EA NEWS

ETHICAL AGENTS
VETERINARY MARKETING

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A Special points of interest:

- Focus on infection control
- Antibiotic and non antibiotic means
- New product launch - Marbocyl P
- D mannose - a non antibiotic approach to urinary infection

Infection Control

When we look at infection control we are launching into a very broad subject. It covers antisepsis, disinfection and also chemotherapeutics.

Antiseptics and disinfectants are broad spectrum chemicals and chemotherapeutic agents are more specifically targeted antimicrobials.

Disinfectants kill most things but are too strong for living tissues, antiseptics are milder in action. They can be used topically, but not ingested (e.g. alcohol, iodine), whereas chemotherapeutic agents can be ingested.

Antimicrobial resistance covers not only the chemotherapeutic agents but also antiseptics and disinfectants. Already there are world-wide concerns about chlorhexidine resistance.

The physical mode of action of Electromicyn means minimal risk of resistance development and SteriGENE also has a very low risk due to the combination of ingredients.

Antimicrobial resistance is becoming increasingly topical in chemotherapeutic agents but prudent use does reduce the risk.

Ethical Agents has actives in all shades of the traffic light system and is ideally placed to be experts in the field and advise accordingly.

In addition, by having the gold standard antiseptic (Electromicyn) and disinfectants (SteriGENE and Swift) company personnel are infection control experts, making the company your one stop infection control shop.

Hence a newsletter entirely devoted to infection control.

The Traffic Light

The traffic light system propounded by the Antimicrobial Resistance Leadership Group (AMRLG) is one of the singularly most successful projects put forward.

Not only has it been rapidly adapted by clinicians around the country, many marketers from pharmaceutical companies have rushed to the fore in advertising their particular antimicrobials as green or first line.

However there is another way to look at the system. When we stop at a traffic light what colour is at the top? It is the red light.

One approach could be to say that the antimicrobials listed as red on the traffic light system are the top shelf products.

"the price may not necessarily be in dollar terms *per se* but there is a social cost."

The term 'top shelf' has a connotation of quality, with the analogy being that of a typical bar, where the expensive drinks are kept on the top shelf.

The more readily used simple beers are close at hand, spirits and wines at the next level and, on the top shelf, are the single malts and the fine liqueurs.

Another instance of top shelf products is at a fairground shooting gallery; the best prizes are on the very top shelf. The reason for this is because they are not reached for very often.

It is the same in the bar; it is the special request that has the barman reaching for the top shelf.

Similarly with antimicrobials, the red light products are top shelf because they are specialized wares that are less often used.

The other way to look at the analogy is the price paid. Clearly, with the bar and the fairground, the more expensive items are those on the top shelf. With antimicrobials the price may not necessarily be in dollar terms *per se* but there is a social cost.

We may reach for the top shelf product because it has special indications, but we do not go there as often because of the cost, and that

cost is the risk of developing resistance in critically important antimicrobials.

Putting it all into perspective, whilst top shelf alcoholic products have a perception of being better but, if all you are after is to get tipsy, then those on the bottom shelf are generally as effective; it is just that the cost is not the same.

Similarly with red light antimicrobials, they are red light or 'on the top shelf' because they are used less often.

The idea that somehow they are stronger than other antimicrobials is totally erroneous.

They are specialized drugs for special indications and are on the top shelf so they are kept for those situations, not used out of hand.

A bit like the fine liqueur or the single malt just being enjoyed on special occasions.

The Replacement

Hillary phoned the president's office shortly after midnight.

"I need to talk to the president, it's an emergency!" exclaimed Hillary

After some cajoling, the president's assistant agreed to wake him up.

"So, what is it that's so important that it can't wait until morning?" grumbled Trump.

"A Supreme Court Judge just died, and I want to take his place." begged Hillary.

"Well, it's OK with me if it's OK with the mortician", said Trump.

