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Corporate Chains

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Special points of interest:

- * Clindacure - clindamycin drops.
- * Oridermyl replaces Oribiotic
- * The myth of Tryptophan

Large corporates often make decisions that impact on our local market in a boardroom far far away .

What can seem like a reasonable sized market in our little neck of the woods may be infinitesimal to the board of a major company and their allegiances must always be to their shareholders. Products that may be useful in our world are discontinued so the company can focus on the big money earners. This is just a fact of life.

Being a New Zealand owned family run company Ethical Agents Veterinary Marketing is not

bound by these corporate chains; EA is able to make its own decisions regarding the local market.

As well as being far more adaptable EA is large enough to have many contacts all around the world. This means EA is better placed than anyone else to be able to source products and service lines for the NZ veterinary industry.

Examples such as the only acepromazine product, the only registered antihistamine, being able to bring Vitamin K to the market when it was unobtainable, abound.



Now, with the corporate discontinuance of liquid clindamycin, EA has been able to rapidly fill the void with the launch of Clindacure; only from The Source!

Something New

Everyone likes something new and, this month, EA have two new products to launch.

Both are featured in the middle spread of this newsletter.

Clindacure is a liquid clindamycin preparation

replacing the discontinued reference product and really is a service line to the profession.

The other product is Oridermyl replacing the popular Oribiotic which was withdrawn from the market a year ago.

Both products are small animal focused and seamlessly replace two very useful tools in the clinician's armoury.

In addition we feature an addition to the staff here at EA, and his initiation rite.

If Agatha Christie Did Science

A recent webinar on the One Health website came up with some surprising news. The webinar was run by Dr Laura Kahn who has recently written of her research in a book entitled “One Health and the Politics of AMR.”

The first of the two part series looked at food animal usage and followed, in particular, vancomycin resistant enterococci (VRE) and its development over the years.

The key to monitoring resistance is surveillance and, with food borne bacteria the Swedes divided the microbes into zoonoses, such as Salmonella, and indicator species such as E coli and other Enterobacteriaceae, the latter living normally in the gut but capable of causing disease if they get into areas such as the bloodstream.

Of special concern was vancomycin resistance as avoparcin, a polypeptide antimicrobial used in animal feed, is closely related to vancomycin, an antimicrobial of last resort in human medicine.

The Scandinavian countries have been reducing antimicrobial use in feeds for some time and there is a plethora of data showing a reduction of growth promotant use, along with a corresponding increase in therapeutic use, since the start of the millennium.

Thus total antibiotic use has not altered a great deal however, in

Denmark, pork production by weight has gone up, especially after a total ban on the use of antimicrobials for growth promotion in 2006.

So how has this impacted on vancomycin resistance? In fact vancomycin resistance has gone down in livestock but has increased in the human population. The waters are muddied further when looking at the American situation. Once again the level of vancomycin resistance, marked by the genome VRECC17, is a rising problem in human medicine and at a much greater level than in livestock.

As a matter of fact avoparcin has never been used in food producing animals in the United States, being banned from inception because of a fear that it may be carcinogenic.

So it seems patently obvious that vancomycin resistance in human pathogens does not come from animals, right?

Well not exactly, it is just not from the animals that one would expect. This is where we get the Agatha Christie twist in the case.

The genomic data suggested a surpris-

ing finding. One or two VRE clones caused initial outbreaks, proliferating into multiple clones, and becoming endemic in hospitals. This strain is VRE CC17 and is genetically distinct from VRE in livestock and from healthy people in the community. Genetic analysis suggests that this VRE precursor came from animals, just not the animals that would be expected.

Ampicillin resistant Enterococcus faecium (AREF) have been isolated in dogs. Studies have shown that 1 out of every 4 dogs in the United States had AREF CC17, which turns out to be a precursor of VRE CC17.

So food producing animals are in the clear, dogs are the ‘culprits.’

This means that antibiotic resistance in pets is potentially an important hidden source of resistance in human pathogens.



A penny's worth:

If you live in Georgia and make the minimum wage of \$7.25 an hour, you make 0.002 per second.

If you see a penny on the ground, pick it up, check to see if it's a real penny and drop it in your pocket, it

would take you approximately 6 seconds.

Therefore it would cost 0.012 to pick the penny up.

More than the value of the penny.



Tartare Tom

Earlier this year well known Dunedin identity Tom Hart joined the EA team in a specialist position. Tom has had some experience in the veterinary wholesale field but most of his career has been on the human medical side, marketing to doctors, dentists and pharmacists.

Therefore his role at EA has nothing to do with the veterinary industry itself but to market lines such as sutures, disinfectants, etc. to the various branches of the medical profession and beyond.

