

Edited by:
Dennis Scott BVSc
MACVSc

EA Veterinary Marketing Ltd
54 Hobill Ave Wiri
PO Box 97-110 Manukau City
Manukau 2241

Ph 09-262-1388 Fax 09-262-1411
Freephone 0800 800-624
email info@ethicalagents.co.nz
website www.eavm.nz

Inside this issue:

| | |
|-------------------------|---|
| Vale Ron | 2 |
| Pyoderma and MPC | 3 |
| Why Not Just Use Bleach | 4 |
| Prudent Use Ear Therapy | 6 |
| Vetamox is Back! | 7 |

Special points of interest:

- * Goodbye to an old mate
- * Why cheap household bleach is not the best option
- * Vetamox is back - and improved!



Looking to the New Year

Another year has gone and a momentous one it has been, from the vagaries of a strange electoral system to the vagaries of the weather.

In most of the country it has been dismally wet

from a, normally dry, autumn through to a saturated spring.

Suddenly, a couple of weeks into summer, many are complaining of the heat and the possibility of drought!

However it spins out the team at EA hope all their clients have an enjoyable festive season and a prosperous year in 2018.

And we hope for a good year for EA as the company turns 50.



Vale Ron



Ron Bruce was one of the iconic reps for EA, serving for many of the formative years of the company. Therefore it was with sadness that we learnt, only recently, of his passing away a couple of months ago.

Ron was an old school rep from another era and he covered the whole South Island in his own inimitable way.

These were the days when there were fewer reps on the road, practices were more isolated and veterinarians were not as time poor as they are today. Hence it was nothing for Ron to have calls lasting half the morning with a good old chinwag about all sorts of things. While that would not occur today it did mean that Ron had a great rapport with his clients.

Ron himself was quite a character, being Scottish born and serving many years in the merchant navy before immigrating to New Zealand in 1956 when unemployment was rife in his homeland.

In the early part of the century Ronnie sadly lost his soulmate, his wee wife Meg who had come out with him from Scotland.

A few years later he remarried, having met Gay, a good Southland lass, and they were happy together.

As well as his many anecdotes from the time he had at sea Ronnie had a large repertoire of jokes that he loved to share, not only with his clients but in sessions with staff at company functions.

He nevertheless took his role very seriously and would carry huge wads of papers into his calls to detail to vets, interspersed with the many jokes, of course.

In 1994, with a nationwide launch of Calol the company had organised talks to veterinary practices throughout the North Island but Ronnie refused that offer for the South. "It is the reps' job to detail to the vets," he asserted and, instead, organised, in concert with the various practices, an impressive array of presentations to be made to the farmers instead. Calol

really took off in the Deep South!

He had his own little oddities, he was not called Mr Bean by company staff for no reason, "I'll give you Mr Bloody Bean", he would sputter!

In two decades of driving in and out of Waimate he had never noticed the giant white horse monument on the hillside above the town and, upon hearing this a client jokingly suggested, "I suppose he hasn't seen the clock in Cromwell either." "What clock?" was Ron's ingenuous reply.

From having his nose almost ripped off by a little dog in a waiting room to seeing him in a frigid motel room in Oamaru with not only the heater full bore, but all elements on the stove and the oven itself, with door fully open, on high the stories about our Mr Bean have passed into legend.

2018 is the year that EA will be celebrating 50 years in existence. The intention was to have had Ronnie invited along, as part of the celebrations. Unfortunately this will not be happening but we know he will be there in spirit.

We may not be talking to you in person Ronnie but, rest assured our wee mate, we will be talking about you. Nicely of course.

McIntyre Tartan - A Ronnie Joke

This Kiwi tourist goes into a kilt shop in Edinburgh and asks for a kilt in a McIntyre tartan.

The assistant goes out back and finds they have none left.

He tells the boss his problem and the boss replies, "give him a Dun-

lop tartan, that Kiwi will never know the difference."

So the assistant brings out the Dunlop tartan kilt but the Kiwi is on to it. "Hey, that's not a McIntyre tartan!"