A Splash Of Colour

Antisepsis unfortunately can be all about perception. Microbes are far too small to see with the naked eye and thus it is difficult for the mind to appreciate what is actually occurring. Therefore it is not surprising to find some of the most widely used antiseptics are brightly coloured compounds such as iodine and chlorhexidine, giving an appearance of total coverage and an illusion of efficacy.

There has even been an attempt to colour hypochlorous acid and market it as such for spraying on wounds. From a marketing perspective this seems an ideal move, from an efficacy perspective it is absolutely the wrong thing to do as stability is compromised but, hey. It's coloured, it must be working!

"It will also be more efficient for the clinic in time terms but less efficient in monetary terms."

We even see this effect with the high quality disinfectant SteriGENE. It comes in two forms, uncoloured and with a green colour. The green one also has a fragrance, both fragrance and colour being there for aesthetic reasons; one form is no more or less effective than the other. However the green one is by far the more popular in the marketplace, the clear mainly being utilised in foggers or food contact areas. Part of the colour attraction being that clinics mix according to colour rather than accurately try to measure. This will undoubtedly mean higher concentrations so more product used, all good for EA, the vendors. It will also be more efficient for the clinic in time terms but less efficient in monetary terms.

As far as antiseptics are concerned the brighter the colour the more it is accepted, but this is deceptive thinking. The new gold standard for on animal antisepsis, Electromicyn is clear, as adding colouring agents would affect product stability, hence efficacy. This does not prevent it being better than other commonly used antiseptic chemicals; it is a mind-set that needs overcoming. It not only gives a better antimicrobial kill than chlorhexidine and iodine but it is also far less cytotoxic. Whether on wounds or as a pre-surgical scrub Electromicyn should be the go to product.

We have had the question, "what if we use Electromicyn but also spray with iodine to show where we have been?" The answer is of course that, that is fine, as long as the Electromicyn has had 30 seconds to do its job because, unlike the others, that is all it needs.

Reference: Rani S et al 2014. The in vitro antimicrobial activity of wound and skin cleansers at non-toxic concentrations. Advances in Skin and Wound Care 27 (2) 66-69

Glasgow Dentist

A Glasgow man phones a dentist to enquire about the cost for a tooth extraction

"85 pounds for an extraction, sir" the dentist replied.

"85 quid! Huv ye no got anythin' cheaper?"

"That's the normal charge," said the dentist.

"Whit aboot if ye didnae use any anaesthetic?"

"That's unusual, sir, but I could do it and would knock 15 pounds off."

"Whit aboot if ye used one of your dentist trainees and still without any anaesthetic?"

"I can't guarantee their professionalism and it'll be painful.

But the price could drop by 20 pounds."

"How aboot if ye make it a trainin' session, ave yer student do the extraction with the other students watchin' and learnin'?"

"Well it' would be good for the students", mulled the dentist. "I'll charge you 5 pounds but it will be traumatic."

"Och, now yer talkin' laddie! It's a deal," said the Scotsman.

"Can ye confirm an appointment for the wife next Tuesday then?"

Marbocyl P is here!

Marbofloxacin has been available in the large animal market for many years but, due to contractual arrangements overseas, not available to small animal clinicians. This has now changed with the registration of Marbocyl P.

Clearly marbofloxacin is a fluoroquinolone so is subject to the regulatory constraints of other fluoroquinolones but it has features and benefits that make it extremely useful in certain specified indications.

These features and benefits not only include spectrum of activity but also the basic kinetics; the best army in the world cannot fight unless it can get to the battlefield.

Like all fluoroquinolones marbofloxacin concentrates intracellularly so that tissue levels are higher than actual blood levels.

There are few barriers and, in certain situations, penetration is superior to other antimicrobial classes. A case in point would be lung infection where the site of infection itself is generally inside the alveoli. That means that the drug has several barriers to cross, from blood across the extracellular fluid, and across another membrane into the alveolus.

