late in the course of the disease and may be partial seizures. Aggressive behaviour change may be seen in addition to other evidence of altered mentation. Once clinical signs are seen they may progress relatively quickly over months.

Carrier dogs are neurologically normal and do not have any abnormalities in their lifetime attributable to the presence of 1 copy of the abnormal allele.

Physical examination findings

Dogs tend to be in good body condition, and have no abnormalities on physical examination.

Ophthalmological examination

The menace response may be present or absent, normal dazzle, normal pupillary light reflexes (direct / indirect) and normal palpebral reflex. Retinal exam in Border Collies tends to be unremarkable (other breeds with NCL may have retinal abnormalities).

Neurological examination

Affected dogs with NCL tend to have normal postural reactions, spinal reflexes and cranial nerve function. Variable generalised ataxia is common. Neurological abnormalities tend to be localised to forebrain dysfunction and generally do not have any lateralizing signs.

No abnormalities are found on biochemistry profile, complete blood count, electrolytes or liver function testing.

Further investigations

DNA testing kits are commercially available through GTC, Fitzroy VIC **(www.animalnetwork.com.au)**. Testing requires a buccal swab and results are available within 14 days. This test can reliably identify the CLN5 mutation in affected and carrier dogs. The test is relatively cheap (approx $150). NCL is an autosomal recessive disease. This test identifies affected, carrier and clear dogs.

Background

Ceroid Lipofuscinosis

Ceroid lipofuscinosis is the most common of the lysosomal storage diseases. It is a heterogenous disease – it can affect various age groups, and various organs. Central nervous system dysfunction is usually predominant. Neuronal *Ceroid lipofuscinosis* is caused by a genetic abnormality, due to reduced production of specific lysosomal enzymes. The lysosome is an organelle responsible for breaking down cellular waste materials and debris. Lysosomal storage diseases occur when the lysosome cannot degrade the metabolic products into diffusible substrates, thus the products accumulate in the cell. Cells throughout the body are affected. In particular, cells within the central nervous system and the brain especially are affected.

In people, several forms are recognised with different genetic mutations. The disease typically affects infants or juveniles (Battens disease) as the metabolic products accumulate in the cells and cause cell death early in life. Occasional adult forms of CL have been identified.

In dogs, NCL is predominantly a disease of purebred dogs. It has been recognised in several breeds and in recent years, DNA analysis has been done to identify specific genetic mutations. There is a differing age of onset in different breeds (less than 1 year to > 4 years) and different clinical signs are identified with specific locations (e.g. cerebellar) more severely affected in different breeds. Lysosomal storage diseases are uncommon, but are a very important differential in a list of possible causes when making a neurological diagnosis, particularly (but not only) in juvenile dogs.

Histopathology

Ceroid Lipofuscinosis is identified as autofluorescent inclusions within neurons, and neurodegeneration. Intracytoplasmic inclusion bodies are found within the cerebral cortex with PAS, Luxol fast blue, Sudan Black and Schmorl stains. Subtle inclusion bodies may be found with hematoxylin and eosin staining.

Treatment

There is no treatment for NCL in dogs or people. It is progressive.

Control in Border Collies

Border Collie clubs in Australia, including the Border Collie Club of NSW (**www.bccnsw.com/cl.html.**), promote CL testing in all breeding dogs. Whereas the registered breeders of Border Collies have been aware of this disease for a long time, non-registered breeders of Border Collies and especially of the 'working type' Border Collie, have not been aware and the genetic mutation has remained in the population. This disease is devastating for both the owners of affected pets and their breeders.

It is recommended that any dog suspected of CL undergoes DNA testing. This may prevent unnecessary (and expensive) investigation for other causes of CNS disease. For any Border Collie with results that are consistent with CL, the breeder of the dog should be informed and all related dogs that are not desexed should be tested. Both the sire and dam must be carriers in order to produce affected offspring (or affected – as dogs may be bred from before 16 months of age and before they show clinical signs).

Identification of affected dogs and carriers and preventing the breeding of carriers with other carriers will reduce the prevalence of affected dogs. Carrier dogs, although neurologically normal ideally, should not be bred from in an effort to reduce the incidence of the abnormal gene.

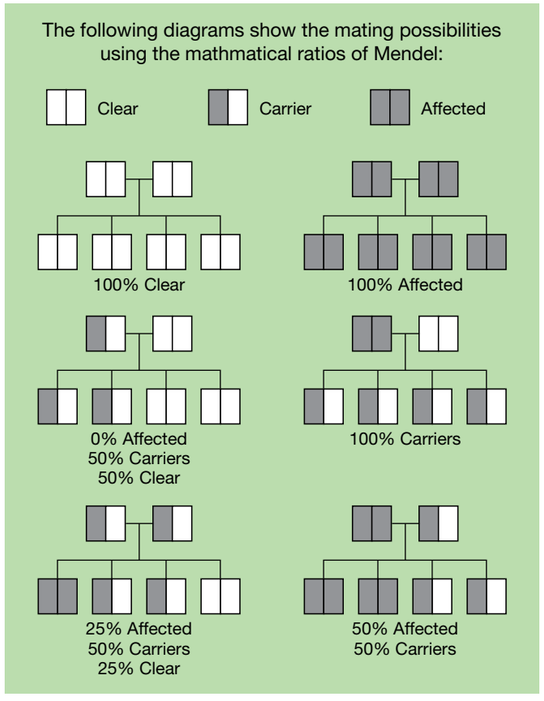


Figure 1. Autosomal recessive mode of inheritance.

Figure 2. A screen grab from the video showing 'Clover' pictured here with Christine Huynh, a 2011 Sydney University vet graduate.

e-book Please go to our e-book version, available at www.cve.edu.au/candtebook to view the accompanying video of 'Clover'. Clover shared the same dam and sire as Jessie, but was born 8 months previously. When Clover's diagnosis was confirmed the breeder notified Jessie's owners who then presented her at the clinic when she showed clinical signs. ▶

Figures 3 & 4. 'Jessie', shown above at 13-weeks-old and at 18-months-old.

Case history

'Jessie' is an 18-month-old FS Border Collie presented with a 2 month history of loss of toilet training and a 1 month history of seeming frightened of people, shying when approached, not responding to previously known commands and, at times, not seeming to recognise her owners. Prior to 16-months-of-age, Jessie had been a very active, intelligent, people-friendly and affectionate dog. In the week prior to presentation, she was exhibiting fly snapping behaviour and mild intermittent unsteadiness. No abnormalities were found on physical or neurologic examination apart from the behaviour described. DNA test for CL indicated she was affected.

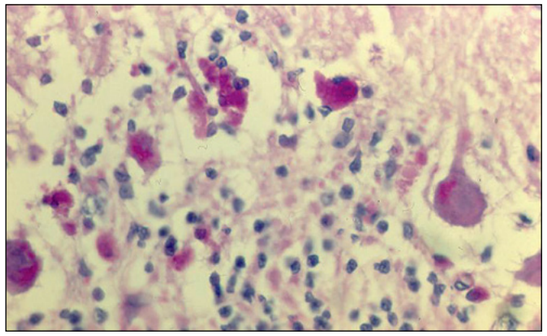


Figure 5. Canine lipofuscinosis or NCL with dark pink stained storage in Cerebellum Group. Description: Brightly eosinophilic NCL material in Purkinje and some other cells in NCL. Sex of Animal: unknown. Desexed?: Unknown. Notes Registry No. C0424 Slide- 171/75 LFBPASH Canine neuro. (Image courtesy of OLIVER, Copyright owned by University of Sydney, Contributors Peter Windsor and Gauthami Kondagari)

CONTROVERSY CORNER:

Puppy vaccination schedule with Protech C3

C&T No. 5204

Mario Viscardi DVM
Ballantrae Drive Vet Clinic
Shop 10B, 91 Ballantrae Drive
St Andrews NSW 2566
T. (02) 9820 2711
E. drmario@optusnet.com.au

I have been using Protech C3 for puppy vaccinations for a number of years, and regularly discuss vaccination protocols with veterinarians employed formerly by Fort Dodge – now Boehringer Ingelheim (BI) – to work out a strategy that both satisfies early intervention and minimises the risk of giving the booster at an age in which the immune response may not be adequate.

The literature accompanying Protech C3 recommends vaccinating pups at 6, 8 and 10 weeks; the last vaccination at this early age is claimed to be adequate. After that the next booster is to be given 1 year later.

Dr Leanne Peebles (formerly Huynh) from Boehringer has confirmed that another vaccination can be given at 12-14 weeks if the vet feels that the above schedule has not been sufficient.

The theory

Puppies are more prone to contract Parvovirus than older dogs, therefore vaccinating early minimises the risk of infection. So my recommendation is to vaccinate with Protech C3 at 6, 9 and 12 weeks. I have applied this schedule for several years, and to my knowledge no dog has developed Parvovirus (in the following year).

The practice

On the other hand, I consistently see pups vaccinated elsewhere (with Protech C3) on a schedule of 6, 12 and 16 weeks, or variants such as 6-8 weeks, 12-14 then 16-18. While I can see some wisdom in vaccinating after 10 weeks (despite the recommendations of the manufacturer), I cannot see the sense of a 4-6 weeks gap between the 1st and 2nd vaccination. Sadly, one of my customers recently cancelled the appointment for vaccination at 9 weeks of age because the Puppy School trainer at another Vet Hospital told her it was too early.

If the vast majority of pups produce enough Parvo antibodies after the 10 week vaccination, why leave such a big gap between 1st and 2nd dose, contrary to the recommendations? What happens if one day a pup, or worse a whole litter, contracts Parvo say at 11-12 weeks of age? And what if the owner of this litter sues the vet, resulting in a court case? What sound scientific evidence did the vet have for an 'off the label' use of the product, which may have been responsible for the infection? Would BI approve of these recommendations?

So, if we are concerned that 10-12 weeks is too early for the last booster, why not give a dose between the high risk time of 6-12 weeks? What wisdom is there in choosing 'to be safe' for the pup's future wellbeing, and gambling on the initial high-risk period?

Reply courtesy of

Peter Bracken BVSc, MACVSc
Technical Services Veterinarian
Boehringer Ingelheim Pty Limited
78 Waterloo Rd, North Ryde, NSW 2113, Australia
T. +61 (2) 8875-8635
F. +61 (2) 8875-8730
M. +61 (0) 412479661
E. peter.bracken@boehringer-ingelheim.com
www.boehringer-ingelheim.com.au

Thank you for the opportunity to respond to Dr Mario Viscardi's comments.

The registered product information leaflet for Protech® C3 does have a suggested primary vaccination program of 6, 8 and 10 weeks. However, veterinarians are encouraged to develop a primary vaccination protocol to suit their clients and local disease conditions. To minimise the risk of infection, pups can be vaccinated every 2 weeks until they pass the susceptible period when maternal antibodies wane; however, realistically, it may be difficult to encourage some pet owners to return to the clinic for multiple visits for cost and convenience reasons. I agree with Dr Viscardi's suggestion of vaccinating pups more regularly between 6 and 12 weeks as this will give pups another opportunity to respond to vaccination in this critical period and reduces the length of time a pup is left susceptible once maternal antibodies have waned.

If any of your readers would like to discuss primary vaccination programs I encourage them to call me at Boehringer Ingelheim Technical Services on 1800 038 037.

WINNER

Proliferative and necrotising otitis externa in a young cat

C&T No. 5205

Dr Nick Lloyd
Paradise Veterinary Hospital
655 Lower North East Road
Paradise SA 5075
E. paravet@internode.on.net
T. (08) 8337 4922

Summary

Proliferative and necrotising otitis externa (PNOE) is an uncommon but severe form of otitis externa affecting cats and dogs, but especially young kittens of 2-6 months.

Clinically, it typically involves rapid development of severe epidermal hyperplasia and hyperkeratosis of the ear canals with tissue necrosis and other secondary effects due to the altered anatomy and micro-environment.

Aetiology is uncertain. An autoimmune basis is mainly suspected especially as it has similarities to hyperkeratotic erythema multiforme in children. There have also been suspicions that it is an immune-side effect of feline herpesvirus -1 infection and some cases respond well to interferon, antivirals (e.g. imiquidmod). Papillomavirus has also been considered as a trigger.

Many cases are said to resolve spontaneously over time (estimates vary from 3-6 months to 2 years).

Treatment in most literature reports is based on tacrolimus (a relative of Cyclosporin but better absorbed through the dermis) along with symptomatic treatment of secondary infections and pain relief. Corticosteroids seem to have little effect.

Clinical History

Two male Siamese kittens were obtained at 3-months-old from a long term breeder in December 2009. My suspicion that they had *Chlamydia* was confirmed by PCR (also Herpes/Calici negative). I started them on a month of doxycycline monohydrate.

Two weeks into this course, one of the kittens, 'Rama' developed bilateral otitis externa; the Gram stain had *Malassezia* yeasts and low numbers of Gram positive cocci, not cultured. On otoscopic exam it had a brown waxy discharge overlaying a slightly inflamed mucosa with a 'cobblestone' (early polypoid) effect. He was started on Canaural®.

Within a few days there was obvious development of hyperkeratotic/hyperplastic tissue (Figures 1 A&B) and by 10 days this was occluding the whole canal, at which point samples were taken for histopathology and attempts made to saline flush as much debris out as possible.

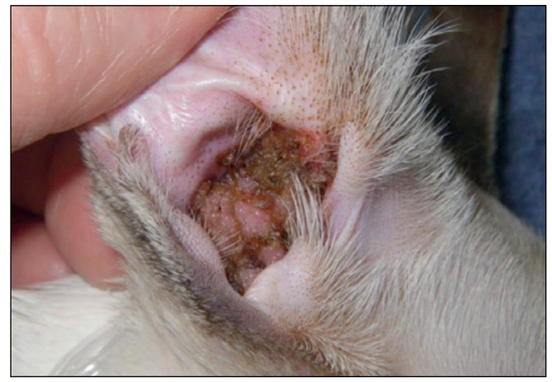


Figure 1A.

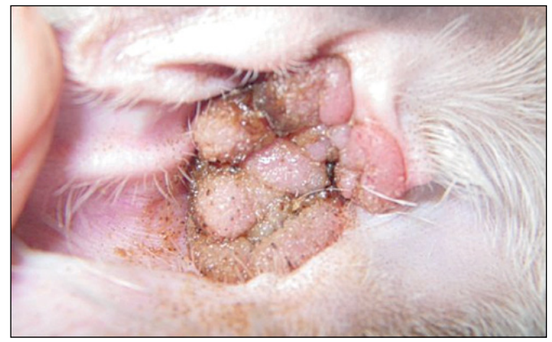


Figure 1B. The ear canal's gross appearance – note the Hyperkeratotic/hyperplasic response in the external ear canal.

Histopathology suggested PNOE and Mauldin's article[1] that the pathologist sent me seemed to confirm it for me, along with several discussions seen on VIN[2].

The article and other reviews of PNOE were all fairly pessimistic about resolution of the condition, mainly indicating that the lesions would regress in time without treatments. This would be fine except that the time frames discussed were between 1 and 2 years!

As Rama was already in considerable discomfort and the lesions prevented access to clean or topically treat the ear canals, some form of treatment was going to be necessary; it would not be kind to leave it to self-resolve.

As the treatment mentioned with most success, I had 0.1% tacrolimus ointment compounded locally and started this topically as well as prednisolone at 1.75mg/kg sid. Oral Clavulox and Ketoconazole were used as it was not possible to gain access to the canals to treat them topically. After 10 days there was no improvement and the lesions were, in fact, worse. ▶

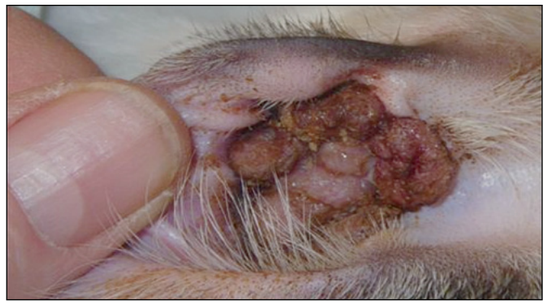


Figure 2. 15/02/2010

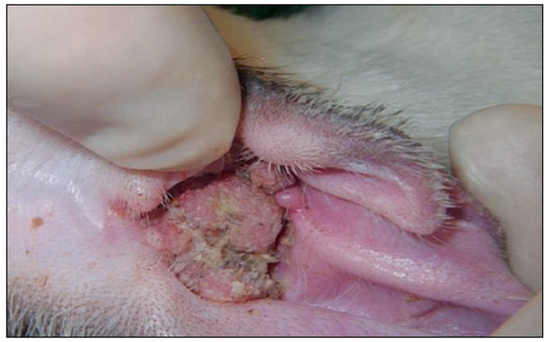


Figure 3. 01/03/2010

After emailing and discussing the case with Ken Mason he suggested trying oral (10mg/kg sid) and aural Cyclosporin instead and this was started.

A few days later, Rama 'screamed' and suddenly started circling to the right with severe nystagmus present as well. I presumed a spontaneous ear drum rupture with resulting otitis media.

Rama was anaesthetised and I excised some portions of the hyperplastic tissue to gain access to the canals and flushed both ears with saline. Due to the presence of inflammatory polypy-type tissue all the way down the canal, I was unable to examine the ear drums.

As Rama was causing himself further grief and trauma by scratching at his ears and was unable to keep on an Elizabethan collar, I performed a bilateral hind foot onchyectomy. This procedure, while undesirable, was very effective in assisting his comfort and ability to run around and play with his brother.

At this stage (5-months-old) he also tested positive for FIV antibodies (FeLV antigen negative) which I presumed was from maternal antibodies. (A later PCR showed him Negative and the mother also tested antibody negative so probably a false positive.)

He was continued on aural and oral cyclosporin and Baytril was added to the Clavulox to give better cover for otitis media. He was anaesthetised about weekly to trim (grown back) tissue and saline flush the ears.

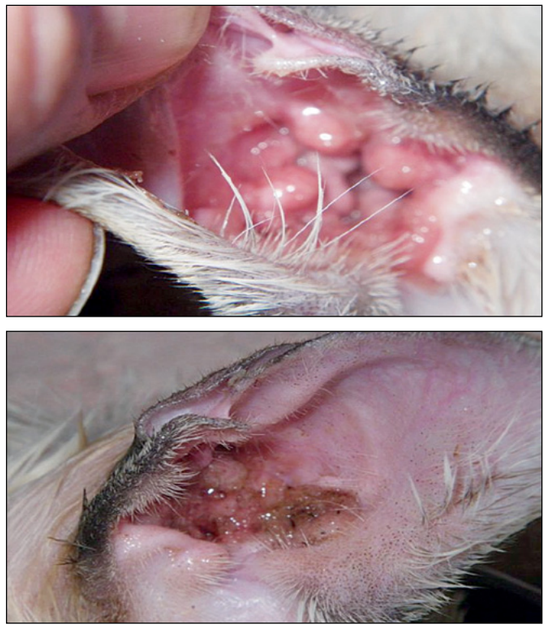
His right head tilt subsequently became a left head tilt so I presumed the other ear drum had gone. I consulted with Dr Davies at the Adelaide Specialist Centre, who was concerned that the high dose of Cyclosporin may encourage a latent infection or Toxoplasma. So I cut back to just topical application pending reformulation of tacrolimus, provided this time by BOVA.

At this stage I also weaned Rama off prednisolone as he needed more pain relief than the intermittent oral Temgesic he was receiving. I also placed him on meloxicam (a previous accidental dose while on prednisolone had made him very happy!). He was also taken off Clavulox/Baytril and started on clindamycin and fluconazole. (Fluconazole was stopped when Dr Mason alerted me to possible toxic interactions with cyclosporin.)

Within a few days of starting Rama on tacrolimus his left ear started exuding a necrotic pasty substance and the canal started to open up as the hyperplastic lesions started to shrink. The right ear also looked as though the lesions were starting to crumble away, too.