"No sir," replied the assistant, "but

this is a Dunlop tartan and they have been McIntyres for years!"



Pyoderma and MPC

A recent webinar on dermatology threw up the concept of using fluoroquinolones above MPC (mutant prevention concentration) for pyoderma in dogs. While there is not a wealth of literature on the subject the concept itself is not new.

This use has been registered for marbofloxacin in cattle diseases (pneumonia and gram negative mastitis) but any such use in small animals is 'off label.' Marbofloxacin has a registered dose of 2 mg/kg and enrofloxacin 5 mg/kg. The recommended dosing for enrofloxacin to be above MPC would be around 20 mg/kg and marbofloxacin 10 mg/kg. Clearly these doses are outside the registration conditions so would be off label use.

Therefore it is important to consider the aim of such therapy and possible risks involved.

The aim of dosing above MPC is to reduce risk of resistance. This is a valid way of utilizing concentration dependent antimicrobials such as fluoroquinolones and aminoglycosides, however there are a couple of caveats. The obvious one is toxicity and aminoglycosides have a much narrower therapeutic window than fluoroquinolones so are far less suited to the technique.



The other is that, while dosing above MPC knocks out first stage mutants so reducing risk of resistance, it is a short term measure as doing it for a long period of time would have the effect of putting more antimicrobials into the environment thus negating the benefits of reduced resistance.

The only fluoroquinolone registered for dosing above MPC in New Zealand is marbofloxacin and that is, as stated above, for cattle. This use is also as a single shot regime and that is where it is better suited. The single shot, at a very high dose, does get levels well above MPC for the target organisms and then, being discontinued, does not result in continued high levels in the environment. It is known as the SISAAB concept (single injection short acting antibiotic) and it really is the smart bomb of antimicrobial therapy.

An additional advantage of the short term therapy is reduced risk of toxicity. Marbofloxacin in safety trials for registration, for example, has low toxicity when dosed at 6 or 10 mg/kg over a four week period so when given as a one off the risk is virtually zero.

Will the technique work? Probably. Is there strong compelling evidence? Not as yet.

However it is tempting to envisage the use of a single, high dose, shot of fluoroquinolone, well above MPC, and then follow up with topical treatment with a strong biocide such as hypochlorous acid.

If effective it would mean that, even though the fluoroquinolone would be a 'red light' antimicrobial, this would be designated prudent use.

One of the tenets of antimicrobial prudent use is that we need to develop smarter ways of using the tools that we have got at the moment. Is this one possible way?

"we need to develop smarter ways of using the tools that we have got"

Ode to the Bureaucrat by Miltspeare

ONE civil servant with nothing to do

Got an assistant and then there were 2

TWO civil servants kept the job alive

'Til more were appointed and then there were 5

FIVE civil servants slaving with the pen

Formed a department and then there were 10

TEN civil servants you'd think would be plenty

But being a department, extended to 20

TWENTY civil servants with a head so haughty

Doubled the number and then there were 40

FORTY civil servants with reasons good & weighty

Needed assistants and then there were 80

So the game went on and on – it's really rather fun

To make a hundred joblets where formerly there was one

Why Not Just Use Bleach?

It has become fashionable, especially in an age of antibiotic awareness and prudent use guidelines, for academics to recommend chlorine technology for treating pyodermas in dogs. Ordinary household bleach is cheap and does have some antibacterial properties but, in the end, there are better options.

One such option is hypochlorous acid, used widely in human medicine for diabetic ulcers, a condition as difficult to treat as canine pyoderma.

The Basic Chemistry

Chlorine gas hydrolyses in water almost completely to form hypochlorous acid (HOCl):



The hypochlorous acid dissociates into hydrogen ions (H^+) and hypochlorite ions in the reversible reaction: $\text{HOCl} : \text{H}^+ + \text{OCl}^-$

While it is also 'chlorine technology', there are differences between it and bleach itself.

Sodium hypochlorite (NaOCl) is commonly used in household bleach often at concentrations of about 3 – 8%.

Because it readily breaks down to produce sodium chloride (NaCl) and sodium chlorate (NaClO_3) most bleach solutions also contain low concentrations of sodium hydroxide which slows down this decomposition.