Marbofloxacin is amphoteric and also both lipophilic and hydrophilic, thus can travel through aqueous media and across lipid membranes.

Metabolism and excretion are also important. Marbofloxacin is active in itself, not a prodrug like enrofloxacin so does not need conversion in the liver, meaning onset of activity is more rapid.

Blood levels are also maintained above MIC for a full 24 hours and in situations such as urinary infections.

The bottom line is that, when a fluoroquinolone is indicated it is better to reach for the best, and that is Marbocyl P.

Marbocyl P is presented as chewable tablets of 20 mg for cats and dogs and 80 mg for larger dogs.

Indications in dogs are: Pyoderma (resistant to other antimicrobials), deep pyoderma, otitis externa (non responsive to topical treatment), urinary tract disease, chronic metritis, respiratory disease and osteomyelitis.

"when a fluoroquinolone is indicated it is better to reach for the best,"

In cats: Cutaneous infections, respiratory disease, urinary tract disease, and bone and joint infections.

A Very Big Number

The next time you hear a politician use the word 'billion' in a casual manner, think about whether you want the 'politicians' spending your tax money.

A billion is a difficult number to comprehend, but one advertising agency did a good job of putting that figure into some perspective in one of its releases.

A. A billion seconds ago it was 1959

B. A billion minutes ago Jesus was alive.

C. A billion hours ago our ancestors were living in the Stone Age.

D. A billion days ago no-one walked on the earth on two feet.

E. A billion dollars ago was only 13 hours and 12 minutes, at the rate the government is spending it.

D Mannose and The Urinary Tract

In a study of more than 300 women with a history of recurrent UTIs, researchers treated the women with either two grams of D-mannose, 50 milligrams of an antibiotic, or no treatment, daily for six months. D-Mannose is a naturally occurring sugar that's closely related to glucose.

Only 15 percent of those taking the D-mannose had a recurrent UTI compared to 20 percent for the antibiotic group (both of which were significantly lower than the no-treatment group). However, the incidence of side effects was significantly lower in the D-mannose group than the antibiotics group.

D-Mannose works in a similar way that lysine works in reducing the effects of herpes virus infections. Viruses rely on arginine for energy but supplementing lysine means lysine occupies the arginine receptors meaning that the virus is starved of energy and cannot replicate.

With UTIs, although similar, the effect of D-Mannose is slightly different.

More than 90 percent of UTIs are caused by Escherichia coli (E. coli), which is normally found in the intestinal tract.

The cell walls of each E. coli are covered with tiny finger like projections called fimbria allowing them to "stick" to the inner walls of the bladder and even work their way upward to the ureter and kidneys.

Because they cling to the urinary organs, they can't simply be washed out by urination. These little finger like projections are made of an amino acid-sugar complex, a glycoprotein called lectin, which makes them sticky.

Lectin on the bacteria's fimbria binds to mannose, which is produced by the cells and covers the internal lining of the urinary organs. This mannose allows the bacteria to adhere—like Velcro. But, when taken, D-mannose sticks to the E. coli so it can be effectively "rinsed" out by the urination.

Unfortunately for the E. coli, D-mannose 'sticks' to E. coli lectins even better than E. coli lectins 'stick' to mammalian cells. With a large quantity of D-mannose ingested, most spills into the urine, literally 'coating' any E.coli present so they can no longer 'stick' to the inside walls of the bladder and urinary tract. The E. coli are literally rinsed away with normal urination!

In the majority of cases, UTIs can be effectively treated without antibiotics by using D-mannose. It's important to note that D-mannose only works for UTIs caused by E. coli, this represents 90 percent (or more) of infections.

D-mannose is very safe, even for long-term use, although with single episodes of bladder or urinary tract infection treatment is only for a few days at most. Although D-mannose is a simple sugar, very little of it is metabolized. It doesn't interfere with blood sugar regulation and it creates no disruption or imbalance in normal body microflora.