Within 2 weeks the external lesions had almost totally resolved. On an anaesthetic to flush out residual debris there was still a mild polypy appearance in the distal canals, so topical tacrolimus was continued. All other treatments were stopped.

Rama remains deaf (and overweight from cortisone) but otherwise healthy and happy. There are possibilities for brainstem auditory evolved response testing and CAT scans to see if anything can be done to restore his hearing, such as bulla osteotomy.



Figures 4&5. 05/03/2010 – response a few days after starting recompounded Tacrolimus.

Conclusions

PNOE is dramatically rapid in its onset and production of these proliferative lesions. While the disease itself is aggressive in onset, I think it is the secondary effects that are the main problem. If it were not for concurrent infections, and in Rama's case ear drum ruptures, it may have been possible to wait for regression.

It is almost certainly immune based and much suspicion centres around FHV-1 infection and the immune reaction to it. (PCR negative in Rama's case.)

In my hands, I think the keystone to the relatively rapid resolution was the relatively high doses of oral Cyclosporin and Topical Tacrolimus. As Dr Davies said, this treatment does have the potential to allow other serious infections to take hold so I would not advocate its use in all cases. I was happy to use it as Rama was an indoor cat and had never contacted others outside his litter. Otherwise, FIV and Toxoplasma testing would be advisable first.

Tacrolimus appears to have been very effective in many vets' hands. I think in my case I was disappointed in its lack of effect probably due to poor local compounding; the second prescription was made up as a reverse thermodynamic gel – kept in the fridge it is liquid, but sets in the warm ear, keeping in contact). Had this been done then it may have been more effective (+/- oral cyclosporin too). Tacrolimus is potentially toxic to humans so care is needed in administering – gloves should be worn and hands washed post administration.

In Rama's case, regular anaesthetics to keep the ears as clean as possible and treatments for secondary infections and analgesia were essential.

Postscript

Rama is my own kitten (of course!) so I was happy (and desperate enough) to throw everything at him to give him relief. Many owners would find ongoing costs prohibitive. I hope this article may make some more vets aware of the problem and its likely cause and possible treatments so they can advise owners accordingly.

Rama being my cat, I plagued many people with emails and phone calls for advice so I give many thanks to: Ken Mason, Richard Malik, Aine Seavers, Mandy Burrows, Peter Hill, David Davies and Elizabeth Mauldin.

References:

1. Proliferative and Necrotising otitis externa in 4 Cats – Elizabeth Mauldin *et al.*
2. VIN Resources.

Sinus tachycardia and possible central diabetic insipidus in a Yorkshire Terrier with pancreatitis

C&T No. 5206

Dr Yuan-pei Lien
Hong Kong Non-Profit Making Veterinary Clinic
No. 24 Ki Lung Street
Prince Edward, Kowloon, Hong Kong
T. 0011 852 2393 2395
E. gogovet101@yahoo.com.hk

The patient was a 14-year-old, neutered female Yorkshire terrier dog (3.2 kg) with anorexia for 2 days preceded by on-and-off inappetence and diarrhoea for several weeks. There was no history of polyuria and polydipsia (PU/PD). Physical examination revealed dehydration, mild fever (39.6˚C) and mild tense abdomen on palpation but not localisable to a specific area. A complete blood count and biochemistry tests were unremarkable except for abnormal canine pancreatic specific lipase level (IDEXX Canine Pancreatic Lipase Test). Urinalysis revealed highly concentrated urine (SG 1.045) and radiology showed 'thickened' intestinal loops. Abdomen ultrasound exam findings were mild pain (Murphy sign) when examining the cranial abdomen area and slow peristalsis of small intestine and stomach. The pancreas was scanned but poorly visualised due to technical limitations.

Presumptive diagnosis: pancreatitis.

The patient was hospitalised for intravenous Lactated Ringer's solution. The rate was based on the hydration status: Buprenorphine (0.1-0.15 mL tid-qid IV). Later on the first day the sensation of pain intensified from mild to severe, just like those more 'typical' pancreatitis cases. Fresh frozen canine plasma CANIPLUS 45 mL was infused intravenously on the second day after hydration had improved.

An ECG monitor was put on because the slow heart rate was auscultated. The rate was 50-70 bpm without pulse deficit and murmur and the rhythm was respiratory arrhythmia. The rate was unreasonably low for a small breed dog with intense pain. The heart rate should be higher in a normal animal, if in pain. The heart rate was supposed to be influenced by pancreatitis (and the Buprenorphine injection). However, at one time the heart rate jumped to 240-260 bpm in sinus rhythm! Carotid massage was performed immediately and heart rate dropped to 70-100 in minutes.

After 7 days of treatment, the patient recovered from the pancreatic disease: appetite was good, no vomiting nor diarrhea and no abdominal pain. IV fluid therapy was discontinued. But 36 hours later the dog started to have neurological symptoms: ataxia, tremor and abnormal mentation. A blood test showed sodium raised to a critical level of 176 mmol/L?! Immediately, the patient was put on a drip with 2.5% dextrose in 0.45% NaCl solution to try to lower the serum sodium concentration. More water was added to the food and also administered by syringe feeding. However, the sodium level was always high (it fluctuated over 160 mmol/L) despite the pure water given and the urine output was so huge that at the peak there was almost 1 litre of urine produced per day! The urine SG was around 1.004 no matter whether the dog was dehydrated or not.

For the numerous causes of PU/PD (although this dog didn't drink much by herself), central diabetic insipidus (DI) was the most suspect. Therefore, trial treatment with MINIRIN® (desmopressin) 1 unit SC bid was commenced. The sodium level was back to normal in 1 day and the urine output dropped gradually in 3 to 4 days to a steady level of 200 mL/day. The urine SG remained steady at around 1.020 when 1 to 8 hrs post injection and dropped to 1.008 immediately before the next injection. The daily water intake was carefully maintained at about 250mL/day to avoid either fluid overload or dehydration. Mentation was back to normal in about 1 week after the sodium level was under control.

I cannot say for certain that this was central DI, although the response to desmopressin certainly fits this diagnosis.

In pancreatitis cases, central DI is not a reported complication or a key reference.

The timing of the 2 diseases suggests causation, but we cannot think of a pathomechanism to link the 2 different disease processes. I'd be interested in any feedback about this case.

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WINNER

‘Seaver’s Slide’ saves the day!

C&T No. 5207

Dave Goodwin
Sussex Inlet Vet Surgery
179 River Road
Sussex Inlet NSW 2540
T. 02 4441 1011
E. dave@sussexvet.com.au

‘Sophie’, an overweight female, desexed Staffy, was seen at our practice 12 hours after being hit by a truck. The owner had been in earlier in the day, wanting some purple spray for abrasions on the dog. Thankfully, he was convinced by our 2 nurses to come in for a check-up!

Sadly, they couldn’t come in till 5.30pm that day and by that time Sophie was markedly lame in the right hind and also had a severely swollen left foreleg, with moderate lameness. In the right foreleg there were several open wounds and abrasions, a nail torn clean off and lacerated pads as well. Her gums were pink, lungs clear, heart racing and she had a chronic otitis with shrunken canals to boot! The left foreleg struck out at an abnormal angle and crepitus was felt across the carpus joint, but otherwise she was pretty stoic (typical Staff!) and never vocalised or complained during examination.

We cleaned her wounds using chlorhexedine, put a Robert Jones bandage on the left foreleg, dressed her wounds with melanin and iodine solution, and put a standard wound bandage on the right foreleg. She was given Tolfedine® for pain relief and Clavulox® Injectable and cage rest overnight. We planned to sedate Sophie the next morning to assess her for drawer sign in the right stifle and to take Xrays to assess suspect fractures of the left foreleg and possibly the right hip.

The next day Sophie was sedated using 0.12mLs Domitor/0.12mLs of Torbugesic and Xrays confirmed over-riding fractures of two metacarpals and the distal ulna. The hind-leg was assessed with no drawer sign in the stifle, but looked to be shorter than the other leg. VD Xrays of her hips confirmed suspicions of a dislocated femur.

Wounds were re-dressed and the owners phoned to advise referral for plating metacarpal fractures and possibly hip replacement at the same time under general anaesthetic but her owners couldn’t afford a referral. My concerns were that it was 24 hours post the initial injury and the hip may not go back in.

Remembering an excellent article I’d read some years ago on replacing dislocated hips by Aine Seavers, I did some searching and found a 2007 *Control & Therapy* article where Aine had replaced some dog’s hips, up to a week after dislocation!

We did a screening Xray of the chest to rule out diaphragmatic hernia prior to anaesthetising ‘Sophie’. Aine recommended using thiopentone, but we had none in stock, so I gave 2.3mLs of Nembutal® IV to effect and I got up on our Xray table holding onto the good leg in one hand and the bad leg in the other – just as Aine described so well – with the nurse supporting the chest and head. On a count of three, we let gravity take over whilst holding onto the right hind and, pop, everything went back into place like a dream!

Xrays below show before and after views, to confirm replacement of the hip, then it was bandaged in place.

Scroll over to see:

- e-book • Enlarged Xrays (digitalised Xrays courtesy of Helen Laurendet, Senior Radiographer, Faculty of Veterinary Science, The University of Sydney)
- e-book • Aine Seaver’s original C&T No. 4785 The Seaver’s Slide – when tables are not just for dancing on. Mar 2007, Issue 246
- e-book • Keith Fletcher’s reply, C&T No. 4923 Reply to C&T No. 4785. June 2008, Issue 251

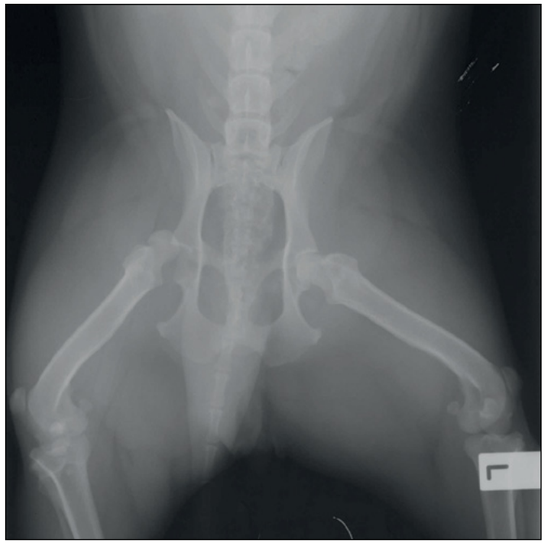

Figure 1. VD view hip before reduction.

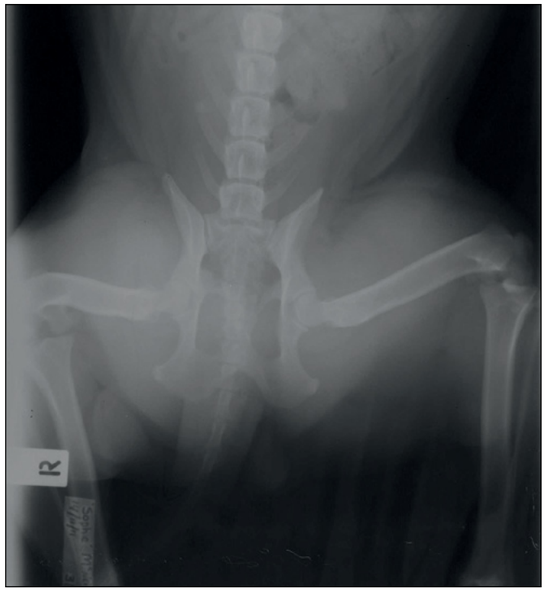

Figure 2. VD view hip post reduction.

Postscript: *Three days post discharge (with EC on and whilst being sedated twice daily with Acepromazine tablets), Sophie chewed off both her Robert Jones bandage and her hip bandage but thankfully, the hip stayed in!*

‘Saffy’ and hypothermia

C&T No. 5208

Geoff Hayres
North Croydon Veterinary Clinic
84-86 Exeter Road
Croydon VIC 3136
T. 03 9726 9616
E. gmh@ava.com.au

Figure 1. ‘Saffy.

‘Saffy’, a female 10-year-old Burmese, was presented to us this winter from a boarding cattery looking terminal.

Saffy was very cold to the touch and was having periodic head twitching. We use only glass thermometers and her temperature was way less than 35ºC; the mercury did not leave the bulb which is 2cm below the 35ºC calibration. Bloods were taken and Saffy was placed on IVF, a heating pad and a blow heater.

The heating pads we use are more than 20-year-old veterinary specific ‘Linda’, a very old brand. Older Vets will recall the advertisements: ‘Sleep wonderfully warm with Linda!’ These pads are designed to never burn an animal; they have a metal case and originally a soft cotton toweling cover. The covers have long ago worn out, now we wrap and seal them with a tough plastic bag. We use them routinely in surgery.

The ‘General Electric’ blow heater we use is also very old. The drip line was dangled into the warm air and Saffy was wrapped in a towel so that the warm incoming air percolated around her body. Bloods revealed nothing significant. Some hours later Saffy was much brighter and felt ‘less cold’ but the mercury was still not leaving the bulb. The owner, obviously on holiday but contactable, wanted everything done and Saffy was referred to our local Animal Emergency Centre for overnight care. On arrival her temperature had reached 34·1ºC, confirming our clinical impression.

Saffy had EXTENSIVE investigation at Melbourne Referral Centre; absolutely nothing of significance was found. Approximately 5 days after initial presentation here she was sent home from the specialist centre and has completely returned to normal. The owner’s theory (and I agree) is that Saffy is a totally indoor cat; the boarding cattery is open air, this winter has been extremely cold and her metabolism was unprepared. Effectively, the only treatment Saffy had was symptomatic, i.e. warming.

We have revived other hypothermic animals with the ‘Linda’ pads and blow heaters and have used the same combination for sedated or anaesthetised poisonings. In the last 2 years we have had 3 snail bait ‘all nighters’ kept normothermic with the blower/pad while anaesthetised. Circulated warm air seems to be the current method of choice and we have had very good results using the blower/pad with both prevention and treatment of hypothermia. Not all heating pads are as safe as the old ‘Linda’ pads we use; fortunately for us, they are obviously of very robust design.

Figure 2. The General Electric fan.

Figures 3 & 4. The Linda heating pad, ‘nude’ and plastic covered.

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Prostate tumour in a 12-year-old beagle

C&T No. 5209

Sally-Ann Williams
Auchenflower Veterinary Clinic
109 Haig Road
Auchenflower QLD 4066
T. (07) 3371 5763
E. sallyvetwilliams@yahoo.com.au

A 12-year-old MN beagle had been examined the day before for its annual health exam. The prostate gland was painless and moderately enlarged and irregular as per rectal palpation. The medial iliac (sublumbar) lymph nodes were not palpable on rectal exam. There was no history of any frequent urgency or difficulty in urinating. He had been desexed around 5-months-of-age.

The following day, the dog represented with frequency, urgency and discomfort when attempting to urinate. Only very small volumes of urine were passed.

A cystocentesis was carried out to reduce the markedly distended bladder. Attempts to pass a urinary catheter were unsuccessful.

Radiographs highlighted foci of tissue mineralisation, of varying intensities, at the pelvic inlet. (Figure 1)

Ultrasound of prostate revealed irregularly marginated hypoechoic regions separated by spurs. The spurs radiated from an irregularly marginated, central intense hyperechoic region with distal acoustic shadowing, indicating dystrophic mineralisation. (Figures 2A & 2B) This was suggestive of a prostatic carcinoma, although chronic prostatitis can present with peripheral mineralisation.

There were no uroliths visible within the bladder lumen.

At exploratory surgery, the bladder wall was thickened, the neck of the bladder felt thickened and constricted with a 'gritty' feel on the left hand side. The constriction seemed to be surrounding the neck of the bladder.

Cystotomy was performed and no uroliths found. Retropulsion of warmed saline through a urinary catheter produced no stones.

A fine needle aspiration was performed on the prostate gland; 4mLs of slightly cloudy fluid with a few flecks of small fine white material was aspirated as well as several samples of the prostate gland.

Aspirating the prostatic fluid alleviated the pressure within the prostatic urethra and a Cooks foley catheter was able to be passed into the bladder from the penis. The catheter was sutured to the external ventral abdominal wall, bandaged and a urine collection bag set-up.

The dog was hospitalised and remained catheterised for 4 days to allow enough time for the bladder wall to heal. Slides were made of all collected aspirates obtained of the prostate gland. Diagnostically, the most rewarding slides were from the aspirated fluid. The fluid that accumulated within the prostate gland was due to necrosis of the central region of the tumour.

Cytology findings confirmed a prostatic carcinoma, modified to an unusual extent by secondary degenerative and inflammatory changes.

I offered to send the dog home with the catheter in place. Despite the probability of an ascending infection, an indwelling urinary catheter could be left in for 4 to 6 weeks. Urine could be regularly examined for any evidence of bacterial urinary tract infection (UTI) and treatment instigated if bacterial UTI developed. The downside to this offer was the possibility that a resistant bug could be isolated. In light of the fact that euthanasia was certainly a possibility, the option of an indwelling catheter was a significant consideration.

However, the owners were not keen on the idea. The dog had separation anxiety, shadowing the owners at all times and barking, panting and pacing even for virtual separation. Therefore, the dog required access to the entire house and the owners were unable to keep him confined on a veranda or in a bathroom.

Piroxicam (Feldene®) was dispensed (0.3mg/kg sid orally) in the hope of reducing the inflammatory response within and surrounding the prostatic carcinoma, as well as reducing the formation of new blood vessels within the tumour. Hence, reduce the tumour size and hopefully increase the size of the urethral lumen.

Unfortunately, the dog developed urethral obstruction within 3 days of discharge and was euthanased.

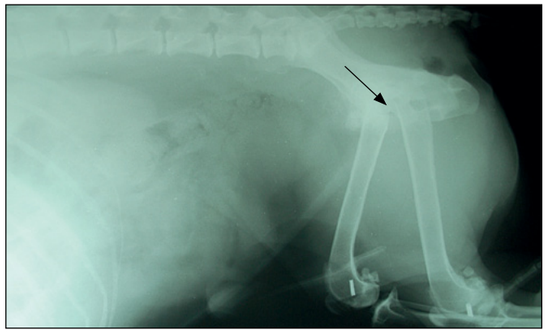


Figure 1. Lateral abdominal radiograph of the dog with dysuria. Note the mineralised region (arrow) at the pelvic inlet.

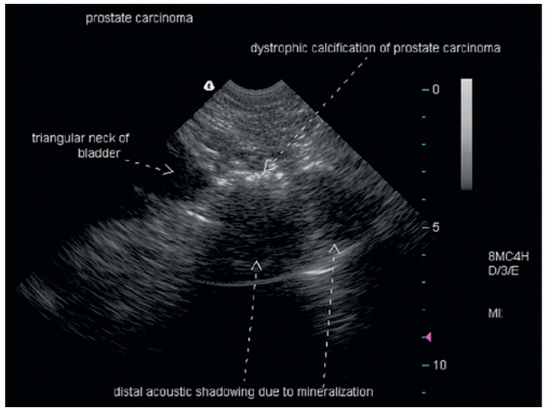


Figure 2A. ABD prostate carcinoma.

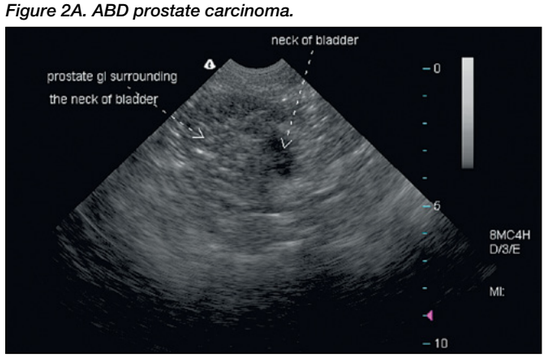


Figure 2B. Transverse image of the prostate.
Figures 2. Ultrasound images of the bladder neck and prostate of a dog with urinary outflow obstruction due to a prostatic carcinoma.