This deliberate buffering is what makes all the difference; it has a huge effect on the amount of hypochlorous acid as opposed to hypochlorite ion in the

solution. According to the MSDS Janola has a pH of above 11.5 so that it is almost exclusively hypochlorite ion.

Proponents of bleach claim that when dissolved in water sodium hypochlorite produces hypochlorous acid, however that is not strictly true. Higher pH results in a preponderance of hypochlorite ions with a lower pH favouring hypochlorous acid.

At very low pH, in an open container, chlorine gas is likely to bubble off and escape the solution. With a pH above 9 the solution is virtually 100% hypochlorite, with pH of 5-5.5 favouring almost total hypochlorous acid.

At a neutral pH, or just below, the solution will be predominantly hypochlorous acid with a small amount of hypochlorite. This is the trade-off for having a more stable form of hypochlorous acid.

Why is this basic chemistry important? There are many references in the literature attesting to the fact that hypochlorous acid in itself is a much more effective biocide than the hypochlorite ion provided in the high pH milieu of household bleach.

The Effect of pH

Hypochlorous acid is a weak acid with a pKa of approximately 7.5 at 25 °C. Hypochlorous acid, the prime disinfecting agent, is therefore dominant at a pH below 7.5 and is a more effective disinfectant than hypochlorite ion, which dominates above pH 7.5.

The rates of the decomposition reactions of chlorine increase as the solution becomes more alkaline, and these reactions can theoretically produce chlorite and chlorate (ClO_3^-); they occur during the electrolysis of chloride (Cl^-) solutions when the anodic and cathodic compartments are not separated, in which case the chlorine formed at the anode can react with the alkali formed at the

cathode. (Chemistry Of Disinfectants And Disinfectant By-Products www.who.int/ipcs/publications/ehc/216_disinfectants_part_2.pdf)

"So why not just use bleach? It simply does not work as well; that's the bottom line."

(Note that Electromicyn is produced using ion exchange membranes so that the chlorine formed at the anode cannot react with the alkali formed at the cathode).

Biocidal Efficacy

Hypochlorous acid and hypochlorite ions are strong oxidants, but their toxicity to bacteria and fungi is not strictly related to their ability to oxidize. For example, the acid, which has an ORP less than twice that of the ion (6), is up to 80 times more toxic to microbes than the ion. (Robbs, *et al.* 1995. Oxidation-reduction potential of chlorine solutions and their toxicity to *Erwinia carotovora* subsp. *carotovora* and *Geotrichum candidum*. Plant Dis. 79:158-162.)

Anti-inflammatory Effect

There is also work in human medicine showing that hypochlorous acid has an anti-inflammatory effect. (Fukuyama *et al.* Hypochlorous acid is antipruritic and anti-inflammatory in a mouse model of atopic dermatitis, Clin Exp Allergy. 2017;1–11).

The neutrophil enzyme myeloperoxidase generates hypochlorous acid (HOCl) at sites of inflammation. Glutathione peroxidase is very quickly inactivated by low concentration of HOCl. Superoxide dismutase should not be easily inactivated by HOCl at sites of inflammation, which may contribute to its effectiveness as an anti-inflammatory agent and in min-

(Continued on page 5)



Why Not Just Use Bleach?

(Continued from page 4)

imizing reperfusion injury. (Aruoma and Halliwell, Action of hypochlorous acid on the antioxidant protective enzymes superoxide dismutase, catalase and glutathione peroxidase Biochemical Journal Dec 15, 1987.)

HOCl has shown to be a potent antimicrobial, a fast acting antipruritic, exhibits anti-inflammatory properties, increases oxygenation at wound

"From an animal perspective it could be envisaged as an Elizabethan collar in a bottle!"

sites and breaks down biofilm. (Gold *et al*, Hypochlorous gel technology – Its impact on post procedure treatment and scar prevention, J Cosmetic Dermatology 2017, 1-6)

This all makes HOCl the ideal post surgical wound spray, the anti-itch effect being particularly important. From an animal perspective it could be envisaged as an Elizabethan collar in a bottle!