"There is the home remedy of drinking cranberry juice for UTIs,"

There is the home remedy of drinking cranberry juice for UTIs, and this is because the active ingredient in cranberry juice is D-mannose.

Pure D-mannose is about 10-50 times stronger than cranberry, non-toxic and completely safe, with no adverse effects. Unlike the large amounts of fructose you'd get by consuming a lot of cranberry juice, D-mannose does not convert to glycogen or get stored in the liver. Only very small amounts of D-mannose are metabolized, so it doesn't interfere with blood sugar regulation or produce metabolic stresses.

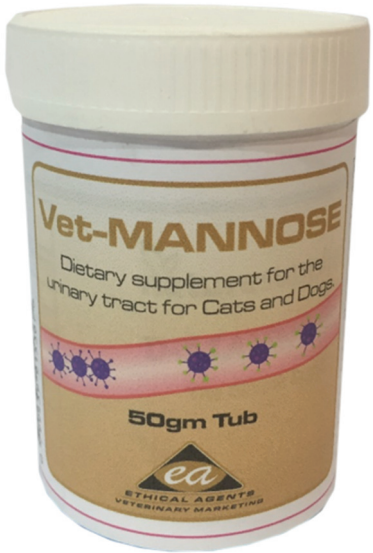
The Report

The State police had a problem. The drug busts over the years had filled their stores with marijuana. It was decided the only solution was to burn all the marijuana in order to free up some space.

The eventful day came and a huge mountain of marijuana was torched. The fire raged and the smoke of the weed rose in a huge cloud in the sky.

At that moment a flock of terns flew through the cloud of smoke. A group of environmentalist were sent out to check on the welfare of the terns. They followed the flock until it landed.

Sneaking up on them the environmentalists were able to observe their behavior. They later issued a report which read, “not a tern was left unstoned.”



Mycoplasma bovis Control

On the way to the Blenheim conference an EA personage and a veterinary decision maker shared a cab when the latter received a call on his phone announcing, confidentially, that Mycoplasma bovis had just struck in the South Island.

The conversation went along these lines: VDM, "Does anything kill it?"

EAP. "Marbofloxacin does."

VDM, "You will get rich."

EAP. "Don't think so."

Marbofloxacin certainly is effective and is registered in Europe for exactly that purpose. While there is a temptation to promote this to the powers that be, the reality of the situation is that it is probably too soon. The M bovis outbreak, while receiving a massive amount of media attention, is still in its early stages and the prime focus is on containment and eradication; treatment is probably not an option right now.

Like all mollicutes, M. bovis is inherently refractory to certain groups of antibiotics because it does not possess a cell wall; furthermore evidence is accumulating that strains of M. bovis are becoming resistant to antibiotics, including tetracycline, tilmicosin and spectinomycin, traditionally used for their control. (Nicholas and Ayling, Research in Veterinary Science, Volume 74, Issue 2, April 2003, Pages 105-112}

"the reality of the situation is that it is probably too soon."

Three fluoroquinolones tested (danofloxacin, enrofloxacin and marbofloxacin) were effective against strains of M bovis, and had a minimum mycoplasmacidal concentration (MMC5o) less than or equal to 1 µg/mI. Gentamicin was poorly effective, having an IIC50 of 8 µg/mI. Many strains of M bovis were resistant to tylosin, spectinomycin, lincomycin, tetracycline and oxytetracycline. (Thomas *et al* Antibiotic susceptibilities of recent isolates of Mycoplasma bovis in Belgium. The Veterinary Record, October 4, 2003).

If the disease does become endemic then marbofloxacin, despite being a red light molecule on the traffic light system, will probably be drug of choice in the lactating dairy cow.

(Continued on page 7)

Speeding Ticket

Nagy was speeding down the highway, feeling secure in a gaggle of cars all travelling the same speed.

However, as he passed a speed trap he got nailed by the speed detector and was pulled over.