Feline hydronephrosis

C&T No. 5210

Sally-Ann Williams
Auchenflower Veterinary Clinic
109 Haig Road
Auchenflower QLD 4066
T. 07 3371 5763
E. sallyvetwilliams@yahoo.com.au

A 16-year-old FN Burmese cat (3.05 kg) was present with a history of intermittent inappetence and constipation over the previous 6 months.

On presentation, the cat was bright, alert and responsive with excellent body condition. He had periodontal disease stage 2-3. No abdominal tenderness was evident. Systolic murmur II/IV. Blood pressure 150 mmHg.

Bloods: azotemia with low SG of 1.020. Urea 17.0 (5.0 - 15.0), Creatinine 0.25 (0.08- 0.20), Potassium 5.6 (3.7 - 5.4). Bacterial culture and susceptibility of urine pending, but suggestive of renal insufficiency.

Ultrasound showed an enlarged right kidney with a markedly dilated renal pelvis and dilated ureter with what looks to be a urolith evident - see Figure 1.

The owner did not want any surgical intervention.

Further follow up as at October 2011.

The cat was diuresed with i/v fluids @ 10mL/kg body weight. He was carefully and frequently monitored for any evidence of pulmonary oedema to suggest over-hydration or cardiac heart failure. Pain relief (butorphine 0.2mL of 3mg/mL) was given every 4 hours for 8 hours then 8-hourly.

The cat improved dramatically within a 24 hour period; interactive, bright, eating and comfortable. He was sent home on Metacam and the owner advised to provide a diet of tinned cat food and no dry food whatsoever.

He was seen for vaccination early this year and had gained weight and was more active (due to NSAID effect on concurrent degenerative osteoarthritis). The owner, an architectural student, was strapped for cash and although offered follow-up bloods and ultrasound was happy with the cat's progress and refused work-up. ▶

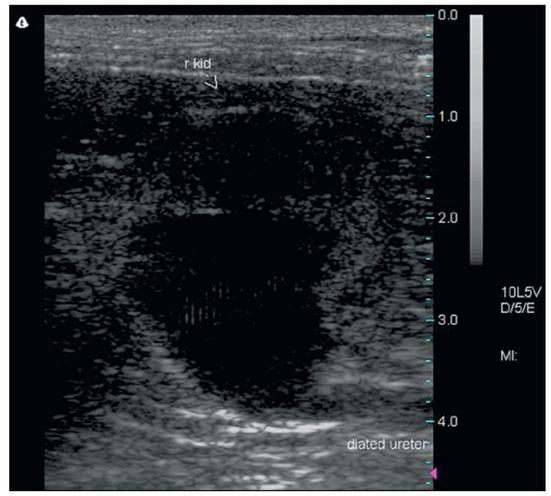


Figure 1. BRT dilated ureter.

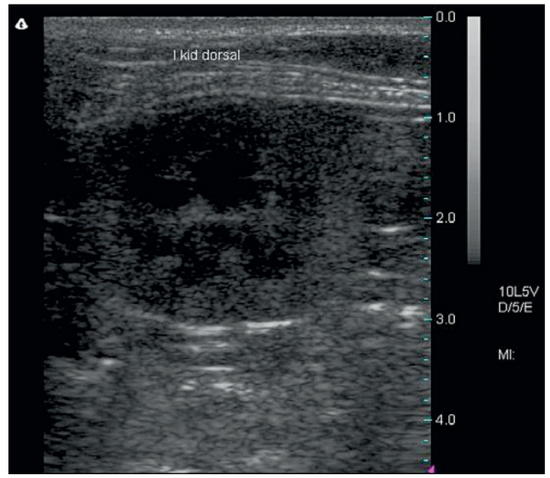


Figure 2. BRT l kid dorsal (001).

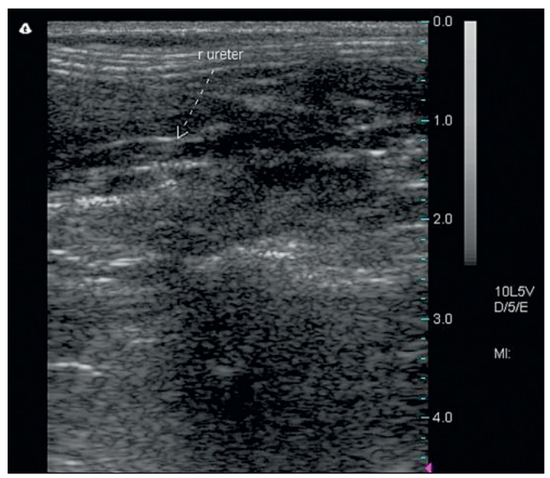


Figure 3. BRT r ureters.

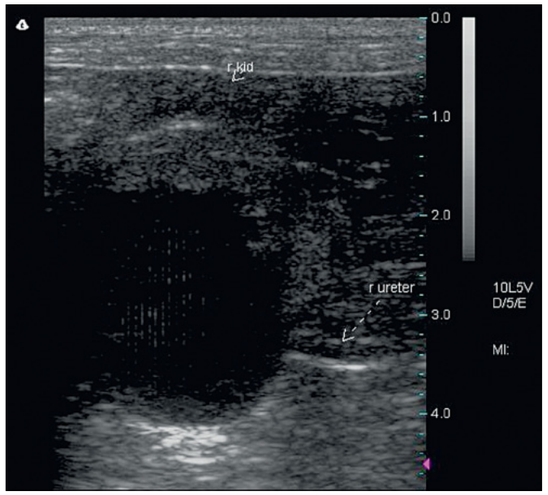


Figure 4. BRT r ureter (001).

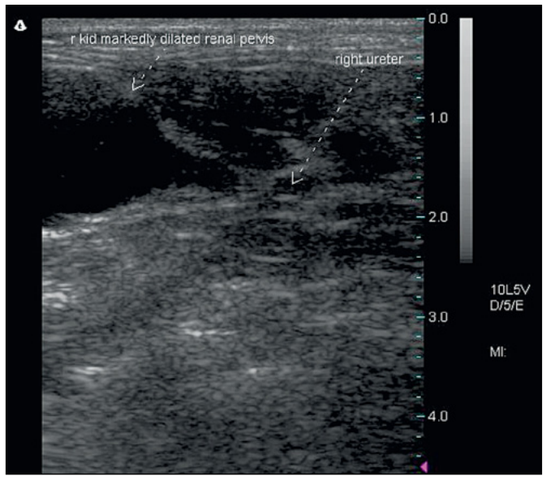


Figure 5. BRT right ureter.

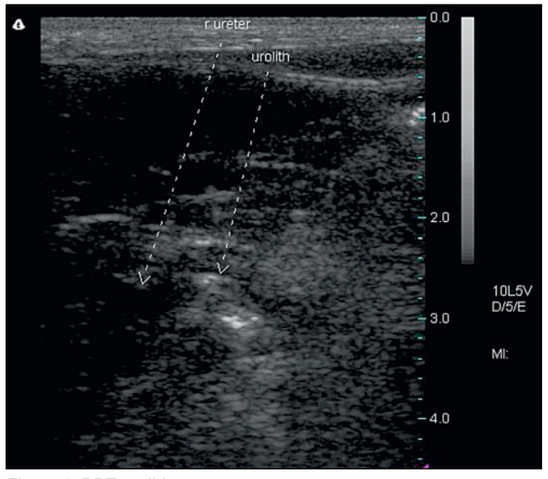


Figure 6. BRT urolith.

WINNER

Flea-related anaemic crisis in a young kitten

C&T No. 5211

Dr Natalie Burke BVSc
RSPCA NSW
201 Rookwood Road
Yagoona NSW 2199
E. nburke@rspcansw.org.au

'Scooter', a 3-week-old male Domestic Short Hair kitten weighing just 260 grams, presented to the RSPCA one afternoon as an emergency case. He arrived with his littermate, who sadly died on the way to the clinic before reaching veterinary care. Both kittens had a marked flea burden. We did not know much of Scooter's history, except that he did not come from a good home and had not been given any flea or worming treatments. The owner also disclosed that the kittens had not been feeding from their mother for approximately one week prior to presentation, so both kittens were thin and weak.

Scooter presented in a critical state. He was depressed and moribund on admission. Indeed, he was barely able to move. Both respiratory rate and heart rate were very low, his mucous membranes were very pale, and a capillary refill time could not be determined. Scooter was rushed immediately into the emergency area and started on emergency oxygen supplementation but did not stabilise. Atropine 0.1mL was administered intravenously to counteract the severe bradycardia; it was moderately effective in increasing the heart rate. Scooter was also hypothermic with a body temperature of 35.7ºC so he was warmed up with heat pads, bubble wrap and warm blankets. Even with the above symptomatic first aid Scooter did not stabilise. A 0.1mL blood sample was retrieved and a PCV measurement was taken. The PCV was determined to be 11% which is life-threateningly low. Due to this result, in combination with the patient's critical state, it was decided that Scooter be given a blood transfusion. There was no time or resources (owners had limited finances) for feline blood typing in this situation, and there was no stored feline blood available at the clinic at the time; because of this, a canine blood transfusion was used. A large Mastiff donated 10mL of blood for the procedure; his PCV was 48% so the sample was suitable for use. 1.3mL citrate phosphate dextrose anticoagulant was then added to the 10mL of blood (the anticoagulant was extracted from an unused blood donor bag). The total blood volume for scooter would be approximately 17.2 mL (66mL/kg for cats – but can actually be up to 80mL/kg for kittens). The amount of blood to infuse was calculated by:

$$\text{Total blood volume} \times \frac{\text{(required PCV – recipient PCV)}}{\text{Donor PCV}} = \text{Amount of blood to transfuse}$$

From this formula the amount to infuse was calculated to be approximately 8mL in total. Scooter was most likely hypovolemic (blood loss due to fleas, plus dehydration) and critical so he could receive as a maximum 20mL/kg/hr which equates to 5mL/hr. We chose to start the transfusion intravenously via the left cephalic vein at 4mL/hr and administer the blood transfusion over a period of 2 hours. Once the transfusion was administered intravenous fluid therapy with 0.9% NaCl at 1mL/hr was started and continued for the next 24 hours, and 5% glucose added to drip after this period. Scooter was also given a small drop of kitten Revolution® off-label to help with the flea burden. Scooter was still moribund 24 hours later and prognosis for survival was guarded, however his vital signs were stable and improving. Approximately 36 hours post blood transfusion Scooter began to recover rapidly, becoming brighter and active, eating small amounts without assistance and gaining weight. After 4 days in hospital Scooter was well enough to go home with a foster carer and was visibly improving each day. Scooter is now 10 weeks old and living in foster care; he will soon be adopted and go to a new home.

It is important to remember that fleas can not only cause chronic debilitating anaemia and reduced quality of life, they can in some cases cause fatality. In small animals such as Scooter with a much lower total blood volume, a lower PCV to begin with, and lower total body iron reserves, it can take very few fleas to cause significant anaemia. It has been reported that it takes just 72 female fleas to ingest 1mL of blood from an animal per day!! This means it could only take a matter of days for a very small animal such as Scooter to have critically low blood levels.

Editor's Comment: *When finances are limiting, it is actually safer to give dog blood to a cat, rather than an unmatched feline transfusion. Just remember, the red blood cells only last 7 days, and you can only try this trick once. It works well when you **KNOW** you can fix the cause of the anaemia quickly and definitively. There are also quick ways to do a cross match – but it still takes time and possibly both Type A and Type B donors.*

Use of dog blood in a FeLV positive cat

C&T No. 5212

Karina Graham
North Shore Veterinary Specialist Centre
64 Atchison Street
Crows Nest NSW 2065
T. 02 9436 1213
E. kjgraham@optusnet.com.au

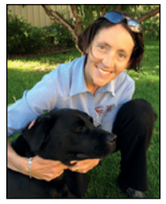
I used the dog blood trick (passed on to me from Richard Malik) for a cat the other day which was a FeLV-positive cat and had severe anaemia. The owners were coming in to euthanase it when it went into respiratory arrest. We had dog packed cells in the fridge that had just expired so I bolused 15mLs into him rapidly and he stabilised reasonably well. I also gave him a smidge of dexamethasone and butorphanol because he was quite restless immediately after, but was very calm and moochy when the owners came.

This is a great trick that I'd like to share with CVE members/ readers. The owners were thrilled they got to say a nice goodbye.

MAJOR WINNER

Management of chronic canine hypophosphataemia

Comment from Hugh White: *This is an excellent article and shows yet again that vets 'in the bush' can see and investigate the most obscure and complex cases. General practice is never dull if you keep looking, thinking and reading!*



C&T No. 5213

Virginia Grice
Inverell Veterinary Clinic
32 Sweaney Street
INVERELL NSW 2360
T. (02) 6721 0266
E. vkgrice@hotmail.com

Patient: 'Meg', an 8½-year-old female spayed Poodle X Silky Terrier.

History and Physical Examination: Meg was presented in September 2009 for a variety of fluctuating symptoms. Her astute owners had noticed that she had become less boisterous, with episodes of intermittent agitation and shaking. Two episodes of agitation had coincided with application of Advantix in the first instance and Program in the second. On physical examination, Meg weighed 3.13 kg, HR-96, mucous membranes were pink and moist, capillary refill, C/S and rectal temperature were normal. No abnormalities were detected on abdominal palpation, although she consistently disliked palpation of the cranial abdominal area. She was eating, drinking, urinating and defecating normally, and ate a balanced commercial dog food. As she was in need of a dental, we decided to:-

1. Watch her closely, and try to bring her in during an episode of agitation, should it recur.
2. Try Advocate (after she returned a negative heartworm test) or Capstar for fleas in case she had had an idiosyncratic reaction to the previously used flea products.
3. Run a general health profile (BUN, CREA, Ca^{2+}, TP, ALB, GLOB, ALKP, TBIL, CHOL, GLU and PCV). ▶

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Initial general health profile results:

Meg returned values within reference intervals except for a slight elevation in ALT of 140 U/L (10-100), slightly low amylase at 328U/L (500-1500) interpreted as insignificant and surprisingly, a low phosphate level of 0.58mmol/L (0.81-2.20). The moderate hypophosphataemia was difficult to interpret, in light of the accompanying normal parameters. We decided to:-

1. Trial 7 days of Clavulox 12.5mg/kg BID and metronidazole 25mg/kg BID in view of the very mild hepatic changes and her gingivitis.
2. Repeat the general health profile at the end of the 7 days and, if within normal reference intervals, admit Meg for a general anaesthetic and dental with IV fluid support.

The dental side of this plan was well and truly abandoned 7 days later! Meg's phosphate level had dropped further to 0.36mmol/L. ALT had increased slightly to 206 U/L, and amylase was low. Meg was diagnosed with moderate (bordering on severe) hypophosphataemia of unknown cause.

Hypophosphataemia in Dogs

Hypophosphataemia is present in dogs when the serum concentration is less than 0.8mmol/L. It is not usually clinically worrisome until the phosphate concentration is less than 0.48 – 0.65mmol/L. Clinical signs may develop when the serum concentration is less than 0.48mmol/L although this is quite variable and can be clinically silent for some time – especially if the drop in concentration occurs gradually. Severe hypophosphataemia of less than 0.32mmol/L is of major clinical concern, as it is known to affect the neuromuscular system causing weakness, ataxia and seizures, and also the haemotological system causing lysis of red blood cells.[1]

A search of veterinary and human literature fleshed out the possible clinical consequences:-

- **Rhabdomyolisis** – dogs fed a low phosphorus diet for 4 weeks demonstrated a reversible decrease in average resting transmembrane potential, and increases in muscle Na+, Cl- and water.[2] In hypophosphataemic dogs a subclinical myopathy might set the stage for rhabdomyolisis if acute, severe hypophosphataemia is superimposed.[3]
- **Haemolysis** – hypophosphataemia can markedly reduce levels of erythrocyte ATP and 2-3-DPG.[4,5] This increases the affinity of haemoglobin for oxygen and diminished oxygen delivery to tissues. ATP is also required for maintenance of erythrocyte bioconcavity and viability in the circulation.[6,7] ATP depletion has been associated with decreased cell membrane deformability and life span, and rarely in humans with haemolytic anaemia.[8]
- **Leucocyte dysfunction** – hypophosphataemia can also reduce the ATP content of leucocytes and ameliorate neutrophil phagocytosis, impairing chemotactic, phagocytic and bacteriocidal activity.[9,10]
- **Respiratory failure** – in human patients, moderately hypophosphataemic patients demonstrated respiratory muscle weakness that was reversed upon phosphate repletion.[11]
- **Impaired myocardial performance** – reversible depression of myocardial performance has been demonstrated experimentally in dogs with moderate diet-induced moderate hypophosphataemia.[12]
- **Perturbed CNS** – several human case reports indicate an association between hypophosphataemia and neurological problems such as altered mental status, irritability and polyneuropathy including cranial nerves, seizures and muscular weakness.[13]
- **Impaired platelet aggregation**[14]
- **GIT disturbances** – may include anorexia, nausea and vomiting[14]
- **Renal tubular acidosis** – phosphorus depletion diminishes renal acid excretion and can lead to distal tubular acidosis.[14]

I had not happened upon a case of non-spurious canine hypophosphataemia before, and felt the need to research the list of causes and differentials for Meg's condition. A search of veterinary and human literature provided a not insubstantial list:-

- **Redistribution of phosphorus from the extracellular to intracellular compartment**
  - Acute respiratory alkalosis
  - Diabetic Ketoacidosis
  - Glucose administration (refeeding syndrome in starved or anorexic patients)
  - Insulin administration or hyperinsulinism
- **Decreased intestinal absorption**
  - Starvation or inadequate dietary intake
  - Chronic malabsorption syndrome, characterised by chronic steatorrhea, vomiting or diarrhea
  - Overzealous administration of phosphate binders (antacids)
  - Vitamin D deficiency
- **Increased renal loss**
  - Primary hyperparathyroidism
  - Hypercalcaemia of malignancy
  - Eclampsia
  - Hypercalcitonism
  - Hypomagnesaemia
  - Hypervolaemic states leading to natriuresis
  - Fanconi syndrome and Fanconi-like syndromes causing renal tubular disorders
  - Metabolic acidosis
  - Diuretic therapy
  - Corticosteroid administration
  - Sodium bicarbonate administration
  - Recovery from hypothermia[1,15]

The majority of these possibilities could be ruled out immediately on the basis of Meg's signalment, her otherwise healthy presentation, her outdoor lifestyle, her adequate diet, her lack of polydipsia or polyuria and the absence of hypocalcaemia, hypoglycaemia, hyperglycaemia or current medical therapy. We had not ruled out all causes of increased renal loss, nor could we completely exclude hyperinsulinism.

I sought the advice of a senior clinician at The Sydney University Veterinary Teaching Hospital (SUVTH) who agreed that Meg's hypophosphataemia warranted further investigation. He recommended I also not rule out hyperparathyroidism yet, as in some cases phosphorus levels drop before calcium levels rise. We also discussed running a Fasting Insulin:Glucose test to rule out hyperinsulinism, and a Phosphate Excretion Test to determine whether Meg was losing phosphorus inappropriately through her kidneys.[16]

We proceeded with the Fasting Insulin:Glucose test, whereby fasted blood samples are taken hourly until the blood glucose level reaches 3.3mmol/L. At this point, a non-haemolysed serum sample is collected for determination of concomitant insulin levels. Meg was fasted overnight, and hourly glucose determination commenced the following morning. By 18 hours post-feeding, Meg's glucose was still within the normal range at 4.4mmol/L (3.89-7.95) and we abandoned the test and fed Meg! Clearly no hyperinsulinism operating here!