Therefore, in conclusion, Electromycin, at a pH of around 6.5 is a much more effective antiseptic than household bleach at a pH of 11.5. It is also more attuned to the pH of the skin of the dog. And has anti-inflammatory

and antipruritic properties as well as having a massively stronger biocidal effect.

So why not just use bleach?

It simply does not work as well; that's the bottom line.



What Day Is It?

Over breakfast one morning a woman said to her husband, "I bet you don't know what day this is." "Of course I do," he answered indignantly, going out of the door on his way to the office.

At 10 am the doorbell rang and, when the woman opened the door, she was handed a box containing two dozen long stemmed roses. At 1 pm a foil wrapped, one kilogram

box of her favourite chocolates arrived. Later a boutique delivered a designer dress.

The woman could not wait for her husband to come home.

"First the flowers, then the chocolates and then the dress," she exclaimed, "I've never spent a more wonderful April Fools' day in my whole life!"



Improving The Game

Nagy was once a keen golfer but was going through a bad spell. Therefore he went to a professional for advice.

"Your trouble is all in your mind," said the pro. "I want you to play a full round of 18 holes with only an imaginary ball. Keep a careful score for each hole and bring me your card."

Nagy followed the advice and presented his card to the professional

"Tomorrow," the pro said, "I want

you to play another 18 holes, this time with a ball but with an imaginary club. Keep a score and bring me your card."

When he submitted the second card the pro examined it.

"Congratulations Nagy," he announced, "these two cards show that you have the best two rounds of your golfing career."

"What should I do next?" said Nagy.

"Quit while you are at your peak."



Prudent Use Ear Treatment

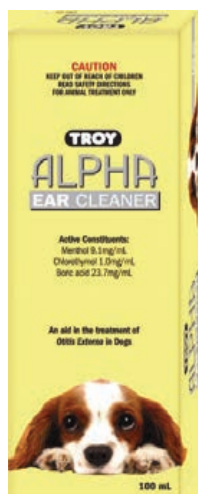
Despite ACVM insisting anything applied to the ear canal must be a registered veterinary medicine most of the veterinary world agrees that the external ear canal is part of the tegument and thus is treated in a topical fashion.

Thus prudent use in ear infections is not a difficult concept and really is a return to basic concepts of topical therapy. The difference between antiseptics, which is what topical therapy really is, and disinfection is a matter of degree, with the latter being harsher on living tissue and so confined to use on inanimate objects.

The basic principle of disinfection is clean then disinfect and that also applies to topical antiseptic, or antimicrobial, therapy. One would never just apply creams to a dirty wound without cleaning it first. The same should apply to the external ear canal, cleaning giving the antimicrobial product the opportunity to work.

Some years ago in vitro work by an Australian laboratory and presented at the ANZCVS science week in 2008 found that most common ear cleansers were no more efficient than plain water and many were actually inferior because they actually adsorbed into a ceruminous mass, just making it larger. The main effective product was the old Leo ear cleaner that was withdrawn from the market some time later as it was deemed to require registration. EA has managed to have the same active ingredients registered and it is marketed under the name of Alpha Ear Cleaner.

Not only is it a top of the line cleaner for clinical cases, it is also used to treat susceptible dogs once a week as a preventative measure. A highly relevant point when one




is talking prudent antimicrobial use.

FOR ANIMAL TREATMENT

TROY
ALPHA
EAR CLEANER

Active Constituents:
Menthol 0.5 mg/mL
Chewyphenol 1.2 mg/mL
Sore acid 2.2.7 mg/mL

An aid in the treatment of
Otitis Externa in Dogs



100 mL

In clinical cases, after the ear canal has been cleaned, just as with disinfecting a table, the antimicrobial is applied. Choice of antimicrobial takes in target organisms and how acute the infection is. As it is a 'topical' application, and as long as the cleansing process has taken place, pharmacokinetics is not an issue.

As an aside, it is now considered by most authors of prudent use guidelines that parenteral therapy is almost never indicated in treatment of external ear canal infections.

