



ETHICAL AGENTS LTD
VETERINARY MARKETING

EA NEWS

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Strengths and Weaknesses

Inside this issue:

Big Brother, Little Brother 2

After Temgesic 4

Penicillin In The Car 7

All products have strengths and weaknesses and nobody knows more about them than the purveyors of those products to the market.

EA markets both meloxicam and tolfenamic acid in the NSAID market and so is well placed to comment on comparisons.

Meloxicam's strengths are mainly around sim-

plicity of dosing but tolfenamic acid has superior kinetics for short term acute use and a wider therapeutic window.

These differences are discussed inside, along with a comparison of Metabolase and the new product Metabolase Forte.

On the one hand we have a direct comparison of two compounds with respect to their suitability for a particular indication and, on the other, we compare the similarities of two preparations as to how they can be companion sold and used to complement each other in a clinical situation.



Special points of interest:

- * New product Metabolase Forte to accompany big brother Metabolase
- * Rationalizing is not necessarily best practice
- * The effect of car temperature on procaine penicillin

Quote Of The Week

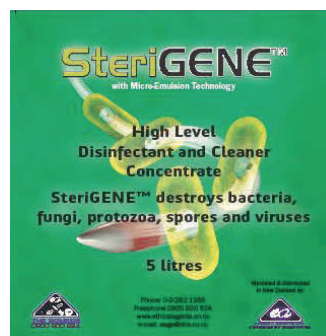
There was an interesting and thought provoking quote in the latest edition of Rural News:

"The way the water's allocated has exacerbated the feed shortage.

The dairy farmers have

used it all...and now there's none left for the cropping farmers to grow the winter feed that's so badly needed."

— South Canterbury farmer Jeremy Talbot



Big Brother, Little Brother

It is almost a year to the day that Metabolase was unveiled in New Zealand and, by filling a niche in the market, it has proven to be a great success. Now the company has launched the companion product Metabolase Forte.

While this may appear to confuse the market the reasons are sound. All products have strengths and weaknesses; to be successful the former have to outweigh the latter. Metabolase's strengths are formidable, which explains its success in the marketplace. Metabolase is a parenteral nutrient that not only contains essential amino acids and vitamins but also antioxidants and detoxicants to reduce excess nitrogen and free radical accumulation in periods of body stress.

It really is a very effective all-embracing product aimed at the poor performing race horse, parvo dogs, the transitional cow and also used to great effect in facial eczema and theileria cases.

The product weakness really is in the administration as, by necessity, it is a large volume infusion given intravenously in most cases, although in cattle it may be given subcutaneously.

The reason for the high volume is that the ingredients are powerful and should not be given too rapidly; therefore it is presented as a dilute high capacity infusion.

"it means the client has to get the vet out to treat the animal."

This often restricts its use to the veterinary practitioner rather than the practice client, be they farmer or horseman. Some practitioners appreciate this fact, having the attitude that it means the client has to get the vet out to treat the animal.

This is all very well and a strong case can be made for leaving such a potent product in the veterinarians' hands, especially since it should be administered in a professional manner.

However the wider indications mean that there is a place for some clients to have a means of rapidly treating animals that may not necessitate or justify a veterinary call out with attendant consult fee. While the non-performing horse, especially with a 'normal blood

count', is still a primary Metabolase target the filly prone to tie up, which is normally treated in a preventative manner by the client, would be an example of this situation. Facial eczema would be another example; both products contain the same amount of d-l acetylmethionine per dose as the previously available Liver-X, a recommended standby for early cases.

They not only have the base ingredient but also other metabolic

(Continued on page 3)



Mixed Religion Seminar

I decided to go to the mixed religion seminar for the first time.

I sat down and then the Catholic Priest came up to me, laid his hands on my head and said "By the will of God the Almighty and Jesus Christ, you will walk today".

I told him I was not paralysed.

Then came the Pentecostal minister and laid his hands on me and

said "By the will of God the Almighty, you will walk today".

Again I told him there was nothing wrong with me.

Along came the Muslim Imam and laid his hands on me and said "By the will of Allah the Almighty, you will walk today".

Again I told him there was nothing wrong with me.

Finally along came The Buddhist monk and laid his hands on me and said "By the will of Buddha, you will walk today".

Again I told him there was nothing wrong with me.

After the prayers and sermons, I stepped outside and lo and behold, my bike had been stolen.