We then perused the possibility of increased urinary loss, and performed a Phosphate Excretion Test. Meg returned a result that was hard to interpret. On that day, her blood and urinary phosphate both measured within normal range at 1.8mmol/L (0.8-2.1) and 22.4mmol/L respectively, and her phosphate clearance was well within the accepted normal limits at 18.7% (<39%). Whatever the explanation for the normal blood phosphate on that particular day, Meg did not appear to be losing excessive phosphate via the renal route. I did reflect later that it would perhaps have been worth repeating this test in the hope that Meg's renal response to a low measured serum phosphate level could be assessed. However, her otherwise perfect renal function as demonstrated by repeated general health profiles made renal loss a very unlikely proposition.

Treatment

At this point, I discussed Meg's condition with her owners. It was difficult to know what to do next, especially since Meg was not at this stage exhibiting any signs referable to hypophophataemia besides occasional tremoring and agitation. We were very concerned however that left untreated Meg would become severely hypophosphataemic (a decrease of a mere 0.04mmol/L from her current level). We still had not ruled out early hyperparathyroidism, and discussed the cost of running a PTH assay. We also considered giving Meg an intravenous infusion of sodium phosphate and sought some guidelines regarding this.

In general, treatment of the underlying cause of hypophosphataemia should be attempted whenever possible.

Mild hypophosphataemia (0.48 – 0.8mmol/L) should be treated by increased oral intake.

Moderate hypophosphataemia (0.32 – 0.48mmol/L) may require intravenous supplementation, particularly when clinical signs of phosphorus deficiency are present (principally weakness) or when total body phosphorus depletion is suspected.

Severe hypophosphataemia (<0.32mmol/L) is usually only seen when total body phosphorus deficiency is present and should be treated with intravenous supplementation.[14] The reported veterinary dose of either intravenous potassium or sodium phosphate is 0.01 – 0.03mmol/L/kg/hr.[17] This requires very careful monitoring of plasma phosphate, calcium, sodium, potassium and glucose levels every 4 – 6 hours, due to the risks of hyperphosphataemia, hypocalcaemia and ectopic calcium phosphate deposition.[2,14]

Taking into consideration that Meg was still (just) in the moderately hypophosphataemic range and her apparent resilience to the clinical effects of hypophosphataemia, we adopted a different tack. We decided to increase Meg's dietary intake of phosphorus by adding phosphorus rich foods[18,19] to her current commercial diet. We were aware that concentrated oral phosphorus is available as sodium phosphate – however, its primary use as a laxative in preparation for colonic endoscopy made it a very unappealing option.[20] Mindful of the need to keep Meg's calcium:phosphorus ratio stable, we decided to add lactose free milk, cheese and ground peanuts, brazil nuts and almonds to her diet for the next month.

After one month, I reassessed Meg. She had had no more episodes of shaking, had maintained her weight, and was well on physical examination. The milk and cheese had not appealed to Meg, but her dedicated owner had persisted with adding cheese and ground nuts to Meg's diet. This time, her blood results showed an increase in phosphorus to 0.42 mmol/L which, whilst still in the low range, was encouraging. We decided to really push the addition of phosphorus rich foods,[18,19] having no real guidelines as to what level of supplementation we should be giving. I could not find any information regarding this in veterinary literature, so I adopted similar levels of supplementation of 1000mg/day as recommended for human patients[15] – whilst monitoring Meg's PCV, calcium and phosphorus levels monthly as part of a general health profile.

For the following month, Meg ate her normal balanced dog food mixed with 2 tablespoons of a power-packed phosphorus mixture of boiled mashed potato or brown rice, beef mince, raw lambs liver, sunflower or olive oil, ground peanuts, sunflower seeds, pumpkin seeds, wheatgerm, ground kelp and egg.

After 1 month, her blood results were extremely encouraging. Whilst still in the low range, her phosphate had increased again to 0.65mm/L. Her ALT remained slightly high (112) and amylase was low (349) as it had been throughout. Meg's owner continued with her home-made phosphorus mixture for the following month.

After 1 further month of serious supplementation, Meg's owners were rewarded for all their efforts. This time Meg's phosphorus measured 0.94mmol/L – within normal range. Interestingly, her ALT also measured 97 U/L – also within the normal range, which had not happened whilst ever Meg was hypophosphataemic.

At this point, Meg's owners had a long holiday due, and we arranged to review Meg on their return in 6 months. It was not possible to keep up with the intense dietary supplementation during this period. When I retested Meg on their return, some disappointingly familiar numbers reappeared. Her phosphate levels had dropped back to 0.36mmol/L, just above the severely hypophosphataemic range, ALT was high again (109) and amylase was low (328). At this stage, some 12 months after initial presentation, I felt able to rule out hyperparathyroidism, as Meg's hypophosphataemia had been responsive to phosphorus supplementation, and her calcium levels were still normal. Also, with primary hyperparathyroidism serum phosphate rarely drops below 0.6mmol/L due to enhanced intestinal absorption and bone mobilisation.[15]

After 2 weeks of resuming her phosphorus rich diet, Meg's serum levels rose to 0.52mmol/L, and will presumably continue to rise back to normal as they did previously.

I have concluded that one more differential for canine hypophosphataemia may need to be added to the current veterinary lists – namely idiopathic selective phosphorus intestinal malabsorption. My association with Meg has shown me that individual dogs can be extremely resistant to the frightening list of possible sequelae for severe hypophosphataemia, and one may ask – why bother? My justification for persisting with treating Meg is fourfold:-

1. We have no information in veterinary literature as to the effects of chronic (low) moderate hypophosphataemia in dogs
2. The sequelae to severe hypophosphataemia as reported for humans and dogs are extremely serious and possibly life-threatening.
3. Untreated, Meg hovers just slightly above the severely hypophosphataemic level; and
4. Meg's owners are brilliant.

At the time of writing, we are monitoring Meg monthly, and are considering engaging the help of a veterinary nutritionist to formulate a long-term phosphorus rich diet for Meg. ▶

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Figure 1. Some of the essential ingredients for Meg's management. Essential ingredient missing from the photo is a dedicated owner

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Comment courtesy of:

Sue Foster BVSc MVetClinStud FACVSc
Small Animal Medical Consultant
Vetnostics
60 Waterloo Rd
North Ryde NSW 2113
E. sfoster01@bigpond.com

Dr Grice should be congratulated on the investigation, management and reporting of this very interesting case. Hypophosphataemia unrelated to anorexia/inappetence, hypercalcaemia or diabetes mellitus is rarely reported in the veterinary literature. There is a paucity of data on the clinical consequences of hypophosphataemia in dogs and recommendations for chronic treatment.

Hypophosphataemia occurs by 3 mechanisms: decreased intestinal absorption, renal loss or extracellular to intracellular shifts. The most common causes are anorexia/inappetence (usually mild decrease), primary hyperparathyroidism, humoral hypercalcaemia of malignancy and diabetes mellitus. Loss in the latter is due to marked renal loss and the true extent of hypophosphataemia may be masked by an intracellular to extracellular fluid shift as a result of insulin deficiency. Insulin administration drives phosphate intracellularly and can result in severe hypophosphataemia. Insulin treatment of diabetic ketoacidosis (DKA) is the most common cause of clinically significant hypophosphataemia, resulting in haemolytic anaemia in cats.[1,2] Haemolytic anaemia is also reported as a sequel to experimentally induced hypophosphataemia in dogs.[2] However, as Dr Grice discussed, dogs are remarkably resilient to clinical consequences of hypophosphataemia.

Until 2008, hypophosphataemia, for me, was just a consequence of another disease and usually clinically unimportant unless it was occurring in DKA patients. However, with the outbreak of acquired proximal renal tubulopathy associated with feeding of KraMar Supanaturals Chicken Breast Strips®, hypophosphataemia became a more common finding in laboratory results. As I was not necessarily privy to the urinalysis findings, hypophosphataemia was sometimes the only marker I had for renal tubulopathy. Of the 108 dogs collated by Dr M Thompson[3] with acquired tubulopathy, 37% had hypophosphataemia. Interestingly, some of these dogs had very severe hypophosphataemia (0.2 mmol/L) despite being asymptomatic. It was also interesting that some of these dogs had unexplained increases in alanine aminotransferase (and one dog had hepatic lesions on histopathology).

After the recall of KraMar Supanaturals Chicken Breast Strips®, I started recording all cases of dogs with hypophosphataemia and no obvious explanation. Vetnostics, North Ryde and QML Vetnostics generously offered to provide urinary fractional excretion measurements free of charge to enable follow-up of these dogs. What I have found is that unexplained hypophosphataemia is mostly associated with 2 disease processes 1) acquired renal tubulopathy due to treats and 2) central nervous system signs, usually seizures. In dogs with CNS signs, the hypophosphataemia is transient and urinary fractional excretion of phosphate is normal. When these dogs are retested, phosphate concentrations return to normal. This unexpected hypophosphataemia could be due to hyperventilation and respiratory alkalosis at the time of seizures. Another hypothesis provided by Dr Chris Holland was that seizuring dogs may have increased sympathetic tone and hypertension resulting in transient hypophosphataemia, as occurs in humans.[4] Knowing that transient hypophosphataemia is associated with seizures does cast some doubt on the hypophosphataemia as a cause of seizures in the diabetic dog reported by Willard and others (1987).[2]

The incidence of hypophosphataemia due to toxic renal tubulopathy was expected to decrease once the KraMar® treats were withdrawn. However, treat-related tubulopathies with hypophosphataemia are still occurring in Australia. The hypophosphataemia usually (but not always) resolves with the glucosuria once the treats are withdrawn. There has not been a consistent 'offender'. We are still investigating each case as best as possible and Vetnostics continues to provide follow up urinary fractional excretions on these cases. If anyone does have a case of acquired proximal renal tubulopathy/Fanconi syndrome, Dr Linda Fleeman, Dr Mary Thompson and I are still very keen to be contacted.

Dr Grice's case is different from the proximal tubulopathy cases in that the urinary fractional excretion of phosphate was normal. However, it was odd that the dog had normal serum phosphate at the time of the test despite hypophosphataemia both prior and subsequently. Dr Grice and I did arrange for the dog to have urinary fractional excretion performed at QML Vetnostics (the owners have moved interstate). The phosphate excretion was normal but interestingly it was relatively high normal for a dog with a borderline low serum phosphate concentration. There is no information as to what percentage of phosphate excretion is acceptable in hypophosphataemia. Physiologically, one would expect phosphate excretion to be low rather than normal in a hypophosphataemic patient but with no data to support this hypothesis, it has to be assumed that the dog does not have renal tubulopathy but instead has idiopathic hypophosphataemia.

A common recommendation in Fanconi's syndrome is to use a Pet Cal-type vitamin D phosphorous replacement.[5] I have been associated with two 'KraMar dogs' which have required long-term supplementation. One of these with severe non-clinical hypophosphataemia has required phosphate supplementation for 2 years. Like Dr Grice, I was concerned about the potential sequelae, even though the dog had no signs. The veterinarian treating this dog (Dr Gary Ashton, Campbelltown Veterinary Hospital, NSW) used a fresh meat diet and Coforta injections in the first instance, around Christmas, when it was difficult to procure parenteral sodium or potassium phosphate. Coforta is registered for phosphorous supplementation and contains 100 mg/mL butaphosphan (17.3 mg phosphorous/mL; 31 mg phosphorous = 1 mmol) and vitamin B12. Dr Ashton then used dicalcium phosphate (DCP) powder, at an empirical dose (1 tspn BID PO) to try and normalise serum phosphate. Once a successful dose was established, calcium and phosphate monitoring were performed to ensure that both calcium and phosphate remained in reference range. The dog was later supplemented with 3 mL Cophos B 3 g Paste® BID PO rather than DCP. Cophos B 30g Paste (Nature Vet) is registered for canine use and contains ethanolamine phosphate 100 mg/mL and cyanocobalamin 50 µg/mL. Attempts to wean the dog off phosphate supplements have been unsuccessful and urinary fractional excretion of phosphate in this dog is still markedly increased. I also monitor a similar case in Queensland, which has also been managed with DCP for over 2 years.

Dr Grice found innovative solutions to Meg's hypophosphataemia. I had previously suggested using red meat (high in phosphate, low in calcium) but had not pursued high phosphate diets any further. I think using low calcium, phosphate rich diets and supplements has significant merit and I will certainly be recommending that in the future. I have learned a lot from both the case and the report with its well-researched references.

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CO-WINNER OF BEST PICS

Cladosporium and posaconazole

C&T No. 5214

Eamonn Lim
Peakhurst Veterinary Clinic
709 Forest Road
Peakhurst NSW 2210
T. 02 9153 7614

'Rocco' is a male neutered 8-year-old DSH cat with indoor and outdoor access. His routine prophylactic treatment was mainly up-to-date and, apart from cat bite abscesses and 2 episodes of conjunctivitis, he had been in good health.

Rocco presented for a routine health check in April 2009. A mass ~ 5 x 5 x 5 mm was found on the medial aspect of his P3 D3 RFL and he also had a presumed eosinophilic granuloma lesion involving his chin. He was started on doxycycline 5 mg/kg BID PO. After 1 week, his chin lesion was regressing nicely and the digital lesion was flatter but it had developed a single sinus discharging bloody fluid. Convenia® was added at the normal dose rate. After 1 month, the chin lesion had resolved and the digital lesion was smaller but still discharging. An excision biopsy was performed. An ulcerated mass was dissected free and routinely closed. To the naked eye, the mass was discrete, dark, soft and completely removed. The wound healed uneventfully, with histopathology showing phaeohyphomycosis with granulomas and infectious organisms close to the margins.

In December 2009, regrowth became evident with lesions on the lateral and medial surfaces of the same digit. The lesions were excised and bacterial and fungal culture and sensitivity performed. Initial treatment was doxycycline. Coagulase positive Staphyloccus was isolated and Convenia® was added. The wounds healed uneventfully. Fungal culture yielded *Cladosporium* spp and griseofulvin was added at approximately 21 mg/kg SID. It is not certain how long Rocco remained on this treatment.

Rocco showed signs of recurrence again in October 2010. There were dark purple masses on the lateral and medial surface of P3, D3, right forelimb. There was a smaller lesion on the lateral aspect of the adjacent D2.

After discussion with Sue Foster (Vetnostics) and Richard Malik (CVE), posaconzole was started 5 mg/kg SID PO. Posaconazole comes as an oral suspension, 40 mg/mL, 105 mL bottle and is approximately $900. The taste is apparently reasonable.

In the 19 days between representation and commencement of treatment there was marked growth of all the lesions. The lesions on P3 D3 had coalesced into one large lesion over the dorsum and sides of the digit. There was also a new lesion on D3 on the dorsal aspect of P1. The approximate sizes of the lesions were as follows:

lat + med D3:	~ 22 x 15 x 10 mm
dorsal D3:	~ 7 x 5 x 2 mm
lat D2:	~ 7 x 4 x 2 mm

After 2 weeks of treatment, the lesions were definitely smaller; the lesions that had coalesced over P3 D3 had regressed to become 2 distinct masses again. ▶

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lat D3:	~ 10 x 6 x 3 mm
med D3:	~ 12 x 8 x 8 mm
dorsal D3:	~ 6 x 5 x 2 mm
lat D2:	~ 8 x 5 x 2 mm

Unfortunately, Rocco was not easy for the owners to medicate. Despite missed doses and incomplete doses, Rocco continued to improve. There was concern regarding lethargy, inappetance and mild weight loss. Clinical examination, BP, UA, FBC, biochem, and T4 were all essentially normal. The owners felt that the issue was most likely behavioural in response to administration of the posaconazole. At 5 weeks of treatment, lesions sizes were approximately:

lat D3:	~ 10 x 5 mm, flat
med D3:	~ 12 x 9 x 4 mm
dorsal D3:	~ 5 x 4 mm, flat
lat D2:	~ 5 x 3 mm, flat

At 9 weeks of treatment, lesions were continuing to regress.

lat D3:	~ 7 x 5 mm, flat
med D3:	~ 10 x 6 x 4 mm
dorsal D3:	~ 5 x 3 mm, very hard to see lesion
lat D2:	~ 5 x 3 mm, very hard to see lesion

At 16 weeks, there was further improvement.

lat D3:	cannot see lesion
med D3:	~ 8 x 2 mm, flat
dorsal D3:	cannot see lesion
lat D2:	cannot see lesion

At 22 weeks, there was slight discoloration on the medial aspect of D3 but otherwise no visible lesions.

At 32 weeks, there was no visible sign of any lesions.

At 56 weeks, Rocco is apparently still on medication. For the first 3 to 4 months, the owners were able to dose Rocco reasonably regularly. As time progressed, he became increasing difficult to medicate. Some days he would not allow medication and other days, the owners would only try a reduced dose to at least have some drug administered. If Rocco was taking every dose, one bottle would last around 3½ months. The first bottle lasted a little over 4 months. The second bottle has lasted 9 months and is still going. It appears that the initial more intensive treatment, followed by lower chronic doses, has been effective but longer term follow up will be necessary to confirm this.

D3 and D2 have been clipped lightly before photography to enhance visualisation of the lesions.

Photos 1 and 2: pretreatment.

Photo 1. Pretreatment. D3 is directly under the thumb. The main lesion surrounds the sides and top of the nail. There is a smaller lesion more proximally near the fingernail.

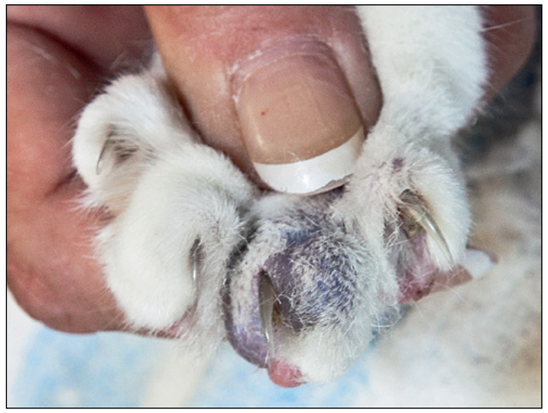

Photo 2. Pretreatment. Close up of D3 showing the main lesion surrounding the nail. The smaller lesion on the lateral surface of adjacent D2 can just be seen.

Photos 3 to 5: 2 weeks of treatment

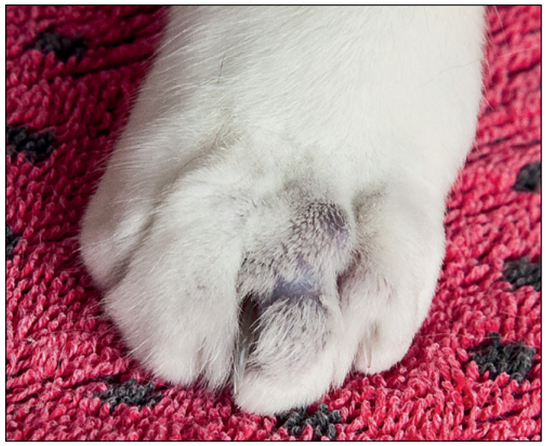

Photo 3. After 2 weeks, the lesions are noticeably smaller.

Photo 4. After 2 weeks. Closer view.

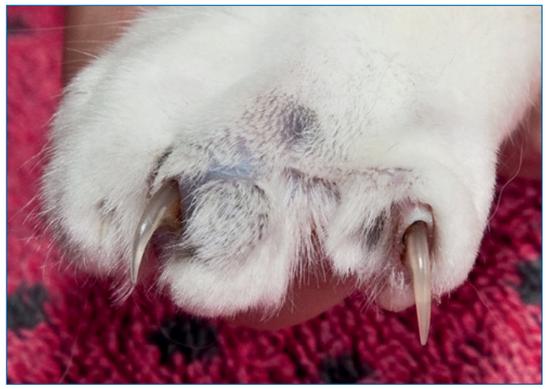

Photo 5. After 2 weeks. Closer view.

Photos 6 to 8: 9 weeks of treatment

Photo 6. The lesions on lateral and medial D3 are still visible but the lesion on the dorsum of D3 and lateral D2 are very hard to see.