This does make Tom one of the happy team however and he joined them all at the recent NZVA Conference in Hamilton. Naturally at a team dinner at the Bluestone Steakhouse in downtown Hamilton Tom was introduced to the longstanding tradition for all new EA employees (well, since June 2016 anyway) of dining on steak tartare as part of his initiation.



His face was a delight to behold when he saw the dish being prepared in front of him; raw mince, a raw egg, some spices and no cooking implement of any kind in sight.

He did not exactly replicate the famous Mr. Bean episode of trying to hide the mixture all around the table and he did valiantly have a go at getting through it. However it did prove too much in the end, not to mention the after effects the next day, with poor old Nagy having to sit beside him on the plane back to Christchurch!



With experience comes knowledge and "Tartare Tom", as the team now call him, has probably ordered his last steak tartare ever.

Why Men Are So Honest

"One day, while a woodcutter was cutting a branch of a tree above a river, his axe fell into the river. When he cried out, the Lord appeared and asked, "Why are you crying?"

The woodcutter replied that his axe has fallen into water and he needed the axe to make his living.

The Lord went down into the water and reappeared with a golden axe. "Is this your axe?" the Lord asked.

The woodcutter replied, "No."

The Lord again went down and came up with a silver Axe. "Is this your axe?" the Lord asked.

Again, the woodcutter replied, "No."

The Lord went down again and

came up with an iron Axe. "Is this your axe?" the Lord asked.

The woodcutter replied, "Yes."

The Lord was pleased with the man's honesty and gave him all three axes to keep, and the woodcutter went home happy.

Sometime later the woodcutter was walking with his wife along the riverbank, and his wife fell into the river. When he cried out, the Lord again appeared and asked him, "Why are you crying?"

"Oh Lord, my wife has fallen into the water!"

The Lord went down into the water and came up with Angelina Jolie.

"Is this your wife?" the Lord asked.

"Yes," cried the woodcutter.

The Lord was furious. "You lied! That is an untruth!"

The woodcutter replied, "Oh, forgive me, my Lord. It is a misunderstanding. You see, if I had said 'no' to Angelina Jolie, You would have come up with Cameron Diaz. Then if I said 'no' to her, you would have come up with my wife. Had I then said 'yes,' you would have given me all three. Lord, I am a poor man, and am not able to take care of all three wives, so that's why I said yes to Angelina Jolie."

The moral of this story is: Whenever a man lies, it is for a good and honourable reason and for the benefit of others.

That's our story, and we're sticking to it!

Clindacure

Clindamycin has long been an incredibly useful antibiotic and that importance has been enhanced in these days of responsible antibiotic prescribing.

With an emphasis on diagnosis and a recommendation to, where possible, use narrower spectrum antibiotics, clindamycin ticks a lot of boxes. With a spectrum mainly against gram positive cocci and also anaerobic bacteria clindamycin is predominantly used for treating skin infections, deep wounds and abscesses, dental infections and osteomyelitis.



A fast action, T_{max} within one hour, and the kinetics allowing once daily dosing in the cat (twice daily in dogs) also makes clindamycin a very practical drug to use.

Whilst readily available in tablet form the liquid drops have been extremely popular as a means of dosing cats and are also beneficial in dental conditions with dogs with sore gums that may resist tablet administration.

Unfortunately for many clinicians the company marketing these drops was faced with a corporate decision to discontinue them and accordingly a letter was sent to practices sometime last year.

Into the breach came EA, not bound by corporate chains and having many tentacles around the world, it was able to source a high class generic from its association with Chanelle manufacturing in Ireland.

The resultant product achieved registration reasonably quickly, thanks to an impressive dossier, and is now readily available in New Zealand marketed as Clindacure drops.

Clindacure exemplifies many of the trends in modern pharmaceuticals. There is always the possibility of board decisions in faraway countries affecting drug availability in



"predominantly used for treating skin infections, deep wounds and abscesses, dental infections and osteomyelitis."

our small corner of the world. Modern generics can fill that breach but require a company based locally being able quickly to react to the market whilst at the same time being also of a size large enough to have the clout to be able to re-source and register product in a quick efficient manner.

That is where EA steps on as "The source of veterinary pharmaceuticals."

The other trend where Clindacure fits nicely is that of the trend now to move away from 'shotgun' antimicrobial therapy towards more specialist treatment.

With a range from front line antibiotics to those deemed critical to human medicine EA has the whole field covered and is expertly placed to advise on antimicrobial therapy.

Historical Fact

Who says building a border wall won't work?

The Chinese built one over 2,000 years ago and they still don't have any Mexicans.

A Short Gun Story

It's the early 1970's. A civilian walked into the bar at the CPO's Mess, HMAS Watson, waving his pistol and yelled,

"I have a 45 calibre Colt 1911 with a seven round magazine plus one

in the chamber and I want to know who's been sleeping with my wife."