Big Brother, Little Brother

(Continued from page 2)

stimulants meaning a better all-round treatment, all for a very similar cost.

Whereas Metabolase, with its fuller array of ingredients, remains product of choice for the downer or the debilitated animal requiring veterinary attention, Metabolase Forte is ideal for rapid treatment of groups of animals at the farmer level.

Looking at the make-up of the two, it is clear that Metabolase has all the essential ingredients of a parenteral nutrient driving metabolism and then some. Metabolase Forte has the basics but is in a more convenient package, in other words it is selling convenience.

Metabolase has carnitine and methionine as its major ingredients plus Vitamins B₁₂ and B₆, energy sources, several antioxidants including lipoic acid, the universal antioxidant, and detoxicants, including the co-enzymes in both the urea cycle and the extra-hepatic detoxification of urea.

Metabolase Forte has the essential carnitine and methionine but only

Vitamin B₁₂ and has Vitamin E as the anti-oxidant; there are no energy sources or detoxicants. Its major advantage is convenience of dosing, hence the concept of companion marketing as 'big brother and little brother'.

"Similarly with Metabolase, those who carry and use it will create greater demand for client access to Metabolase Forte,"

Metabolase Forte is not only 'little brother' by way of ingredients but it also is a much smaller volume injection. It is also an intramuscular presentation and should not be used intravenously. This is because too rapid an application may result in a reaction and the product is so chock full of the active ingredients it is highly concentrated, thus the word Forte in the name. The parent product Metabolase gets around this situation with its dilute high volume presentation.

So there is certainly a place on the shelf for both products, Metabolase for veterinary treatment of the individual animal and Metabolase Forte to leave as farmer or trainer

follow up, or to have on hand for group therapy in 'tie up' or facial eczema.

In the dairy world the practices where the vets carry and use Calol in their trucks are the ones that have the highest volume sales out of the clinics. Similarly with Metabolase, those who carry and use it will create greater demand for client access to Metabolase Forte, yet still retain the 'big gun' for their professional use.

Those Welsh

A guy was driving down a motorway in England with his blonde girlfriend and she piped up,

"I think those people in the car next to us are from Wales".

"Why do you think that?" he said.

"Well, the kids are writing on the window and it says

"stitt ruoy su wohs".

Maths Instruction

A high school teacher was arrested today at Auckland International airport as he attempted to board a flight while in possession of a ruler, a protractor, a compass, a slide-rule and a calculator.

At the press conference, the Attorney General said he believes the man is a member of the notorious extremist Al-Gebra movement.

He did not identify the man, who has been charged with carrying weapons of maths instruction.

'Al-Gebra is a problem for us', the Attorney General said. 'They derive solutions by means and extremes, and sometimes go off on tangents in search of absolute values.'

They use secret code names like "X" and "Y" and refer to themselves as "unknowns;" but we have determined that they belong to a common denominator of the axis of medieval with coordinates in every country. As the Greek philosopher

Isosceles used to say, "There are three sides to every triangle."

When asked to comment on the arrest the Prime Minister said, "If God had wanted us to have better weapons of maths instruction, He would have given us more fingers and toes."

Colleagues told reporters they could not recall a more intelligent or profound statement by the Leader.

After Temgesic...?

The title does not intend to suggest Temgesic will disappear from the market, far from it in fact. Despite the fact that it really would qualify as an off label use, there is no buprenorphine registered for animal use but there are a myriad of butorphanol products, Temgesic is probably the most common opiate used for surgical analgesia, especially in cats.

Opiates are used peri-operatively for analgesia as they have fewer side effects than NSAIDs in the low renal flow states of surgical anesthesia. The problem is that all opiates have a relatively short duration of action and so are replaced by NSAIDs to extend the analgesia in the recovery process.

While some NSAIDs do have peri-operative use as a registered label claim in dogs, (but not in cats) it is considered best practice to still use opiates during surgery and NSAIDs after. Therefore the above title really refers to what is best practice for NSAID use post-surgery.

It is becoming more and more common for practice managers to 'rationalize' the range, for reasons of inventory, but often this is a misuse of the word as it does not actually mean rational usage but expedient, for the bean counters at least, use. In short the drug cabinet is filled for the wrong reasons and patients are made to fit the drugs, not the other way around. It

is like the old farriers adage, "make the shoe fit the horse, do not trim the horse to fit the shoe."