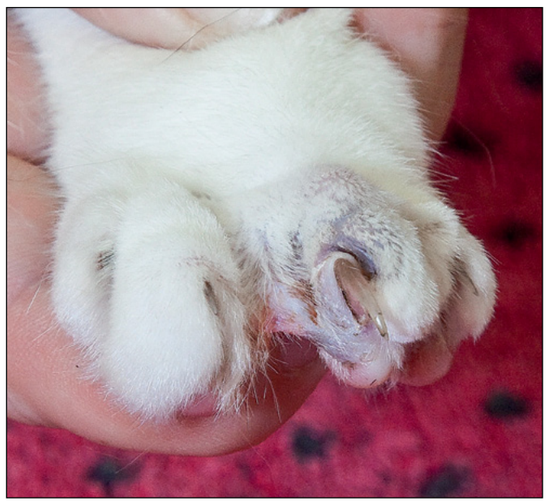

Photo 7. The marks on lateral D3 are due to the clipper.

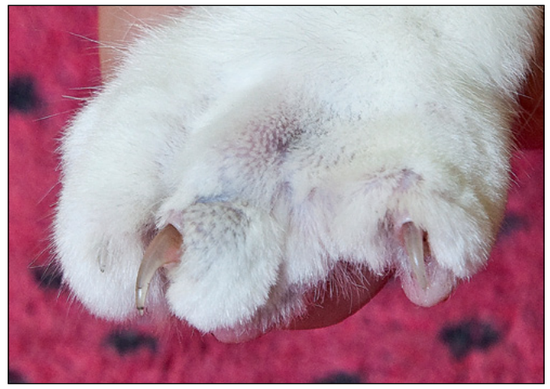

Photo 8. Closer view.

Photos 9 and 10: 16 weeks of treatment

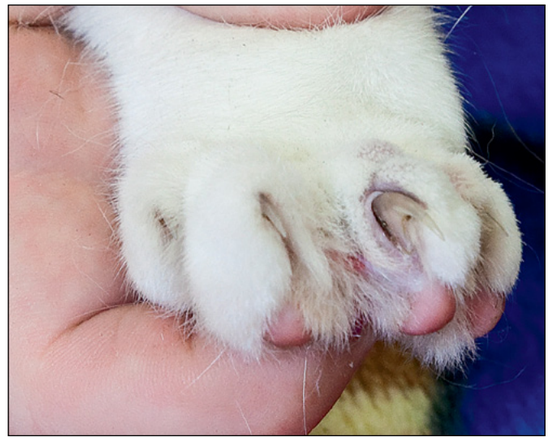

Photo 9. The mark on lateral D3 is due to the clipper again. The lesion on lateral D3 and dorsal D3 are no longer visible.

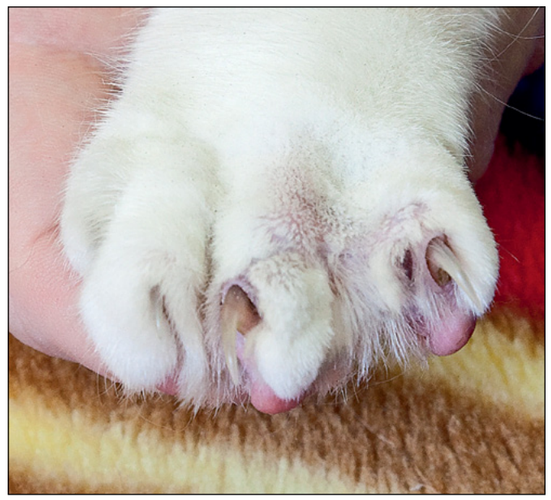

Photo 10. The mark on the lateral D2 is due to the clipper (Rocco was not easy to clip). The lesion on D2 is no longer visible. The lesion on medial D3 is still present but not visible on the photo.

Authors' views are not necessarily those of the CVE

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How to deal with concurrent pancreatitis and diabetes in dogs and cats

C&T No. 5215

Linda Fleeman BVSc PhD MACVSc
Animal Diabetes Australia
at Boronia Veterinary Clinic
181 Boronia Rd, Boronia VIC 3155
T. +613 9762 3177
F. +613 9762 9480
E. L.Fleeman@AnimalDiabetesAustralia.com.au
www.AnimalDiabetesAustralia.com.au

Linda Fleeman is an international expert on canine diabetes and has published numerous papers on the clinical management of diabetes in dogs and cats. Linda has now left university practice to establish ***Animal Diabetes Australia***, a clinical service specifically for diabetic dogs and cats at the Boronia Veterinary Clinic in Melbourne.

Abstract

Management of concurrent pancreatitis and diabetes mellitus presents a significant clinical challenge in dogs and cats. Pancreatitis can sometimes be difficult to diagnose and typically has an unpredictable clinical course. Acute pancreatitis results in metabolic derangements that can be life-threatening in otherwise healthy animals, and are further complicated in diabetic patients by development of ketoacidosis. Chronic pancreatitis can lead to loss of beta cells in diabetic dogs and cats, as well as progressive loss of exocrine pancreatic function. Diabetes mellitus is recognised as an important risk factor for pancreatitis yet there is still little information published on the best management strategies to reduce the risk of acute pancreatitis or slow the progression of chronic pancreatitis in these patients.

Dogs and cats with uncomplicated diabetes mellitus classically present with polyuria, polydipsia, weight loss, an increased appetite, and lethargy. The onset of these classic clinical signs is typically insidious, ranging from weeks to months in duration[1], and may initially be unnoticed or considered insignificant by the owner. Polyuria is the result of osmotic diuresis caused by persistent glucosuria. The animal compensates for this by increasing water intake to prevent dehydration. Weight loss and lethargy occur because insulin deficiency results in decreased ability to metabolise the nutrients absorbed from the gastrointestinal tract, and loss of glucose and amino acids in the urine. Diabetic dogs and cats compensate for these effects by increasing their food intake.

The importance of the compensatory role of polydipsia and polyphagia in the pathophysiology of diabetes mellitus becomes apparent when these compensatory mechanisms fail. Any concurrent illness in diabetic patients that causes inappetence or anorexia and vomiting is rapidly complicated by dehydration, depression, and ketosis. The majority of diabetic dogs and cats that present with diabetic ketoacidosis have at least one concurrent disease, with acute pancreatitis the most common diagnosis in dogs[2], while liver disease and pancreatitis are the most common concurrent conditions reported in cats[3].

Acute pancreatitis in diabetic dogs and cats

The most frequent presenting signs of acute pancreatitis in dogs are anorexia, vomiting, and dehydration[4]. Clinical signs in cats with pancreatitis are less specific, with inappetence and lethargy more commonly present than vomiting[5]. In both species, the clinical course tends to be unpredictable, the outcome can be fatal, and there is no specific treatment. The diagnosis of pancreatitis can be difficult because all of the available diagnostic tests have limitations. The most sensitive test in both dogs and cats is serum pancreatic lipase immunoreactivity (cPLI and fPLI, respectively)† while the most specific test is ultrasonography performed by a skilled operator.

Management of acute pancreatitis is primarily directed at its various clinical sequelae and the goal of treatment is to support the animal until there is spontaneous recovery. Concurrent diabetes mellitus with or without ketoacidosis presents an additional treatment challenge in these patients. With appropriate therapy, dogs with both acute pancreatitis and diabetic ketoacidosis have a similar chance of survival as those with diabetic ketoacidosis alone, although they typically require hospitalisation for a longer period[2].

Longer-acting insulin preparations such as Caninsulin® (Intervet) should be discontinued and replaced with short-acting insulin until the animal is recovered and eating well. Suitable preparations include regular insulin (for example, Actrapid® Novo Nordisk) or lispro insulin (Humalog® Eli Lilly)[6]. Administration protocols involving either constant rate intravenous (CRI) infusion or intermittent intramuscular/subcutaneous injections are effective[7], however CRI infusion protocols are simpler and less labour intensive for management of prolonged anorexia in diabetic dogs and cats. The main constraint is that a separate fluid administration line and infusion pump is required in addition to those used for supportive fluid therapy. An initial insulin infusion rate of 50 mU/kg/hr is recommended, which is easily achieved by administering a 50 mU/mL solution (25 U insulin in 500 mL saline) at 1 mL/kg/hr8. This rate is halved to 25 mU/kg/hr (0.5 mL/kg/hr of this solution) when the patient's blood glucose concentration reaches 10-15 mmol/L. At the same time, the maintenance fluids should be changed to contain 2.5% dextrose. A reliable means of achieving a fairly stable blood glucose concentration in an anorexic diabetic dog or cat is to balance intravenous infusion of insulin at 25 mU/kg/hr with 2.5% dextrose in 0.45% saline at 6 mL/kg/hr8.

Potassium depletion results from decreased intake due to anorexia and increased loss due to vomiting and diuresis. Fluid therapy causes dilution of circulating potassium levels and promotes further renal loss, while insulin therapy and correction of acidosis results in movement of potassium from the interstitial fluid into cells. Diabetic animals with acute pancreatitis therefore have a high risk of hypokalaemia and maintenance fluids should be supplemented with 30-40 mmol/L of potassium ▶

† This test can also be used on abdominal effusions, when present.

(KCl or a 50:50 combination of KCl and KPO[4]) from the outset. In critically ill patients, adjustment of the amount of potassium supplementation should ideally be based on serum potassium concentration monitoring[7].

Once the diabetic dog or cat with acute pancreatitis has recovered and has a normal appetite, therapy with short-acting insulin can be discontinued and a maintenance protocol using a longer-acting insulin preparation administered every 12 hours can be introduced or resumed.

Chronic pancreatitis in diabetic dogs and cats

Chronic pancreatitis is defined as permanent, irreversible damage of the pancreas due to inflammation with the key histological finding being fibrosis. This is likely the result of recurrent episodes of subclinical or clinical acute pancreatitis. Necropsy evidence indicates that chronic pancreatitis is very common in both dogs[9,10] and cats[11]. Chronic pancreatitis can progress to an end-stage where there is substantial loss of both endocrine and exocrine function resulting in diabetes mellitus with or without exocrine pancreatic insufficiency. This process of pancreatic destruction can be associated with minimal clinical signs in some cases, while other animals have recurrent episodes of clinical acute pancreatitis of variable severity. Extensive pancreatic damage due to chronic inflammation is responsible for the development of diabetes in approximately 28% of diabetic dogs[12]. The contribution of pancreatitis to the development of feline diabetes is unknown, although it is frequently present in non-Burmese diabetic cats[13].

Chronic pancreatitis in diabetic animals can have important clinical implications. In addition to the possibility of episodes of acute pancreatitis, progressive destruction of both endocrine and exocrine tissue will result in loss of insulin-secreting beta cells, glucagon-secreting alpha cells, and exocrine acinar cells. Glucagon has an important role in the counter-regulatory response to hypoglycaemia and is therefore crucial in protecting diabetic dogs and cats from the life-threatening consequences of insulin over-dose. Impaired glucagon counter-regulatory response to insulin-induced hypoglycaemia has been identified in diabetic dogs and was associated with episodes of clinical hypoglycaemia[14]. Avoidance of insulin over-dose is one of the primary goals of treatment of diabetic animals and this is especially important in patients suspected of having chronic pancreatitis.

Loss of body weight and condition despite polyphagia are presenting signs for both diabetes mellitus and exocrine pancreatic insufficiency. Treatment of diabetes usually results in weight loss being arrested before optimal glycaemic control is achieved. If weight loss continues despite adequate glycaemic control, the possibility of concurrent exocrine pancreatic insufficiency should be considered and serum trypsinogen-like immunoreactivity (TLI) concentration assayed and/or treatment with pancreatic enzyme supplementation trialled. The goal is to identify exocrine insufficiency early in the clinical course so that pancreatic enzyme supplementation can be started before there is excessive loss of body condition. A positive response to pancreatic enzyme supplementation comprising substantial weight gain and decreased gastrointestinal signs is typically seen within days in affected dogs.

Reducing the risk of pancreatitis in diabetic dogs

Hypertriglyceridaemia has been proposed as a possible inciting cause of canine pancreatitis[15,16] whereas there is no evidence for a similar role in feline pancreatitis. Increased serum triglyceride (TG) concentrations are commonly seen in diabetic dogs[17] and so the diabetic state might also be a risk factor for pancreatitis. Restriction of dietary fat is an important part of the management of hypertriglyceridaemia in dogs[18,19] and is recommended for diabetic dogs when hypertriglyceridaemia cannot be corrected by exogenous insulin therapy.

Fasting serum TG concentrations can be monitored to identify persistent hypertriglyceridaemia and to monitor the response to feeding a fat-restricted diet. Dietary fat restriction <30% of metabolisable energy (ME) should be recommended for all diabetic dogs with fasting serum TG concentration >5.5 mmol/L. For diabetic dogs with good glycaemic control, dietary fat restriction <30% ME is recommended if fasting serum TG concentration is >4.4 mmol/L. It is expected that fasting TG levels will decrease in response to dietary fat restriction. Therefore, if fasting serum TG concentration is >4.4 mmol/L when the dog is being fed a diet with <30% ME fat, further restriction of dietary fat to <20% ME is recommended.

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To bleed or not to bleed? – That is the question...

What dose and duration of Vit K prevents canine haemorrhage in rat bait toxicity?

C&T No. 5216

Aine Seavers
Oak Flats Vet Clinic
58A Central Avenue
Oak Flats NSW 2529
E. reception@oakflatsvet.com.au

The rat bait epidemic has died down but not gone away as the rains have flushed the rat bait out of their protective stations.

The treatment **oral dose** of Vit K1 on product labels of available patented and generic Vit K oral products varies from 1-12.5mg/kg! This reflects the difference in whether 1st Gen or 2nd Gen poisons are to be treated. This is not clear on many pill-pot labels.

The overwhelming impression clinicians and owners have of rat bait toxicity cases is the financial cost involved, even in an uncomplicated case. I have had animals die from lack of available finances not from a disease syndrome *per se*, so making treatment affordable and safe is a passion of mine.

If I have a valuable working dog or beloved family pet – often some hours' drive from a vet clinic – *I can't risk that the first bait the owner saw was the first bait the dog ingested* (always do a faecal scoop as well) so a suggested option of sending it back up the mountain road to wait for 2-3 days to re-test to see if bait had been ingested is a time bomb waiting to happen. Equally, the additional cost and travel inconvenience of regular on-going blood test monitoring is often not an option for many owners.

Thus an extended dose of Vit K is often employed once ingestion is suspected.

The concerns would be:
- The side effects from dosing for an extended period of time.
- The cost outlay to the client.

Side effects

Vit K is perceived to be safe. A fat-soluble Vitamin, it behaves biologically similar to a water-soluble Vit. It has a short half-life with no significant storage pools. The Heinz body anaemia issue seems mostly traceable back to human infant reports – 1 canine case has been reported in 1984. (Haemolytic anaemia is an issue with cats.) Equally, other formulations of Vit K – i.e. Menadione-K_3, not K_1, were implicated in adverse drug reactions.

Mount's work found that in a cohort of normal dogs given higher doses of Vit K, higher serum concentrations did not reveal accumulation of Vit K within the blood. Serum Vit K levels plateaued in these dogs from day 8-25, presumed to be enzyme induction of the Vit K enzyme complex and or other microsomal systems which may have allowed for more rapid clearing of Vit K.

So, on balance, perhaps it is safer to treat for longer than stop too early?

Cost

I do have to address treatment cost as this is not a plug for any one product. Finding affordable care for a client on limited funds is a daily reality of practice for those of us battling it out at the front-line of first opinion practice.

- A new **50mg** chewable tablet **(Mavlab)** produced by the makers of the earliest registered veterinary formulation here (10mg) is now available. Over a month of treatment, the 50mg option can end up costing 50% less than using their own 10mg tablet.
- Equally, another company's 25mg tablet **(Ceva)** in a smaller pot **(25)** makes a very economical option to have sitting just-in-case on the shelves of practices where rat bait ingestion by pets would be an uncommon presentation.
- There is also a **syrup** formulation from a third manufacturer **Koagulon 100mL** for difficult to orally dose smaller pets.

Published treatment **intervals** range from 5-7 days for 1st Gen to 5-24 days for 2nd Generation baits...

- Even 24 days for 2nd Gen may not be sufficient.
- Mount (*AM J Vet Res* 1989 50;10;) found no detectable levels of Vit K1 but found prolongation of prothrombin time in a 2nd gen exposed dog 3 days after a 24 day treatment regime ceased.
- A critical period after therapy was days 27-32 when the coagulation system was still impaired so that any insult to vascular integrity could lead to severe haemorrhage. Dogs given 5mg/kg/day x 21 days were better at limiting pathogenic changes at day 26-36 post ingestion with lower increases in OSPT levels than dogs on 2.5mg/kg/day. Coagulation was resolved by day 32 in Mount's study.

Treatment Regimes

1. Plumb (7th edn, 2011) recommends: A loading dose of 2.5-5.0mg/kg PO followed by 3-5mg/kg divided and given PO twice daily.

2. The iconic UK 2010-11 BSAVA formularies suggest:

- Regime for known **2nd Gen** to be: S/c 5mg/kg in several sites followed in 6-12hrs with 2.5mg/kg orally twice daily for 3 weeks.

Other options.
Still s/c for 24-48hrs if PO is not an option in a critically ill case... Maintain on 2.5mg/kg if regular monitoring an option. Otherwise use 5mg/kg/day for a minimum of 3 weeks if regular revisits are not an option.

- Toxin Generation **Type Unknown or Inandione (Diphacinone)** - BSAVA.

Treatment of 2.5-5mg/kg SC then 2.5mg/kg PO divided every 8-12hrs for 3-4 weeks. Test 2 days later and if PT elevated therapy should be for 2 additional weeks. If PT not elevated then test again 48hrs later.

Clinical practice feedback is vets have had dogs, treated for 4 weeks successfully for some 2nd generations, then sadly succumb to fatal haemorrhage in the ensuing 2 weeks. Equally, there have been cases tested at 4 weeks clearly showed aberrant blood results requiring a total of a 42 day treatment regime. This had led to some clinicians using a standard 42 day treatment regime routinely. ▶

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The gold standard protocol of daily PT testing to determine treatment duration is simply not affordable for the average owner.

The majority of poison cases are small to medium size dogs. Even a single lab test costed out at the laboratory set basic price can represent 10-24 days of drug treatment for a small dog – before any vet professional service time for consultation and blood collection is added. Therefore, on-going serial blood sampling can far exceed the cost of the actual lifesaving part of the therapy – the vitamin medication. As a result, *some vets thus choose, for financial and preventative reasons, to supply a 42 day not 28 day drug treatment regime to protect against potential catastrophic haemorrhage late in the equation.*

- Treatment Regime for **1st Gen** ie Warfarin etc.
  Vit K at: 2.5mg/kg SC in several sites, then 1-2.5mg/kg divided daily e8-12hours for 5-7 days (BSAVA).

Or

0.25-1mg/kg Vit K1/kg/BW i/m, s/c or orally in divided doses for 5-7 days (Woody JVIM).

Or

0.25-2.5mg/kg /BW small dogs – 0.5-2.5mg/kg/BW large dogs.

Warfarin does not inhibit the Vitamin K enzyme complex hence 1 week treatment– some 2nd gens can inhibit Vit K for 3-4 weeks.

Miscellaneous Points

The lipophilic nature of Vit K makes s/c injection with the smallest gauge needle in several sites a safe effective alternative to the high risk anaphylaxis of i/v option (reserve for severest cases) or the potential post injection muscle haemorrhage and necrosis of i/m injections. Use injection route for longer in any malabsorption, cholestatic patients.

Vit K returns PT and APTT to normal within 48hrs.

The longer plasma half-life of Vit K in dogs allows twice daily dosing of 2.5 or 5mg to be protective.

The half-life of some 2nd Gen can be 4-6 days.

Individual animals can be clinically affected with a smaller dose of rat bait. A clinically unaffected Dam can have affected foetus/neonates with both detectable levels of 2nd gen and severe clinical signs.