Acute infections are generally caused by *Staphylococcus intermedius* but gram negative organisms such as *Pseudomonas aeruginosa*, along with fungi, proliferate in the conditions provided by the general milieu. Therefore antimicrobials with s gram negative cover are required, especially after the acute phase.

Neomycin is an aminoglycoside with both gram positive and gram negative activity so is an ideal antimicrobial for first choice topical treatment. This is the core antibiotic, along with antifungal and corticosteroid therapy, in the Vetoquinol product Oridermyl.



Oridermyl is available as a once per day gel formulation that also contains a miticide for treating one of the instigating conditions.

Another 'first of the shelf' product, if drops are preferred, is Dermotic that contains, as its mainstay antibiotic, polymyxin B.

"parenteral therapy is almost never indicated in treatment of external ear canal infections."



Dermotic is manufactured by Troy Laboratories.

For persistent infections, unresponsive to the first choice therapies then the big gun, Aurizon can be wheeled out. Another Vetoquinol product Aurizon has the fluoroquinolone, Marbofloxacin, as its antibiotic component and is the ideal fall back for recalcitrant infections.



Vetamox is Back!

The team at EA were proud of the fact that the very first generic form of amoxicillin/clavulanic acid tablets registered for animal use in New Zealand was Vetamox. Originally registered as Synermox for human use the tablets were an ideal size for larger dogs especially and were able to come to the market at a very economical price.

A little while back the manufacturer, Ranbaxy, made some alterations, for the better, to the product. However this meant that, for a period of time, Vetamox was unable to be supplied and so became out of stock, something every agency company dreads.

The good news is that production is now back in full bore and Vetamox is now back on the shelves at EA, albeit in slightly different form.

So what are the changes? First of all the tablets are scored deeper, making division much simpler. The

other major change is the fact that they are blister wrapped instead of being loose.

This means that any risk of being deliquescent is neutralized, thus ensuring better stability and also dispensing is so much easier.

The old Vetamox, being loose tablets in a bottle, meant dispensing to clients required the use of other containers or packets. The new, improved Vetamox comes in blister wrapped cards inside a small carton instead of a large bottle and dispensing is simply a matter of cutting the card with the required amount of tablets.



So what has not changed? Two vitally important facets have not changed. First of all the size of the tablets remains the same, 625 mg. Secondly, and crucially to many, despite the improvements and the blister wrapping the highly competitive price of the original Vetamox remains much the same. A real win/win situation.

Inside Story Headline

A pair of honeymooners check into the Watergate Hotel in Washington DC. That night, as the husband was about to turn off the light, his bride asked, "Do you think this room is bugged?" "That was a long long time ago sweetheart," he reassured her.

"But what if there is a microphone somewhere? I would be so embarrassed."

So the groom searched under the tables and behind pictures. Sure enough there was a funny looking gismo on the floor. He took out the screws, got rid of the hardware and climbed into bed.

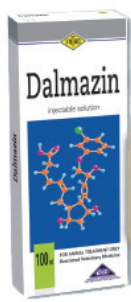
The next morning the newlyweds were awakened by the hotel clerk

who asked if they had slept well.

"We did," replied the groom, "why do you ask?"

"It's rather unusual," the clerk answered. "Last night the couple in the room below yours had the chandelier fall on them."





Bilingual

Walking down the street a dog saw a sign in an office window, "Help wanted, must be able to type 7- words a minute. Must be computer literate. Must be bilingual. An equal opportunity employer."

The dog applied for the position but was quickly rebuffed.

"I can't hire a dog for this job," the office manager said but, when the dog pointed to the line that read "An equal opportunity employer," the office manager sighed and asked, "Can you type?"

Silently the dog walked over to a typewriter and flawlessly banged out a letter.

"Can you operate a computer?" the manager inquired.

The dog then sat down at a terminal, wrote a program and ran it perfectly.

"Look, I still can't hire a dog for this position," said the exasperated office manager.

"You have skills but I need someone who is bilingual. It says so right in the ad."

The dog looked up at the manager and said, "Meow."