A voice from the back of the Mess called out, "You'll need more ammo!"

Ori-dermyl is Here!



Oribiotic was an ear preparation favoured by many practitioners but it became discontinued a year ago. The news is not at all bad however.

The reason for the product being discontinued was that it was superseded in Europe by Ori-dermyl, which is basically the same product that also contains a miticide, thus taking the European market. Ori-dermyl can therefore be considered as Oribiotic Plus!

The original Ori-dermyl formulation contained lindane, an organochlorine, as the miticide and so was not able to be registered in New Zealand.

The parent company, Vetoquinol, reformulated it to contain permethrin instead; just as effective and environmentally friendly.

Toxicity for cats is not an issue as it is applied topically inside the ear

and a cat would have to eat a whole 10g tube to receive a toxic dose.

The other ingredients are nystatin as antifungal, the antibiotic neomycin and triamcinolone for its anti-

inflammatory effect.

Thus Vetoquinol have the ear infection field covered as the gold standard product for pseudomonas infection, Aurizon, is from the same stable. Product placement is quite simple and fits in well with the current climate of responsible antimicrobial usage.

Ori-dermyl is a first line product, containing a less critical antibiotic in neomycin.

Thus it is targeted at everyday use and especially in acute cases, where the miticide removes what is often the inciting cause and the other ingredients take care of the accompanying infection and inflammation.

Aurizon has marbofloxacin, a fluoroquinolone, as the antibiotic and so is aimed at the more chronic, difficult to treat cases.

So, for new infections, reach naturally for Ori-dermyl, for revisits or difficult cases Aurizon will take over.

The two products both share the same type of atraumatic nozzle that is also transparent so that the administrator can see whether the preparation is actually moving into the ear.

One point of difference, apart from the active ingredients, is that Aurizon is in drop form and relies on penetrating through the infectious milieu that is in a chronically infected ear.

However Ori-dermyl, as befits a product targeting acute infections is in a gel that can be placed deep in the ear and melts at body temperature to be easily massaged around if required.

The beauty of both products are that they are indicated for once daily dosing, ensuring greater compliance.

"The beauty of both products are that they are indicated for once daily dosing,"

Differing ideas about sport.....

In England, they will thoughtfully select the most suitable tree, cut it down, carefully remove all of the branches and the bark until they are left with a cylinder.

Next, they will take the cylinder of wood and turn it on a lathe and then whittle away until they are

left with a perfectly formed bat.

The bat will be cured and treated to strengthen it and then, when it is finally ready, they will use it to knock a leather ball around a park.

While in Scotland, they just throw the bloody tree.



A Platypus in New York

A little knowledge is dangerous, as the old saying goes. When science goes wrong we can get some amusing, and some alarming, results. Most of us would struggle at the best of times to follow sciences such as metagenomics, which is the development and validation of novel methods that use next-generation DNA sequence data to detect pathogens from complex ecosystems. In particular, these methods are important in studies of the built environment and of agricultural systems, where the correct detection of pathogens represents enormous public benefit and where incorrect detection creates fear.

For example, in a recent study of the New York subway, due to in-

correct taxonomic classifications, the authors reported observing *Yersinia pestis* (the causative agent of plague) and *Bacillus anthracis* (the causative agent of anthrax) as part of the "normal subway microbiome." These observations led to high-visibility news reports. One could just imagine the field day American media could have with such a scenario.

However, improved reanalysis of the same data found that these pathogens were not part of the normal subway microbiome, either in New York or in an independent sample set from the Boston subway. This study drew the more plausible conclusion that the surfaces were dominated by inputs of

normal human skin bacteria, consistent with other studies, and found that the subway was not a reservoir of bacterially encoded

toxins or antimicrobial resistance elements.

So, where does our platypus (*Ornithorhynchus anatinus*) come in? Well not actually in the subway itself but, when using metagenomics to determine the presence of *Salmonella* from fresh produce, shotgun analysis came up with not only the *Salmonella* but also red jungle fowl, the house mouse and our wandering platypus. While not actually roaming the subway, environments in which the platypus was reportedly found include diverse areas from the built environment to the human gut.

Suffice to say the authors of this paper were able to solve the problems by using an inclusion database and an exclusion database, such as the platypus to demonstrate the presence or absence of the pathogen in question.

Reference

Gonzalez, Vazquez-Baeza, Pettergill, Ottesen, McDonald and Knight. Avoiding Pandemic Fears in the Subway and Conquering the Platypus. American Society for Microbiology, Volume 1 Issue 3 2016



A Modern Church

The elderly priest, speaking to the younger priest, said, "You had a good idea to replace the first four pews with plush bucket theatre seats. It worked like a charm. The front of the church always fills first now."