Feeding with a fatty meal of tinned food increases absorption 4-5 fold. However, Mineral oil reduces absorption.

The **Secondary Relay toxicity** question

All baits are not equal in their primary or secondary relay toxicity risk. Some authors say impossible, a dog would need to eat half their body weight in poisoned rat to be affected. Perhaps for 1st Gen but 2nd Gen relay poison is again often seen in practice. Mount clearly shows that one rat poisoned by 100gm of bait (0.005% active ingredient) could well cause lethal poisoning in a 13.6kg dog. Given that close to 70% of cases in Haines' (6/2008 *AVJ* review of 252) cases were small to medium dogs, it is no surprise that general practitioners see this scenario not infrequently.

‹e-book› *Some country vets, as in Dec 2012* C&T Series, *Issue 265, seeing hundreds of cases noted that 1mg/kg still left prolonged bleeding times at D=3 and D=9 of therapy so they commenced using doses of Vit K at 2.5mg/kg and higher, up to 5mg/kg as routine.*

* ‹e-book› *Emma Harding. Sept 2007. Haemothorax Requiring Transfusion from Suspected Rat-bait Poisoning.* C&T Series, *C&T No. 4843. Issue 248, Sept 2007 is an excellent case study on Tomcat poisoning.*

- REM systems do an in-clinic Rodenticide kit test. For more info contact: pparas@remsystems.com.au

References – A full list of references is available in our ‹e-book› or in the C&T Resources page: www.cve.edu.candt2012

Interesting website and articles on lipid rescue

C&T No. 5217

Katrin Swindells
Perth, Australia
E. kswindells@hotmail.com

In response to queries from Wayne Mizon, CVE DE Feline Tutor, Katrin Swindells, formerly of Murdoch University, has kindly alerted us to the following worthwhile website: www.lipidrescue.org

Intravenous lipid is useful for treatment of life threatening local anaesthetic toxicity (lignocaine and bupivacaine) and may be useful for treatment of neuro-excitatory toxins due to highly lipophilic chemicals. Katrin also advises that she expects 2 more articles on this topic to be published in the next 6 months and refers readers to the following published article, and case studies:-

- Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. *2011*. The use of intravenous lipid emulsion as an antidote in veterinary toxicology. *J Vet Emerg Crit Care. 21(4):309–320*
- Erratum: Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. *2011*. The use of intravenous lipid emulsion as an antidote in veterinary toxicology. *J Vet Emerg Crit Care. 21(5):570*

Case studies

- Pritchard J. *2010.* Treating ivermectin toxicity in cats. *Vet Rec. 166(24):766.*
- Crandell DE, Weinberg GL. *2009.* Moxidectin toxicosis in a puppy successfully treated with intravenous lipids. *J Vet Emerg Crit Care. 19(2):181-6*
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- O'Brien TQ, Clark-Price SC, Evans EE; Di Fazio R; McMichael MA. *2010;* Infusion of a lipid emulsion to treat lidocaine intoxication in a cat. *J Am Vet Med Assoc. 237(12):1455-8.*

Interesting website

www.wemed1.com

Whittemore Enterprises, based in California USA, has grown from a small business operating out of a garage to a worldwide concern, selling refurbished medical equipment at an excellent price, including warranties.

Thanks to Hugh Bain for alerting us to this website.
If you have any interesting websites to share with your colleagues, please contact Lis Churchward, CVE Editor, at **cve.publications@sydney.edu.au** for publication in our next issue.

WINNER

Isospora causing diarrhoea and weight loss in hand-reared kittens

C&T No. 5218

Nathalie Dowgray BVSc MRCVS
NCAC Veterinary Officer
Cats Protection, National Cat Centre
Chelwood Gate, Sussex, UK
E. Nathalie.Dowgray@cats.org.uk

'Thomas', 'Emily' and 'Percy' were the 3 surviving kittens from a litter of 5 kittens found under the floor boards of a steam train carriage at Bluebell railway in Sussex. Their mother was a feral cat who chose the train as a safe place to give birth one night. Unfortunately, once staff came on site to work in the morning she didn't return to feed the kittens and they were suffering from hypothermia and hypoglycaemia when they were brought into the National Cat Adoption Centre (NCAC) vet clinic. One kitten had already died and another wasn't able to be saved. Thomas, Emily and Percy responded to warming and feeding and were hand reared by members of the NCAC staff.

They had been at the NCAC for 6 weeks when they developed diarrhoea. They were being weaned from milk to kitten food so initially the diarrhoea was thought to be due to this. The milk was stopped completely and they were feed 50% kitten food and 50% Hills i/d®.

After 48 hours there had been no improvement with the diarrhoea. All three kittens were bright and eating, the diarrhoea was associated with a lot of straining and mucus. Samples were collected and sent for faecal analysis. The results showed a significant number of oocysts identified as *Isospora* sp. The kittens were started on Septrin suspension® (sulfamethoxazole/trimethoprim) 15mg/kg bid for 7 days. This drug is coccidiostatic. After 5 days there was some improvement with the faecal grade but this then worsened again over the following 2 days.

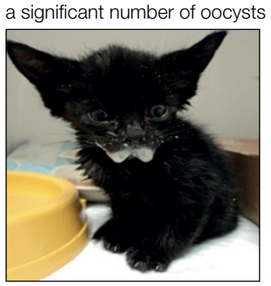
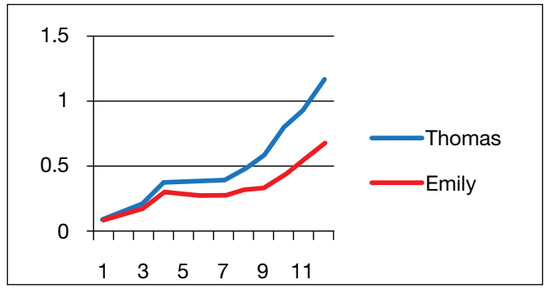


Figure 1. 'Percy'.

The Septrin® caused the kittens to hyper-salivate profusely and they were anorexic for 2-3 hours after administration.

By Day 7 all the kittens had lost weight and Percy was passing blood with his faeces. Subcutaneous fluids were given to all 3 kittens; Emily and Thomas improved but Percy became severely dehydrated and was euthanased. Necropsy results from Percy showed *Isospora* was still present but the cause of death was thought more likely to be due to a secondary bacterial infection.



After posting their case on a feline medicine forum I received the information that toltrazuril (Baycox®) was safe to use in cats. I had previous used this drug for treating coccidiosis in calves and knew it was very effective.

Thomas and Emily were treated with Baycox® multi (50mg/mL) at 20mg/kg. This amounted to 0.14mL. I administered this in a gelatine capsule as it can be very bitter tasting and cause hyper-salivation and vomiting although this side effect is less pronounced when the more concentrated Baycox® is used. This wasn't successful as the capsules burst in their mouths but the salivation was no worse than that caused by the Septrin.

Within 12 hours the diarrhoea stopped and Thomas and Emily started to gain weight. A 2nd dose of Baycox® can be given 10-14 days after the first if the diarrhoea returns but was not necessary in this case.

Infection with *Isospora* occurs following ingestion of either sporulated oocysts from a contaminated environment or from ingestion of a paratenic host (mice usually). Oocysts are passed unsporulated in the faeces; they become infective in warm humid environments within 12-24 hours. Infected cats are usually asymptomatic but kittens may show clinical disease, usually transient watery diarrhoea. In some cases the diarrhoea may be haemorrhagic and occasionally severely infected kittens may die. Diagnosis is by demonstration of oocysts in faecal floatation. Frequent removal of faeces from the housing will help to remove oocysts from the environment before they sporulate.

In this case it is likely that the *Isospora* contributed to the cause of Percy's death. Thomas and Emily both suffered from a small amount of weight loss but also didn't gain any weight for nearly 2 weeks. Previously we have used Septrin solely for treating *Isospora*. Thomas and Emily had this for 10 days without any real improvement. Future cases of *Isospora* will be treated with Baycox® as the first line of treatment.

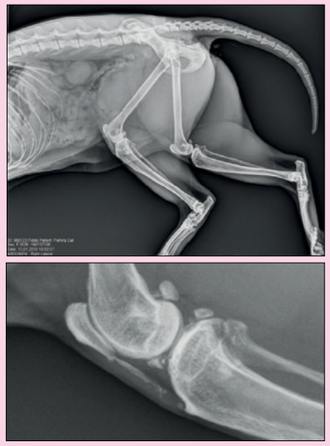
Reference

CR O'Brien, SE Pope and R Malik. 2002. Vomiting, diarrhoea and inappetence in a young cat with hypoproteinaemia. *AVJ.* Vol 8 No 9 2002

Answer to C&T No. 5176
(Dec 2011)

Another unusual manifestation

C&T No. 5219



Images courtesy of Taronga Zoo, Sydney

Graeme Allan
Veterinary Imaging Associates
PO Box 300, St Leonards NSW 2065
T. 300 300 892 F. 300 300 894
M. 0438 133 844 Mob
www.online-vets.com
via@online-vets.com
E. graeme.allan@sydney.edu.au

Mineralisation of the patella ligament, also either meniscal calcification or synovial osteochondrosis (depends upon who you believe) in a Fishing cat.

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Send us a pic of your case

If you have a picture which would be suitable for the 'What's YOUR diagnosis?' column, please sent it to Lis Churchward – Editor, as above.

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What's YOUR Diagnosis?

C&T No. 5220

Amy Lingard – CVE DE Feline Tutor
The Cat Clinic
1 Miller Street, PRAHRAN VIC 3181
T. 03 9533 8955
E. amylingard@gmail.com

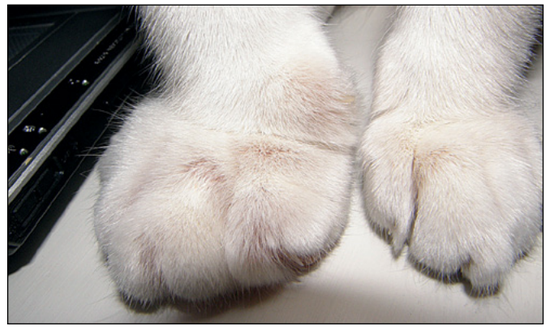

Figure 1.

Figure 2.

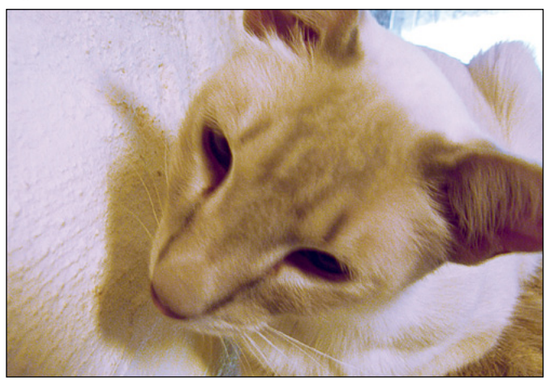

Figure 3.

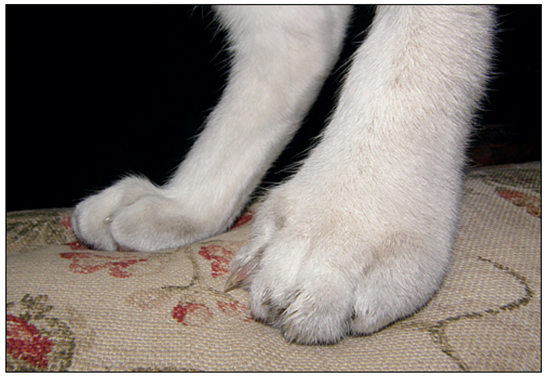

Figure 4.

Vet's summary

'Mia' is a 7yo FN Siamese with a history of pancreatitis and diabetes mellitus, currently in diabetic remission. Recently she has had a few episodes where she has developed marked swelling of her distal limbs or ears (see photos). She has been taken to her local clinic each time and responded to therapy with antihistamines. Physical examination is very limited due to her, shall we say, less than compliant demeanour!

She is an indoor cat, but has access to an outdoor cat enclosure. There are no known insects/spiders in the area and the owners have cleaned all debris from the enclosure.

She is on a homemade diet. Vaccinations are up-to-date and currently she is not on medication.

Further observations from her owner:

I think Mia has always had allergies. She used to twitch and pull out her fur and have bald patches. I think everyone believed it was because she was highly strung and had the habit of pulling her fur but we came to see that it occurred at different times of the year and believed it to be an allergy.

She was sent once for an allergy test to a specialist but she bit the specialist and they rang me to come and get her telling me they couldn't do the test - very naughty girl!

Since Mia's diabetic diagnosis and since I changed her food to a balanced raw diet her coat has improved so much, being thicker and silkier and whilst I do see her twitch and pull her fur a bit she never has bald patches anymore.

She has 3 episodes now of this unusual swelling.

The first occurred on the 15th June. She woke up with fat big ears that were so heavy she couldn't hold them up. There was nothing different with her paws. Her ears went down the next day but her blood glucose levels were higher for a few days. She was given a bump shot of insulin which helped her back down.

The second started on the 6th of August. Her ears were swollen at the base but not as big and heavy as the first time. The next day her ears were coming down but one paw swelled up really big (see photo) and continued to swell up her leg. The next day that leg and paw started to come down but a back leg started to swell but not to the same size. The next day they were still swollen but coming down. The day after all her legs started to swell.

That afternoon we gave her a antihistamine injection and a bump shot of insulin as her numbers were going up again and she was OK after this.

The third started on the evening of the 16th of September. Her ears and ankles were starting to swell and a few hours later her paws were getting bigger, too.The next day her ears were still swollen but her paws had reduced except for one. Late afternoon we gave her a anti-histamine shot but an hour later her back paw became really swollen (see picture). The next day her back paw was slightly reduced but that evening her nose swelled up and was very wide. I gave her a bump shot of insulin this evening as her blood glucose levels were going up. The next day her nose was still swollen.

Today she appears quite normal.

Every time there was a new swelling during this episode it happened early evening?

What's YOUR diagnosis?

Answer to: Rice crispy: C&T No. 5142 (Sept 2011)

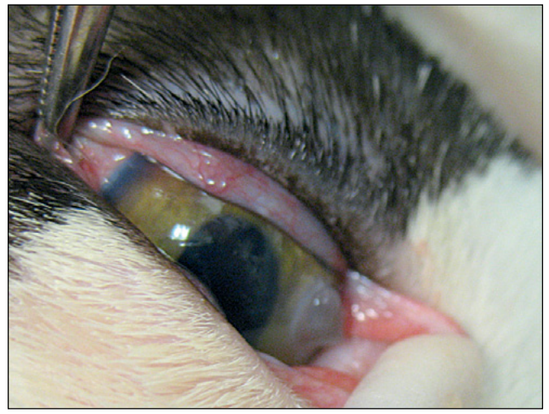

Figure 1. A 2-year-old DSH, male neutered with watery discharge from the affected eye (courtesy of Agnieszka Zoltowska)

Answer courtesy of Dr Jim Euclid's excellent website: www.felipedia.org

C&T No. 5221

Acute bullous keratopathy

Acute bullous keratopathy is one of many corneal diseases in cats. In this syndrome, there is acute, severe, bullous keratopathy of unknown etiology. Young cats are most commonly affected and the problem is usually bilateral[1]. The lesions either resolve with little or no scarring or progress rapidly to corneal perforation. A conjunctival pedicle graft is usually an effective means of preventing corneal perforation if applied sufficiently early[2]. Thermokeratoplasty may also be of benefit[3].

Acute bullous keratopathy begins as a corneal ulcer with rapidly developing secondary edema (bulla). In cats, the bulla can range from a few millimeters in diameter to the complete cornea[4]. ▶

Several small vesicles may coalesce to form a larger bulla. This condition is usually bilateral, but initially it may appear unilateral[5,6].

Etiology

The etiology and pathogenesis of feline bullous keratopathy is unknown. In published reports, tests for feline immunodeficiency virus, feline leukemia virus, feline infectious peritonitis virus, feline herpes virus (FHV), aerobic bacteria, *Mycoplasma spp*, *Chlamydia spp*, and fungi were negative[7]. Microbial cultures are usually negative and organisms were not detected on cytologic examination.

There are several theories as to how this condition develops in cats.

The first is that it may be an inherited stromal dystrophy, as has been reported in the Manx cat. Ultrastructural examination indicates severe stromal edema, as well as abnormalities in Descemet's membrane. However, abnormalities are not detected in the endothelium[8]. In contrast to cats with bullous keratopathy, the entire cornea eventually becomes involved and the corneal lesions are usually progressive over a period of several years.

The second theory is that the bullae are caused by a localized breakdown in the ultrastructure of the collagen fibers through an enzymatic degradative process. This results in a breakdown of the collagen fibers, causing a lack of structural support, as well as breakdown of the ground substance, whose function is to help imbibe fluid within the stroma.

A third theory is that an underlying condition, such as pre-existing uveitis, may cause bullae formation, as the inflammatory process taking place in the anterior chamber may disrupt the ability of the corneal endothelium to draw fluid from the corneal stroma[9]. However, there is no histological evidence of inflammation in any of the reported cases of acute bullous keratopathy. The relationship between uveal disease and the corneal changes remains unclear. Finally, in cats that develop bullous keratopathy, there is anecdotal evidence of prior treatment with topical or systemic dexamethasone. However, there is no evidence that this predisposes the cornea to develop this condition, and several cases of bullous keratopathy have been published that have not received steroids[10,11].

Similar conditions occur in dogs and humans; however, the clinical presentations, histopathology, and etiologies vary from the condition in cats. In dogs, formation of multiple small superficial corneal bullae occurs as a complication of severe corneal edema usually seen in chronic cases of endothelial dystrophy. In humans, the condition of keratoconus is a noninflammatory corneal thinning disorder that usually involves a focal area of the cornea, much like feline bullous keratopathy. However, keratoconus is usually more chronic in nature. Occasionally, there have been incidents of edema (known as acute hydrops) and rupture seen after long-standing cases. The light microscopic findings in human keratoconus differ from those of feline bullous keratopathy. In keratoconus, ferritin deposits are often present, and breaks in both the Bowman's and Descemet's membranes are seen. The edema seen in acute hydrops is the result of these breaks in Descemet's membrane, which has not been documented with feline bullous keratopathy. The etiology of keratoconus is also unknown, but theories have been proposed, including genetic mutations (it is suspected to be an autosomal dominant trait), eye-rubbing, atopy, Down's syndrome, and systemic collagen disease such as Ehler-Danlos syndrome[12].

Diagnosis

The diagnosis is made on the basis of clinical presentation and ophthalmologic examination, although the condition must be differentiated from septic ulcers with collagenolysis. Light microscopic examination confirms the diagnosis by revealing marked edema separating the collagen fibrils of the corneal stroma. Inflammatory cells are inconsistently present; when present, they are usually scant and occasional polymorphonuclear cells will be noted within the stroma. No abnormalities are seen in Descemet's membrane or the endothelium on light microscopy. The cornea surrounding the lesions appears normal[13,14].

Treatment

Treatment of feline bullous keratopathy consists of procedures that provide pressure or structural support to the bulla. The most common treatment is a combination of a keratectomy, conjunctival flap, and temporary tarsorrhaphy[15]. If these surgical procedures are not an option for owners, a long-term third eyelid flap may be successful. The use of topical antibiotics, mydriatics, and analgesics are indicated. Bullae may recur in the same spot as previous bullae or in new locations within the cornea. Some bullae resolve without treatment. The prognosis for bullous keratopathy with surgical treatment is good[16].

Figure 2. Domestic shorthair with bullous keratopathy of unknown etiology.