The office handed him the ticket and was about to walk away when Nagy asked, "officer, I don't think it is fair.

There were plenty of other cars around me that were going just as fast, so why did I get the ticket?'

"Ever go fishing?" the policeman asked Nagy.

"ummm,,,,,,,yeah" a startled Nagy replied.

The officer grinned then added, "Ever catch all the fish?"

Mycoplasma bovis Control

(Continued from page 6)

Even so, with our extensive farming system, it is difficult to see the disease reaching pandemic proportions, instead hopefully being rather sporadic.

In the meantime containment is the big issue and that involves infection control or, more bluntly, disinfection. Various bodies have proposed disinfectant protocols although there is not a lot of science involved.

There does seem to be a dearth of information available but some reports mention efficacy with chlorhexidine and iodine based teat dips to control M bovis mastitis.

SteriGENE has proven efficacy against Mycoplasma gallisepticum so, while awaiting direct evidence, it can be reasonably assumed to be effective against M bovis, which is a lot more than can be said for most in the marketplace.

There is also agreement in the literature that true chlorine dioxide would be extremely effective. The

"true chlorine dioxide would be extremely effective."

Tristel product Swift, a stablemate of SteriGENE is proving a very economical source of true chlorine dioxide and is already popular in several regions for use in calf sheds. It would be ideal for M bovis sanitation.

In summary, while the emphasis on M bovis control is focused on containment, SteriGENE and Swift would be ideal. If the problem becomes endemic and treatment is an option Marbocyl would fit the bill admirably.

The team at EA are infection control experts and have certainly got this.

Google's pizza.

Hello! Gordon's pizza?

No sir it's Google's pizza.

So it's a wrong number? Sorry.

No sir, Google bought it.

OK. Take my order please.

Well sir, you want the usual?

The usual? You know me?

According to our caller ID data sheet, in the last 12 times, you ordered pizza with cheeses, sausage, and thick crust.

OK! This is it.

May I suggest to you this time ricotta, arugula with dry tomato?

What? I hate vegetables.

Your cholesterol is not good, sir."

How do you know?

We crossed the number of your fixed line with your name, through the subscribers guide.

We have the result of your blood tests for the last 7 years.

Okay, but I do not want this pizza I already take medicine.

Excuse me, but you have not taken the medicine regularly, from our commercial database, 4 months ago, you only purchased a box with 30 cholesterol tablets at Drugsale Network.

I bought more from another drugstore.

It's not showing on your credit card statement

I paid in cash

But you did not withdraw that much cash according to your bank statement

I have another source of cash

This is not showing as per you last tax form unless you bought them from undeclared income source.

What the hell

I'm sorry, sir, we use such information only with the intention of helping you

Enough! I'm sick of google, Facebook, twitter, WhatsApp. I'm going to an Island without internet, cable TV, where there is no cell phone line and no one to watch me or spy on me

I understand sir but you need to renew your passport first as it has expired 6 weeks ago

Fast Bike

A man decided he was going to ride a ten speed bike from Auckland to Wellington. He got no more than halfway there, around Taupo, when the task got too great and he could go no farther.

He stuck his thumb out but, after about three hours, not a single person had stopped. Finally a guy in a Corvette pulled over and offered him a ride but, of course, the bike would not fit in the car. The owner of the Corvette found a piece of rope lying on the side of the road and tied it to his bumper. He tied the other end to the bike and told the man that, if he was going too fast, to honk the horn on his bike and he would slow down.

Everything went fine for the first 50 kilometres when suddenly another Corvette flew past them. Not to be out done the Corvette pulling the bike went after the other. A little later the two Corvettes, both doing over 120 kph, flew through a speed trap.

The police officer noted the speeds on his radar gun and radioed ahead to the other officer that he had two Corvettes coming towards him at over 120 kph.

He added, "you are not going to believe this but there's a guy on a 10 speed bike honking to pass!"