



The food re-challenge we were forced to have thanks to AQIS!

C&T No. 5181

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Whilst it is Gold standard to re-challenge any suspected food intolerance/reaction with re-exposure to the offending allergen, most first opinion cases will not have this happen to them on the basis that we have fixed the patient and no-one wants to re-trigger disease and suffering in a stable pet.

Equally, this means that many diet induced skin cases never get seen at specialist level in most countries and so the perception is that like *Ododectes*, *Trombicula* and contact reactions, food too is a less common cause of dermatological conditions.

Recent peer reviewed publications in the last 2 years have seen, however, some redressing of the imbalance and acknowledgement that general practitioners are often quite correct in finding diet as a main player in skin disease.

The whole drama with AQIS (Australian Quarantine Inspection Service) and updating paperwork for premium pet foods saw many of us, however, forced into a de-facto food challenge when the superb Hills z/d® became unavailable. I was lucky to have sufficient stock of canine z/d® to keep my cases supplied – including some mast cell tumour cases – but we hit a major wall of problems late July when Feline z/d® ran out.

In the space of 3-4 weeks my stable, drug-free cases 'fell apart' – some had been stable for 7 years – and immense suffering and distress ensued. Nothing would settle these cases: no other foods, no drugs – the cats ripped flesh from their faces in a manic attempt to ease the itch, they hid, became phobic and fearful – and in the case of the Devon Rexes – had wall to wall diarrhoea.

(Those pesky Devon Rexes should be born with z/d® and/or i/d® tattooed on their heads because so many of them need and do so well on these diets. We ran a rescue society for Devon Rexes some years ago and ended up rehoming them all with a free bag of Hills z/d® or i/d® to keep their variant attempts at ill health under effective control).

I accessed an emergency supply with Hills' help and within 5 days my cats had the agony that had been their life lifted and they returned to full health.

Equally, I hate to think of the loss of Royal Canin's Canine Renal Dry Diet – in my opinion no better renal diet or kidney disease management tool for dogs exists. In my hands, I had some cases, when caught early, where kidney levels of urea 20-30 and creatinine 3 times normal returned to base levels. On this diet, more advanced cases still decreased the values sufficient for the animals to have regression of PM4 ulceration/stomatitis/gastritis, emesis and distressing polyuria to live 18mths-3years and to advanced ages of 17 years.

I understand the biosecurity needs of an island nation, but when human foods riddled with disease flood our shores and only get picked up by *ad hoc* inspections but premium processed high quality pet foods that have never been incriminated regarding disease outbreaks in this country are held up to an intense inspection, then immense suffering ensues.

The restrictions on the importation of any the therapeutic formulae, especially of these premium high quality pet food diets, would impact heavily on animal welfare. Additionally, it forces Australian vets back on to antibiotics to symptomatically rather than causation treat these cases at a time when globally we need to be reducing our use of antibiotics, not increasing our usage!

We, as vets, could be forced by extreme restrictions to offer lower quality care that is available to animals anywhere else in the world. We risk becoming the derriere of the globe when it comes to disease management if therapeutic formulae with a spotless bill of health here get pulled from our treatment armoire.

I sincerely hope a balance can be struck between any perceived threat risks from tightly processed and quality controlled premium pets foods and the medical benefits such foods provide to pets, their owners and vets and to the reduced use of antibiotics such foods provide to Australia.

Use of mirtazapine in feline medicine

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Mirtazapine is used as an antidepressant in humans. However, it has recently attracted interest in veterinary medicine owing to several desirable effects, namely significant anti-nausea, anti-emetic and appetite stimulating properties.

Mirtazapine is a presynaptic α_2 -adrenergic receptor antagonist. The α_2 -adrenergic receptors normally act as a negative feedback mechanism that inhibits norepinephrine release. By blocking these receptors, there is a net increase in norepinephrine which contributes to the appetite stimulating effects of the medication. Mirtazapine also antagonises several serotonin (5HT) receptor subtypes such as 5HT₂ and 5HT₃ receptors. Antagonism of 5HT₃ receptors accounts for the anti-nausea and anti-emetic effects of this drug.

An initial uncontrolled clinical trial conducted by Cahill, 2006 and anecdotal reports have encouraged the continued clinical use of mirtazapine in vet medicine – it is especially popular with feline practitioners.

Cahill, 2006, recommended a dose of 1.88mg or 3.75mg (1/8 or 1/4 of a 15mg tablet) every 3 days. However, no pharmacological studies have been reported to date in support of these extrapolations. Anecdotal observations noted that in most ►



cases, the effect of the drug appears to have dissipated by the second day after administration, implying a shorter dosing interval may be more appropriate.