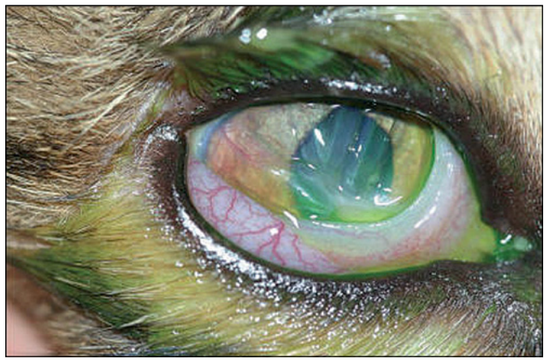

Figure 3. Right eye on presentation. The eye has been stained using fluorescein. Note the wrinkled appearance of the flattened anterior chamber of the ruptured corneal center.

Figure 4. Left eye on presentation. The eye has been stained using fluorescein. Note focal region of corneal edema.

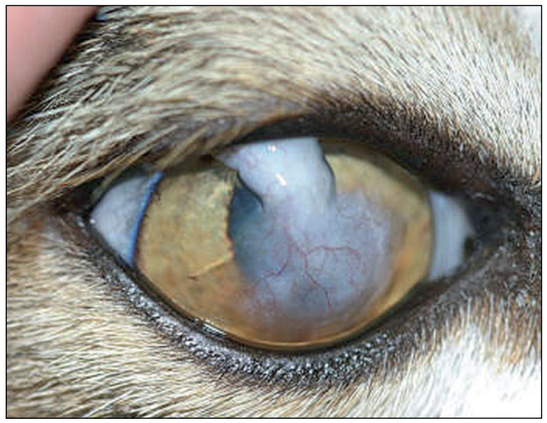

Figure 5. Right eye 4 mo post-surgery. Conjunctival grafts are healed and well incorporated into the cornea.

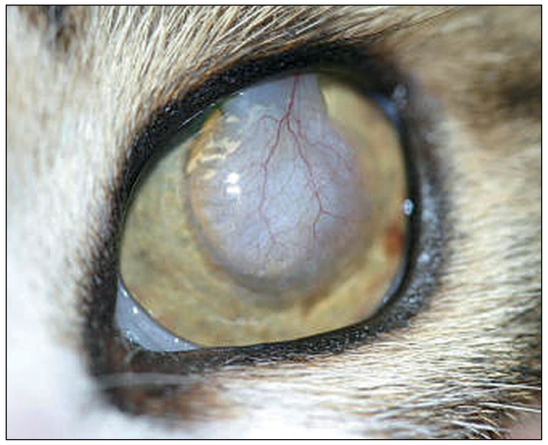

Figure 6. Left eye 4 mo post-surgery.

References

Due to space constraints, we are unable to publish them here. Please go to: www.felipedia.org/~felipedi/wiki/index.php?title=Bullous_keratopathy

APVMA encourages vets to report adverse product experiences

Reply to C&T No. 5182 page 44, 5183 page 46, 5187 page 48 in December Issue 265

C&T No. 5222

Australian Pesticides and Veterinary Medicines Authority (APVMA)
PO Box 6182 Kingston ACT 2604
T. +61 2 6210 4806
FreeCall: 1800 700 583 (within Australia) - charges apply for calls made from mobile phones
Fax: +61 2 6210 4813
Email: aerp@apvma.gov.au
www.apvma.gov.au

The December 2011 issue of C&T contained 3 articles relating to incidents of permethrin poisoning, bifenthrin toxicity and suspected diazepam toxicity in a cat.

None of these incidents was reported to the adverse experience reporting program—AERP—that is one key way in which the Australian Pesticides and Veterinary Medicines Authority (APVMA) obtains post-market feedback on the safety and efficacy of registered chemicals.

Each of these incidents was of direct relevance and interest to the AERP and the APVMA welcomes the opportunity to provide further details about this important element of Australia's chemical regulation system to C&T readers.

The APVMA regulates veterinary medicines and pesticides up to and including the point of sale. Regulated chemicals include veterinary medicines such as antibiotics and vaccines, nutritional products with specific health claims, insecticides, fungicides and herbicides.

The role of the AERP within this framework is to provide post-market feedback on the efficacy and safety of all of these registered products.

The AERP collects data relating to adverse reactions to veterinary medicines as well as to agricultural chemicals. These reactions may involve an animal ingesting a garden pesticide and is not limited to surveillance of reactions in 'target' species (such as a typical vaccine reaction).

Most reports received are submitted by product registrants. However, the APVMA would like to see more reporting by veterinarians in particular as they are the ones that see cases first-hand. This can include reactions involving agricultural chemicals that may have resulted from accidental exposure.

The AERP uses the database of reports to identify recurring events or trends over time. This can enable the APVMA to take further action for example implementing label changes to alert users to potential hazards or side-effects.

While 'off-label' usage of ag-vet products is beyond the official scope of the AERP, the reporting of such reactions and ▶

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usage allows us to become aware of patterns of use that may affect the safety and efficacy of a product, and is therefore encouraged.

There may be a misapprehension that 'you submit a report to the APVMA and nothing gets done'. However, although one report may not instigate immediate regulatory action, it will certainly contribute to the big picture in terms of building our database and taking appropriate action when issues are identified.

And finally, it is most helpful to the APVMA if the reporter has a rough idea of the type of product used as the more information you provide, the better the result.

PUBCRIS on the APVMA website (www.apvma.gov.au) contains details of agricultural and veterinary chemical products which are registered for use in Australia and may be of assistance with reporting.

As the data includes the product name, registering company, active constituents and product category, PUBCRIS can be used to identify the poison when the owner can only remember the name of the product they used and not the active.

The APVMA looks forward to hearing more from our veterinary colleagues as we work together to ensure that products in the market meet high standards for safety, quality and efficacy.

Ethical dilemmas – pedigree dog breeding

Reply to C&T No. 5185

C&T No. 5223

Marshall Thornton
West Cessnock Veterinary Hospital
2a Percy Street, Cessnock NSW 2325
T. 02 4990 4400
E. wcvh@tpg.com.au

The article by Dr Whitehead was very interesting. I have a strong interest in this topic. He makes the comment that vets should have been more 'out there', but the problems is the breeders do not want to know! They know best. They are totally obsessed by their breed and can see no wrong in breeding defective animals that have major problems.

Two quick examples come to mind for me. One is the pug breeders who are breeding dogs with laryngeal dysplasia which can hardly breathe the airway is so obstructed. To compound this, the nasal fold is causing chronic corneal disease and most of them are badly hip and elbow dysplastic.

Another example is a guy who breeds and shows show-winning Golden Labradors. All are hip dysplasia scored with the conventional AVA type positioning which has now shown to be not that useful (from 2 orthopaedic lecturers at conferences, plus reading on this). When advised that the Penn - Hip radiographs are more diagnostic for HD and would he like to confirm his dogs were 'HD free' he emphatically declined!

On this topic of AVA hip radiographs, I was 'tutored' by a GSD breeder I once had as a client on how to hold the dogs for the 'correct position'. Whereas I could get a perfect positioning with the usual extended VD view under anaesthesia method, this showed the dog to be dysplastic on the radiograph. When trying his method, which was to force the femoral heads into the sockets and still get the perfect position in order to eliminate the hip joint distraction, I was unable to achieve a perfectly aligned view.

For me this was an experimental exercise, as I had heard via the breeder grapevine that this could be (and allegedly is) done by practitioners skilled in taking HD radiographs. I could not achieve it experimentally, and would do so for ethical reasons.

Comment on: Use of mirtazapine in feline medicine (C&T No. 5181)

C&T No. 5224

Martin Whitehead
Chipping Norton Veterinary Hospital
Albion Street, Chipping Norton
Oxfordshire OX7 5BN
United Kingdom
E. martin.whitehead@virgin.net

Amy Khoo suggests that mirtazapine can be given daily without serotonergic effects. Quimby and others (2011a) found that CRF decreased clearance of mirtazapine. However, I have encountered 'serotonin syndrome' in a cat after 3.75 mg mirtazapine q72h. This 14-year old male domestic shorthair had multiple problems including plasmacytic glossitis and inflammatory bowel disease (both reasonably well controlled on long-term, low-dose prednisolone), diabetes mellitus (well controlled on Caninsulin), hypocalcaemia after a bilateral thyroidectomy (well controlled on oral calcium and vitamin D3 supplementations) and chronic renal failure (CRF). The CRF was treated with a 'renal' diet, phosphate binder, home administration of subcutaneous fluids, and intermittent use of antacids. As the CRF progressed and he became inappetant, mirtazapine was added at 3.75 mg q72h. After the second administration the owner noticed dilated pupils and odd behaviour that resolved within a day but after the third administration the dilated pupils and odd behaviour – hyperactivity and restlessness – were more marked and there was also rapid breathing. As these signs were consistent with serotonin syndrome the mirtazapine was stopped. The signs resolved without any treatment and did not recur. Quimby and others (2011a) found that CRF decreased clearance of mirtazapine.

Our practice, like many others, has been treating inappetant cats with mirtazapine 3.75 mg q72h for a few years. However, over the last couple of years we have largely stopped using it, not through any evidence-based decision but because we had subjectively felt that it seemed to make no difference. The results of the small studies by Quimby and others (2011a,b) will encourage us to give mirtazapine another go, this time giving it daily, and at the lower (1.88 mg) dose.

References

Quimby, J. M., Gustafson, D. L., Lunn, K. F. (2011a). The Pharmacokinetics of Mirtazapine in Cats with Chronic Kidney Disease and In Age-Matched Control Cats. *J. Vet. Int. Med.* 25(5), 985-989.
Quimby, J. M., Gustafson, D. L., Samber, B. J., Lunn, K. F. (2011b). Studies on the pharmacokinetics and pharmacodynamics of mirtazapine in healthy young cats. *J. Vet. Pharmacol. Therap.* 34(4), 388–396.

Perspective 89

Clinical Review: Non-infectious inflammatory CNS disease in the dog

Dr Amy Lam
BVSc (Hons I) GradCertVetStud MACVS (Small Animal Medicine)
Registrar in Small Animal Medicine, Small Animal Specialist Hospital
North Ryde NSW 2113 E. dr.ames@gmail.com

This article has been republished courtesy of The Veterinarian.

Amy is an Australian trained registrar in Internal Medicine currently working at Willows in the UK. She has worked in private practice in Melbourne and Canberra (with her Dad), undertaken a rotating internship at the University of Sydney, and a residency at the Small Animal Specialist Hospital (SASH) in Sydney. She is currently working towards her fellowships, and loves medicine of both dogs and cats.

It's always a challenge when a dog presents to your clinic with signs consistent with central nervous system (CNS) disease. Inflammatory brain disease can occur in any breed, at any age, with any neurological examination findings.

The CNS is unique. It is walled off by several barrier systems: the vertebral column and cranium, the meninges and the blood brain barrier. This makes it a challenge, but not impossible to assess, despite the budget. With a good (and repeatable) neurological and clinical examination combined with a patient's signalment and history, the problem can be localized, and then a differential list made. This list should then help target your future investigations or therapy.

Inflammatory disease of the CNS

Broad categories of inflammatory CNS disease include:

1. Location: Brain (encephalitis), meninges (meningitis), spinal cord (myelitis) or a combination
2. Infectious or Non-infectious

Non-infectious and presumed immune mediated meningoencephalomyelitis are more common than infectious causes in dogs. Specific disease processes include: granulomatous meningoencephalitis (GME), necrotizing meningoencephalitis (NME) – with increased prevalence in Pugs, Maltese and Chihuahuas, necrotizing leukoencephalitis (Yorkshire Terriers), steroid responsive meningitis arteritis (SRMA) and necrotizing vasculitis. Since a definitive diagnosis is made on histopathology these can be difficult diagnoses to establish. Future advancements in stereotactic biopsies in veterinary medicine may provide us with histopathology in live patients in the future. Currently, diagnosis of these conditions is made on the basis of signalment, clinical and neurological examinations, elimination of infectious, metastatic and certain vascular diseases, and combination of advanced imaging and cerebral spinal fluid (CSF) analysis. It may not be possible to make a definitive diagnosis on the results of diagnostic tests.

Therefore the term: meningoencephalitis (or meningoencephalomyelitis) of unknown aetiology (MUA) or meningoencephalitis of unknown origin (MUO) has been proposed as a more accurate diagnosis. Other proposed or previously used descriptions include non-pathogenic meningoencephalomyelitis, non infectious inflammatory CNS disease, non suppurative meningoencephalitis, reticulosis etc. To simplify the terminology for the rest of this review – we will use the term non-infectious inflammatory CNS disease. This review will not specifically discuss corticosteroid responsive meningitis in younger dogs and shaker dog syndrome as both of these diseases, although presumed to be immune mediated, cause characteristic clinical signs in a different population of dogs and have a much better prognosis than other inflammatory CNS diseases. The cause of both disorders is not known.

1. Signalment:
Age: 0-1y, 1-10y, 10+y
Breed: Toy breed, Terrier (including Staffordshire Bull Terriers), other
Sex: Female / Male, Entire / Desexed

Non-infectious inflammatory CNS disease is most common in toy breeds and terriers: particularly: Maltese, Yorkshire Terriers, Pugs. However, it can occur in any breed or cross breed. GME is most commonly seen in middle aged dogs 4 to 8 years of age. NME and necrotizing leukoencephalitis (NLE) tend to occur in younger dogs (Granger, 2010). It has been reported to occur more often in females than males. Non-infectious inflammatory CNS disease may represent up to 25% of all cases of CNS (especially brain) disease in dogs.

2. Clinical Examination:
History: Acute, peracute, subacute, chronic or episodic
Mentation: Dull or bright
Evidence of systemic disease?
Heart rate / respiratory rate and effort
Systolic blood pressure: >160mmHg without pain or stress?
Neurological examination: focal, multifocal or diffuse disease

These findings may help distinguish more behind the nature of the disease. For example – increased systolic blood pressure, decreased heart rate and altered respiration may be signs of increased intracranial pressure. Evidence of non-CNS disease. should be evalulated, as non-infectious inflammatory brain disease does non-result in systemic illness. Generally there are no abnormalities on physical examination. Pyrexia may be seen but is uncommon.

Patients with inflammatory CNS disease usually present with acute onset of CNS disease. Left untreated it is usually progressive and may be fatal! It is often multifocal – multiple regions of the brain (optic nerve, forebrain, cerebellum, brainstem), spinal cord and or meninges can be affected. Patients tend to have cervical hyperaesthesia. Many dogs will hide and yelp or scream for no apparent reason. They are often quiet or dull and have gait abnormalities. Clinical signs vary depending on the neuroanatomical location of the disease. Generally we try to differentiate them into forebrain (mentation, seizures, compulsive circling, ataxia, pacing, ventral visual impairment with normal pupilliary light responses, ▶

caudal fossa (ataxia, vestibular disturbance, cranial nerve abnormalities, obtunded mentation, hemiparesis to tetraplegia, vestibular dysfunction) or spinal cord disease (paresis, paralysis, ataxia proprioceptive deficits). Spinal cord disease may be multifocal but cervical involvement is most common.

Optic neuritis is recognized in veterinary patients with unilateral or bilaterally dilated pupils that are unresponsive to light stimulation. Fundoscopic examination may reveal a hyperaemic, oedematous optic nerve and vessels may be dilated and focal haemorrhage may be present. Inflammatory CNS disease has been differentiated into disseminated, focal or ocular forms. This distinction may or may not be important and made on the basis of clinical signs only rather than histopathology!

The ocular form (optic neuritis) affects the retinal or postretinal portions of the optic nerve. Some reports suggest better prognosis with the ocular form of GME in comparison to focal or disseminated disease. Some dogs with ocular GME may subsequently develop the disseminated or focal form of the disease.

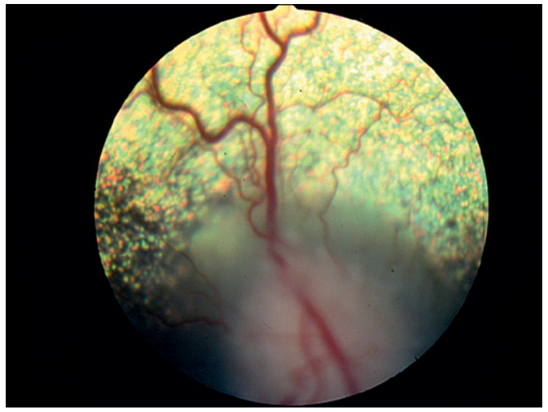

Figure1: Fundic examination: Optic neuritis. Note swollen optic nerve. (Photo courtesy of John (JRB) Mould and Mark Billson)

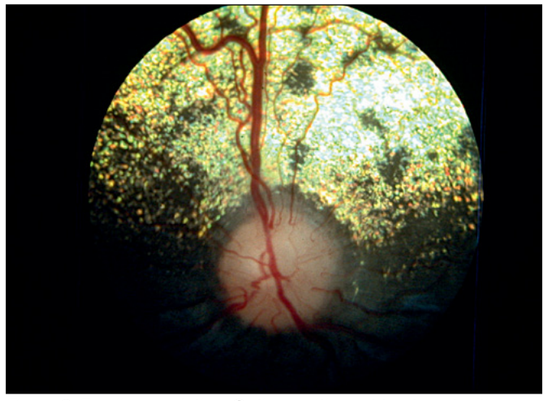

Figure 2: Fundic examiation: Optic neuritis post treatment with immunosuppression. Note marked improvement in swelling of the optic nerve. (Photo courtesy of John (JRB) Mould and Mark Billson)

3. Further diagnostics:
Imaging
Clinical Pathology

Clinically, inflammatory CNS disease usually results in multifocal neurologic deficits. The diagnosis of non-infectious inflammatory CNS disease is made on clinical examination findings and exclusion of infectious agent, congenital malformations, metabolic derangements, intracranial neoplasia and exposure to toxins. In many cases a tentative diagnosis or short differential list can be made given the patients signalment, history and clinical signs. The combination of advanced imaging and clinical pathology (serology, CSF analysis) findings, are the most clinically used diagnostic tests used for the diagnosis of non-infectious inflammatory brain disease.

Biochemistry, haematology, abdominal and thoracic imaging tend to be unrewarding in assessing inflammatory CNS disease. However, they are essential in excluding metabolic causes of CNS disease – for example hypoglycaemia and hepatic dysfunction. Survey radiography of the thorax and abdominal ultrasonography can help to diagnose primary neoplasms that may metastasise.

Imaging
- Radiography
- Computed Tomography (CT)
- Magnetic Resonance Imaging (MRI)

Plain radiology

Survey radiography of the cervical vertebral column should be performed if clinical signs of spinal disease are seen. Radiographs have largely been superseded by the extended availability of advanced imaging (CT and MRI). Myelography is usually contraindicated in patients with inflammatory disease. Examination of craniocervical developmental abnormalities can be performed on plain radiographs if there is a suspicion of atlanto-axial or craniocervical malformation (right signalment and age) or a history of trauma. Radiological technique and then interpretation of craniocervical developmental abnormalities can be challenging. Another indication for contrast radiography includes thoracolumbar disease. Extradural lesions such as disc protrusions can be seen by a defect in the myelogram. In rare situations these defects may be neoplastic, abscesses or other. All of these are other differentials for a focal spinal cord lesions; neoplasia is not rare. Imaging decisions should be made on lesion localization and most likely differentials.

Computed Tomography (CT)

CT is mostly used for assessment of bone and vascular lesions. It is not the ideal diagnostic for non-infectious inflammatory CNS disease. CT is less sensitive especially in evaluating caudal fossa lesions (beam hardening artifact from the petrous temporal bones). 'Mass effect' – deviation of the falx or disruption of normal brain anatomy may or may not be seen in either CT or MRI.