The young priest nodded, and the old priest continued, "And you told me adding a little more beat to the music would bring young people

back to church, so I supported you when you brought in that rock 'n roll gospel choir. Now our services are consistently packed to the balcony."

"Thank you, Father," answered the young priest. "I am pleased that you are open to the new ideas of youth."

"All of these ideas have been well and good," said the elderly priest,

"But I'm afraid you've gone too far with the drive-thru confessional."

"But, Father," protested the young priest, "my confessions and the donations have nearly doubled since I began that!"

"Yes," replied the elderly priest, "and I appreciate that - but the flashing neon sign, 'Toot 'n Tell or Go to Hell' cannot stay on the church roof!"

Tryptophan - Busted!

It was almost like an episode of Mythbusters. For years we have had the mantra of how efficient tryptophan is in calming nervous horses and a myriad of products have gone on the market based on this premise. It has grown to such a level that racing authorities have been endeavouring to establish a threshold level for tryptophan, an essential amino acid, in the horse.

Worry no longer industry bosses, it seems the matter has been cleared in a couple of recent trials that were set up to prove how effective tryptophan is in calming nervous horses. One such work, by Noble *et al* in Australia, could not show a beneficial effect for tryptophan and concluded "While the safety of these doses of TRP can be confirmed, there was no evidence to suggest that a single dose of TRP is an effective calmative for horses." – Busted!

This follows on from earlier work by much the same team in 2008 which concluded "Plasma tryptophan increases when tryptophan is administered at a dose used in some commercial products, but this is not reflected by marked behavioural changes in the horse."

The research work was probably prompted by this abstract by Grimmett and Sillence in 2005 which raised the query:

"Preparations that contain tryptophan are marketed world-wide as calmative agents to treat excitable horses. Tryptophan is the amino acid precursor for serotonin, a neurotransmitter implicated in seda-

tion, inhibition of aggression, fear and stress, in various animal species and humans. Experiments have shown that tryptophan supplementation decreases aggression in humans, dogs, pigs, poultry, and fish, and that it may reduce fearfulness and stress in calves, vixens and poultry.

However, behavioural characteristics more closely linked to excitement, such as hyperactivity in dogs, are not modified by tryptophan supplementation. Research using a variety of animals other than horses, has shown that the behavioural response to tryptophan supplementation varies with age, breed and gender, and can be modified by diet, exercise, social status, and level of arousal.

Significantly, the response is species-dependent, and there are no scientific publications that confirm the efficacy of tryptophan as a calmative in excitable horses.

The few studies where tryptophan has been administered to horses suggest that low doses (relative to those contained in commercial preparations) cause mild excitement, whereas high doses reduce endurance capacity, and cause acute haemolytic anaemia if given orally, due to a toxic hindgut metabolite.

As tryptophan continues to be used as an equine calmative, there is an urgent need for research to confirm its efficacy in horses, and to establish a safe therapeutic dose range. In the meantime, available data suggest that it would be imprudent

to rely on tryptophan to calm the excitable horse, and instead, that a greater effort should be made to identify the underlying causes of excitability, and to explore more appropriate non-pharmacological remedies."

So there is no hard evidence that tryptophan is effective in the horse and, on the contrary, there appears to be some evidence that it is not of much use at all. The stock standard treatment, thiamine or vitamin B1 remains not only the most economical remedy but, anecdotally, the most effective.

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Ethnicity

Nagy meets a man at the Rio Olympics who is carrying an eight-foot-long metal stick.

"Excuse me," says Nagy to the man. "Are you a pole vaulter?"

"No," says the man, a bit stunned.

"I'm German, but how did you know my name is Walter?"



Mother's Driver's License

A mother is driving her little girl to her friend's house for a play date.

'Mummy', the little girl asks, 'how old are you?'

'Honey, you are not supposed to ask a lady her age', the mother replied. 'It's not polite.'

'OK', the little girl says, 'What colour was your hair 2 years ago?'

'Now really', the mother says, 'those are personal questions and are really none of your business.'

Undaunted, the little girl asks, 'Why did you and Daddy get a divorce?'

'That's enough questions, young lady! Honestly!' The exasperated mother walks away as the two friends begin to play.

'My Mum won't tell me anything about her,' the little girl says to her friend.

'Well,' says the friend, 'all you need to do is look at her driver's license. It's like a report card, it has everything on it.'

Later that night the little girl says to her mother, 'I know how old you are. You are 32.'

The mother is surprised and asks, 'How did you find that out?'

'I also know that you used to have brown hair.'

The mother is past surprised and shocked now. 'How in Heaven's name did you find that out?'

'And,' the little girl says triumphantly, 'I know why you and daddy got a divorce.'

'Oh really?' the mother asks. 'Why?'

'Because on your driving licence it says you got an "F" in sex'