A recent study by Quimby *et al.* in the *Journal of Veterinary Pharmacology and Therapeutics*, 2010, found mirtazapine as an efficacious appetite stimulant in cats. This study demonstrated a significant increase in food consumption after administration of the drug. 88% of healthy cats that refused to eat their normal diet while in hospital subsequently ate when mirtazapine was administered.

The results of this study also suggest that the dosing interval in cats is significantly different from that previously postulated by Cahill. **The half-life of mirtazapine at the lowest effective dose (1.88mg) is approximately 9 hours i.e. shorter than that previously postulated. Based on this half-life, the drug could theoretically be administered daily in normal cats without substantial drug accumulation. This is supported by the almost negligible trough serum concentrations that were measured during the daily dosing study.** Although only a small number of cats were used, 24 hours trough concentrations were close to the limits of detection and no accumulation was seen after daily dosing for 6 days.

These findings will change the way feline practitioners use mirtazapine. Instead of giving $\frac{1}{8}$ (1.88mg) to $\frac{1}{4}$ (3.75mg) of a 15mg tablet orally every 3 days, mirtazapine can be given once a day without the 'serotonergic' effects i.e. increased vocalisation, pacing etc. Mirtazapine appears to work better than cyproheptadine in some cats to stimulate appetite. It also has added advantages i.e. anti-nausea and anti-emetic properties.

Recommendations from Bova Compounding

- Inappetent cats with chronic renal failure (CRF) have increased levels of gastrin (which is normally cleared by the kidneys). Gastrin stimulates the parietal cells to secrete more HCl so it may be worth adding H₂ receptor antagonists or proton pump inhibitors to treat subclinical gastric ulceration. Mirtazapine can be used concurrently with omeprazole or famotidine compounded in 1 capsule to be given once daily. This combination can also be used as an adjunctive treatment of GI effects (anorexia, nausea, vomiting) associated with cats with alimentary lymphosarcoma.
- Hypertension is an extremely common complication of cats with CRF. Between 29-69% of cats with CRF are hypertensive. Mirtazapine can be compounded in one capsule with amlodipine to be given once a day.
- 84% of cats with CRF have renal secondary hyperparathyroidism. There are 2 reasons why this occurs. The phosphate levels in blood increases due to reduced renal excretion. This leads to reduced plasma calcium levels which in turn causes increases in parathyroid hormone (PTH). The other cause of renal secondary hyperparathyroidism is due to the reduction in functional renal tissue causing reduction in the formation of calcitriol. Since calcitriol has a negative feedback function on PTH, reduction in calcitriol causes increases in PTH. Calcitriol can be compounded with mirtazapine (in liquid form) to be given once daily. If required, calcitriol, amlodipine and mirtazapine can be compounded in liquid to be given once a day. However, most veterinarians prefer to compound amlodipine, omeprazole/famotidine and mirtazapine in 1

capsule and have calcitriol liquid separate to enable doses of calcitriol to be titrated based on calcium and/or PTH levels.

References

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Coopex poisoning: a sad tale of official indifference

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Mrs C was advised that her house had termites.

Being an age pensioner, she asked her friends and relatives for the name of a competent but cheap pest exterminator to do the job.

Mrs C is also a kind hearted cat lover. Over the years she has taken in many unloved and sickly cats and provided them with a home. To this end she has had built a lavish network of outdoor tunnels and sun rooms, all connected to the house. The cats could enjoy an indoor/outdoor existence while still being confined. A few elderly ones could be trusted to go outside during the day by themselves.

The pest man came and put white powder into the door frames of the door that led outside. Mrs C was concerned because some white powder fell out onto the floor. She cleaned it up and called a second pest man for an opinion, as she didn't want her cats to be poisoned. The second pest man dug out more powder with a knife, left it on the ground and firmly told Mrs C that it was a substance called 'Termidor' that should not have been placed like that. Mrs C did what she could to clean the place up.

The next morning she found 'Skeeta' dead.

Racked with guilt and agonised with grief she brought Skeeta in for a post mortem.

He was a vigorously healthy young vaccinated cat, yet to reach his prime, with no obvious illness. He had been found with his jaws clenched on the wire of his cat house outside, and his posture suggested his having had a fit.

Mrs C felt she owed it to Skeeta, who she rescued from abusive owners, to continue.

She was worried he had eaten Termidor and been poisoned. However, where to start? Termidor did not seem that toxic. She insisted she had been told by the second pest man it was lethal. It is, in fact, fipronil = Frontline. ►