Magnetic Resonance Imaging (MRI)

MRI is the diagnostic modality of choice in non-infectious inflammatory CNS disease. MRI uses the fluid characteristics and change to magnetic signals to create an image of the soft tissue of the brain and spinal cord, which is superior to any other technique. MRI sequences are selected depending on scout images and suspected disease process. There are no 'typical' MRI findings for non-infectious inflammatory brain disease. Infectious, vascular or neoplastic diseases may look similar. Lesions may be single or multiple. Various sequences are used (T1, T2, Fluid attenuating inversion recovery (FLAIR)). Contrast is commonly used as part of the standard examination. Typically the features of lesions seen on MRI of non-infectious inflammatory brain disease are as follows:

- T1: hypointense
- T2: hyperintense
- FLAIR: hyperintense
- Contrast enhancement (with gadalinium) is variable.
- Meningeal enhancement is variable

In some cases no abnormalities are seen. In our practice, all patients are anaesthetized for MRI, as the area scanned must be completely motionless. We have not had any adverse reactions to anaesthesia nor to contrast administration.

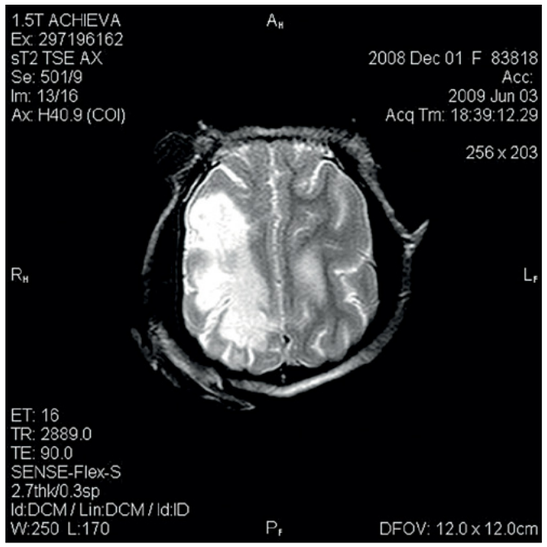

Figure 3: Multiple hyperintense lesions on T2 image. (Courtesy of Dr Georgina Child and SMRI)

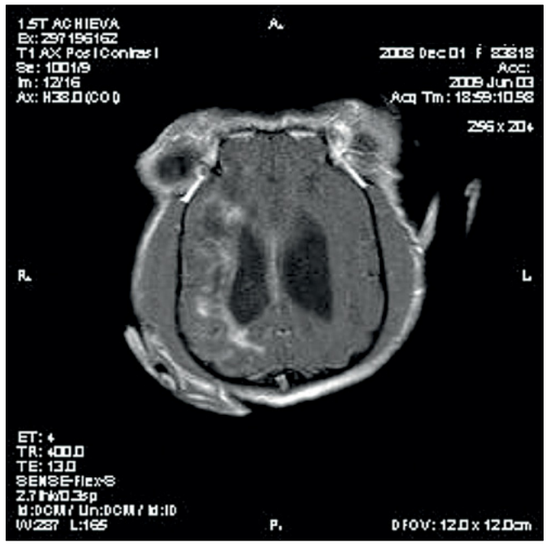

Figure 4: Cavitated lesions on T1. This is consistent with NME (Courtesy of Dr Georgina Child and SMRI)

Clinical Pathology
- Serology
- CSF collection
- Histopathology

Serology

Serology is vital in excluding infectious causes of inflammatory brain disease. Further testing should be performed as indicated in Australia.

- Viruses: are very uncommon in Australia.
- Fungus
  - Cryptococcosis (LCAT or identification – serum or CSF)
  - Aspergillosis
  - Exotic pathogens: Blastomycosis, histoplasmosis, coccidiomycosis
- Protozoa
  - Toxoplasma (Serum IgG and IgM levels, IgM of doubtful value in dogs. Rising titres may be of more diagnostic significance)
  - Neospora (Serum IgG + rising titres)
- Parasites
  - Aberrant parasitic migration usually young animals – roundworm and Angiostrongylus cantonensis (possibly vasorum but very rare in Australia).

In our practice, we recommend latex cryptococcal antigen testing should be performed on all patients prior to the use of corticosteroids. We will still use corticosteroids during the short delay whist waiting for the LCAT results due to the higher-prevalence of the non-infectious inflammatory CNS disease in comparison to CNS cryptococcosis. A recent paper also suggests clinical signs and the outcome may be improved if used in the initial treatment.

CSF analysis

CSF collection from patients with non-infectious inflammatory brain diseases generally show mild to moderate pleocytosis with a predominance of mononuclear cells and variable elevation in the concentration of protein in the CSF.

WBCC: variable between <10 cells to > 5,000 cells/µl 2 (Normal: <5uL)

Mostly small lymphocytes (60-90%)

Monocytes (10-20%) and large macrophages

Neutrophils usually <20%, but can be the predominate cell in some cases

Eosinophils occasional

Protein: variable: normal to >4g/L

Normal CSF protein is <0.3g/L cisternal tap, <0.5g/L lumbar tap (see FIGURE LUMBAR TAP)

CSF can be cultured for bacteria aerobically / anaerobically and fungi. Cultures are rarely positive. CSF can also be submitted for LCAT and cryptococcal assessment. ▶

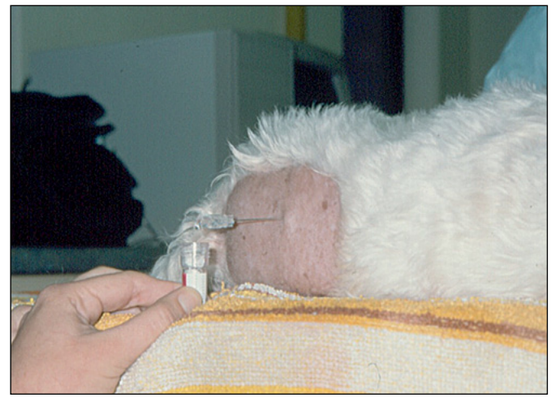

Figure 5: Lumbar CSF collection (Photo courtesy of Dr Georgina Child)

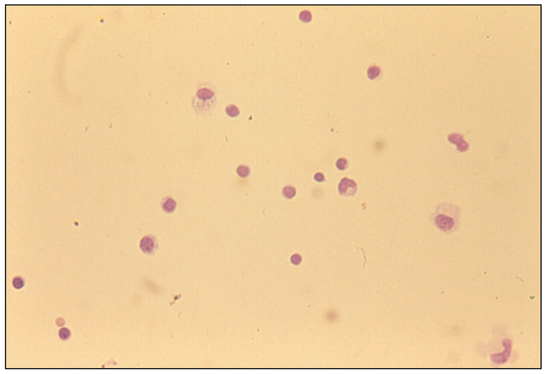

Figure 6: Cytospin preparation of inflammatory CSF – small and large mononuclear cells. (Courtesy of Dr Georgina Child)

CSF findings represent what is happening in the meninges and ependymal lining or tissue slow to the CSF pathways. CSF may be normal in 12-22% of dogs (Granger, 2010). When CSF appears inflammatory, and infectious diseases have been ruled out, it can be used as supportive evidence for non-infectious inflammatory brain disease. Remember that neoplasia, vascular, traumatic and degenerative disease processes may cause inflammatory changes in the CSF not just primary inflammatory or infectious disease.

CSF collection

With the advent of advanced imaging, CSF analysis is used less frequently in our practice as a diagnostic test. It is important, especially in cases of suspected meningitis or in animals with spinal cord signs, and to add another piece of 'the puzzle' in animals with intracranial neurologic signs. However, empiric treatment based on index of suspicion should be discussed with owners prior to recommendation of a CSF tap in animals with evidence of intracranial disease.

Collection of CSF has significant risks.

1. <u>Patients with increased intracranial pressure</u>. CSF collection in patients with increased intracranial pressure have significantly increased risk of brain herniation. Clinical signs (see box) may not be evident. In patients with severe brain disease, auto-regulatory responses may be altered, particularly under anaesthesia. CSF collection can thus be associated with changes in cerebral perfusion, thus deterioration in neurological status.

Increased Intracranial Pressure

+/- Cushing's Triad

1. Increased systolic blood pressure > 160mmHg
2. Significant bradycardia (rate dependant on the size of the dog).
3. Abnormal respiration

+/- Other signs

- obtundation, stupor, head pressing, panting, inability to settle

2. <u>Damage to neural tissues</u> – spinal cord (lumbar tap) and medulla oblongata (cisternal tap). This is more common in small dogs and dogs with craniocervical junction abnormalities such as Chiari-like malformation which is most common in small breeds of dogs, as is non-infectious inflammatory brain disease.

Histopathology

A definitive diagnosis of non-infectious inflammatory brain disease can only be made on histopathology which can be achieved by brain biopsy. Stereotactic CT guided biopsies are the gold standard for biopsies ante-mortem. At this stage, this skill is extremely specialized, and is only performed at a limited number of centres overseas. Microscopically GME is characterized by perivascular lymphocytic and /or macrophage-cuffing. These lesions may coalesce into macroscopic granulomas.

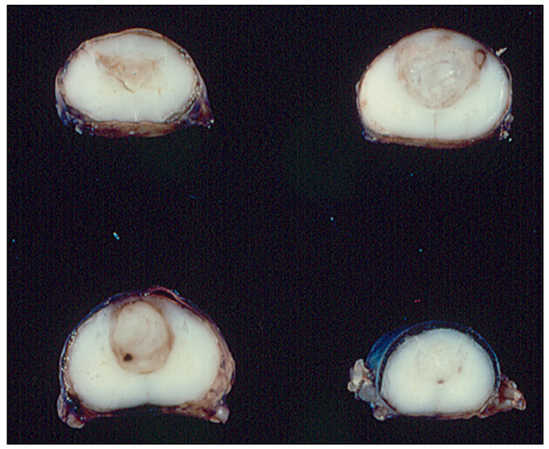

Figure 7: Cross sections of granumatous meningoencephalitis in the cervical spinal cord of a dog. (Photo courtesy of Dr Georgina Child)

GME (granulomatous meningoencephalitis), NLE (necrotizing leukoencephalitis) and NME (necrotizing meningoencephalitis)

GME, NME and NLE tend to have characteristic locations of lesions and therefore characteristic findings from advanced imaging. NME is commonly seen in Pugs, Chihuahuas, Pekingese, Lhasa Apsos, Shih Tzus, and Maltese. NLE is more commonly seen in Yorkshire terriers. MRI and histopathology of dogs with NME and NLE show extensive inflammation, predominantly cerebrocortical necrosis and cavitation of the brain parenchyma. They are differentiated by the presence or absence of meningeal lesions. MRI findings closely mirror the histopathologic lesions at necropsy. Specific regions tend to be more commonly affected in specific breeds. Prognosis for dogs with NME and NLE is very guarded.

4. Therapy

The cause of non-infectious inflammatory brain disease is not known. It is most likely an auto-immune response, as it mostly responds to immunosuppressive therapy. It is suspected to represent a T-cell-mediated delayed-type hypersensitivity reaction with organ specific autoimmune disease.

Prognosis:

Non-infectious inflammatory brain diseases can be acute and rapidly progressive diseases. They can be fatal despite treatment. They can recur despite being in remission for many months to years with no changes in therapy. The prognosis is thus difficult to predict.

In practice, non-infectious inflammatory brain diseases can often be readily treated. The severity of clinical signs on presentation or the degree of abnormalities on MRI or CSF analysis do not necessarily correlate with neurologic deficit or response to treatment or prognosis.

Treatment

Corticosteroids:

Initially, immunosuppressive doses of corticosteroids are vital in the treatment of cases. Improvement is mostly seen within 72 hours, however some patients may take longer to respond. In many cases, empiric treatment is indicated without a more definitive diagnosis. Treatment with steroids will change CSF analysis, however if used for <48 hours, it is less likely to change MRI findings, and may stabilize the patient before diagnostic tests can be performed

Recommended initial doses of Prednisolone:

- Small dogs 2-4mg/kg/day divided
- Larger dogs >40kg: 50mg/m^2/day divided. Maximum dose: 40mg/dog q12hrs

Clients are always warned about the significant side effects of corticosteroid use prior to treatment. Typically the doses are tapered after the first 2-4 weeks, slowly over the following 6 months or more; dose reduction depending on the clinical response of the patient. If remission is achieved most animals will need to be maintained on prednisolone (0.5-1mg/kg every other day or 2-3x a week) for the following 1-2 years. If the patient remains disease free, further dose reductions can be made again at this time. If the patient has recurrence of disease, or the side effects of prednsiolone are excessive, alternative treatments should be combined with corticosteroids. Larger dogs tend to not tolerate long-term therapy well. Early adjunctive treatments should be considered; most patients require low doses of corticosteroids.

Significant side effects of corticosteroids

- urinary accidents (polyuria/polydipsia)
- polyphagia and weight gain
- excessive panting and lethargy
- iatrogenic hyperadrenocorticism
- muscle wasting
- calcinosis cutis
- gastrointestinal ulceration (from anti-prostaglandin effects)
- pancreatitis (due to polyphagia and hypertriglyceridaemia)
- diabetes mellitus (from chronic hyperglycaemia)
- infections (especially urinary tract infection from reduced urine concentration)
- ligamentous and tendon injury
- pulmonary thromboembolism

Survival times: 2 – 1200 days. (Granger 2010)

Azothioprine

Azathioprine is used in non-infectious inflammatory brain disease as an immunosuppressive therapy. It acts to inhibit T cell function. It does not cross the blood brain barrier in normal dogs. Effects tend to be variable. Side effects include: idiosyncratic pancreatitis, gastrointestinal disturbance, liver failure and myelosuppression. Liver failure and myelosuppression tend to occur in patients treated at high doses for extended periods of time. Recommended dose: 2mg/kg PO SID for 7-10 days, then 1mg/kg PO/day = 7mg/kg PO/week. We recommend azathioprine should be handled with gloves, not be split or crushed due to the possibility of human toxicity including drug-related neoplasia or mortality with this treatment.

Recommended dosing:

Initial: 0.5-1.0mg/kg q48 hours

Maintenance: 2mg/kg q24 hours for first 5-7 days.

Survival times not reported.

Cytosine Arabinoside (Cytarabine, Ara-C)

Cytarabine is a parenteral anti-neoplastic therapy. It has commonly been used to treat CNS lymphoma, lymphoreticular neoplasms and myeloproliferative diseases in dogs. It prevents DNA synthesis. It readily crosses the blood-brain-barrier and has immunosuppressive its immunosuppressive effects. It has a short duration of action. Cytarabine has been described as a treatment for non-infectious inflammatory brain disease as a continuous IV continuous infusion 100mg/m^2 over 24 hours every 3 weeks (Smith, 2010). It has also been used at 50mg/m^2 by subcutaneous injection twice a day for 2 consecutive days with this cycle repeated every 3 weeks. This dose is lower than doses generally used as part of chemotherapeutic protocols for neoplasia. Side effects are uncommon, but include myelosuppression. Myelosuppressive effects are most pronounced with IV administration and are usually seen within the first 10-14 days, thus patients on chronic therapy should be assessed with a CBC 10-14 days after the first and second cycle of treatments, then every 3 months. Gastrointestinal side effects are uncommon.

Cytarabine is relatively inexpensive and patients can be treated as outpatients. In our experience, this treatment has been very effective. The frequency of administration can be reduced to every 4 weeks, after 6 months of successful treatment, and again the frequency of administration reduced every 6 months depending on the stability of the patient's neurological status. Chemotherapy handling practices should be adhered to by the clinician and the client. Cytarabine is best used in conjunction with prednisolone. The dose of prednisolone dose can be reduced incrementally after each 2 cycles of cytarabine if an animal's neurologic status is stable. Cytarabine can be used indefinitely.

Recommended dose:

A: 100mg/m^{2}IV over 24 hours in saline every 3 weeks

B: 50mg/m^2 SQ twice a day for 2 consecutive days with this cycle repeated every 3 weeks.

Survival times: 46-1025 days (Granger, 2010)

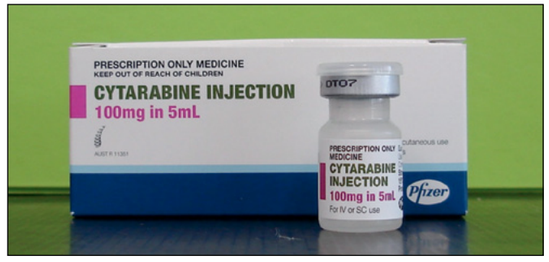

Figure 8: Cytarabine 100mg/5mL (Photo courtesy of Dr Georgina Child)

Cyclosporine has also been proposed as a treatment for non-infectious inflammatory CNS disease, as it is a recognized therapy for T-cell mediated immune disease by modulating interleukin 2 and α-interferon. Cyclosporine is lipophillc. It modulates T-cell mediated immune responses. The blood brain permeability of cyclosporine is increased in dogs with perivascular disease – thus achieves higher concentrations in the CNS with meningeal inflammation. Side effects are predominantly gastrointestinal – causing vomiting, diarrhoea and anorexia. Myelosuppression is rare. Gingival hyperplasia and hypertrichosis is occasionally observed.

Recommended dose:

Initial dose 6mg/kg BID with cranberry juice (to increase absorption) with a blood cyclosporine trough level target of 200-400ng/mL. The trough level should be tested 5-7 days after starting therapy and reevaluated in 1 month and every 4 months thereafter. Best absorption on an empty stomach.

Cyclosporine can be an expensive medication long term, particularly in larger dogs. It is not recommended in dogs with hepatic metabolism. ▶

Survival times: 6-1290 days sole therapy, with corticosteroids median: 930 days (Granger 2010).

Alternative treatments:

Leflunomide is an immunomodulatory drug used in humans primarily in the treatment of rheumatoid arthritis. It has been used in dogs in conjunction with corticosteroids, or as a sole maintenance therapy in dogs with unmanageable steroid side effects. It is not a first line therapy for non-infectious inflammatory disease in dogs.

Recommended dose: 2mg/kg once a day initially.

Procarbazine is an antineoplastic drug that is lipid soluble and readily crosses the blood brain barrier and used predominantly in human medicine to treat lymphoma. Side effects include myelosuppression, gastrointestinal signs and hepatic dysfunction.

Recommended dose: 25-50 mg/m^2/day.

Lomustine is an antineoplastic alkylating agent. It is highly lipid soluble therefore crosses the blood brain barrier. It can be used when there are concerns that the underlying cause is CNS lymphoma, or primary brain tumors. It is not recommended for dogs with idiopathic non-infectious inflammatory CNS disease i.e. GME, NME. Treatment can cause myelosuppression, gastrointestinal ulceration, and hepatotoxicity.

Recommended dose:

Brain tumours: 60mg/m2 every 5-8 weeks for 6 months.

Lymphoma: 60-90mg/m2 every 3 weeks for 3 treatments, then ever 4-6 weeks.

Additional therapies:

1. Animals with seizures should also be treated with an anticonvulsant in addition to immunosuppressive medications.
2. It is recommended that dogs placed onto corticosteroids (and phenobarbitone) be put onto a low fat, high fibre diet. This diet tends to increase satiety, and reduce polyphagia which commonly leads to pancreatitis, intestinal foreign bodies, and bloat.
3. Long-acting injections such as vaccinations, and pro-heart injections are non-recommended in dogs with immune mediated disease, unless absolutely necessary. There is no evidence to support vaccines, other injections or other causes of antigenic stimulation as a cause of non-infectious inflammatory CNS disease; however, relapses have been anecdotally reported after vaccination.

Intranasal vaccines, and vaccinations depending on serum titres and prevalence of disease are preferred.

Response to therapy

Response to treatment is usually gauged on clinical signs. Repeated CSF or MRI assessment can be performed, but is generally not required in the initial management of the disease. In our experience, the majority of dogs respond well to therapy with corticosteroids initially. We tend to add cytosine, and / or azathioprine and / or cyclosporine for steroid sparing effects – to enable possible earlier reduction in corticosteriod dose. Cytarabine can also be used as a first line treatment in animals with severe neurologic abnormalities and/or in those where clinical response is incomplete with high dose prednisolone during initial treatment. Therapy is usually for 6 months, with many dogs requiring long-term therapy, with low-doses of corticosteroids.

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