In the Auckland area at least most practices, when asked about post-surgical analgesia, respond with Temgesic and meloxicam, but is this actually the best approach? The differences in buprenorphine (Temgesic) and butorphanol are the basis for another article but the indications for NSAID use are highly relevant. NSAIDs, like all drugs, have different attributes between drugs in their own class and kinetics and the therapeutic window, in addition to efficacy, should be the major prescribing factors. Cost is very much secondary and 'rationalization' well down the list.

Marketing of prescription remedies is really no different from the marketing of other commodities, especially 'professional' type products. A supreme example came in the 1980's when video recorders became available for public use. There were two major systems, VHS and Beta. It is now history how VHS took the commercial market, yet all the professionals maintain that it is clearly an inferior system. To this day professional major communications media have persisted in using the Beta system.

Similarly with the battle between Microsoft and Apple, Microsoft definitely won that battle with home

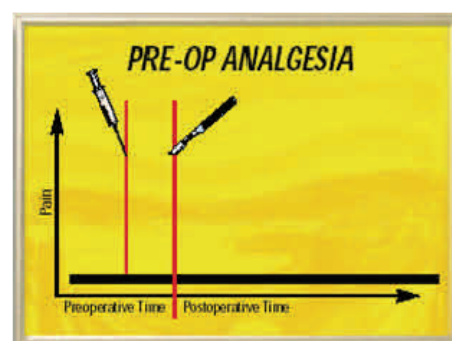
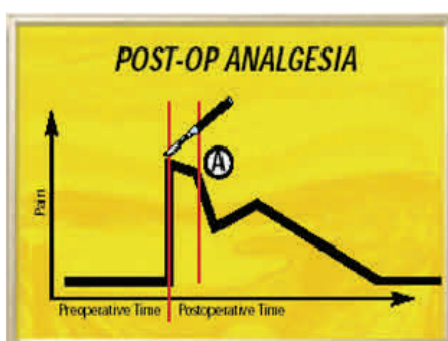
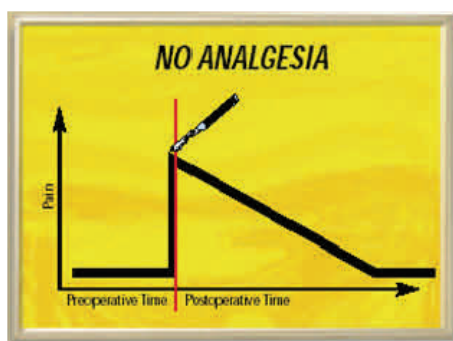
computers but the professionals insist on using Apple software. With prescription drugs the professionals are the practitioners but the marketing war is often aimed at the managers rather than the prescribers.

"The chains of habit are too weak to be felt until they are too strong to be broken."

The concepts of NSAID use can be difficult to get across, particularly when habits form in a practice, and veterinarians used to a particular regime are loathe to alter it. However time moves on and, as Charles Darwin famously stated, "It is not the strongest of the species that survives nor the most intelligent, but the ones that are the most responsive to change." Samuel Johnson, the prolific 18th Century writer also had a little gem, "The chains of habit are too weak to be felt until they are too strong to be broken."

Advantages for meloxicam in long term NSAID use are ease of dosing and simplicity, neither of which are of particular relevance in short term acute indications such as surgery or trauma. Clearly effective pain relief is an overriding factor as well as the therapeutic window, which assumes even greater im-

(Continued on page 5)



After Temgesic...?

(Continued from page 4)
portance with NSAIDs, in particular, at the time of surgery.

Effective Pain Relief

All experts agree that pain relief is far more effective when the analgesia is applied before the onset of pain itself; this has been the basis for the advocacy of pre-operative analgesia.

With the now accepted method of opiate peri-operatively and NSAID at extubation (post-operatively), it is clear that there needs to be a smooth transfer of analgesia from opiate to NSAID.

Considering the short duration of action of opiates then a major requirement for an NSAID would be

short T_{max} , i.e. a rapid onset of activity.

This then highlights a major weakness in meloxicam usage, of the NSAIDs available to the veterinary market meloxicam has the slowest onset of activity by a considerable margin.

It is not considered good practice to use long term NSAIDs as panaceas and, in a situation where pain lasts less than 5 days, time to T_{max} should be a major consideration. So it makes sense to choose a rapid onset of activity product if one really wants to consider rational drug use post-surgery.

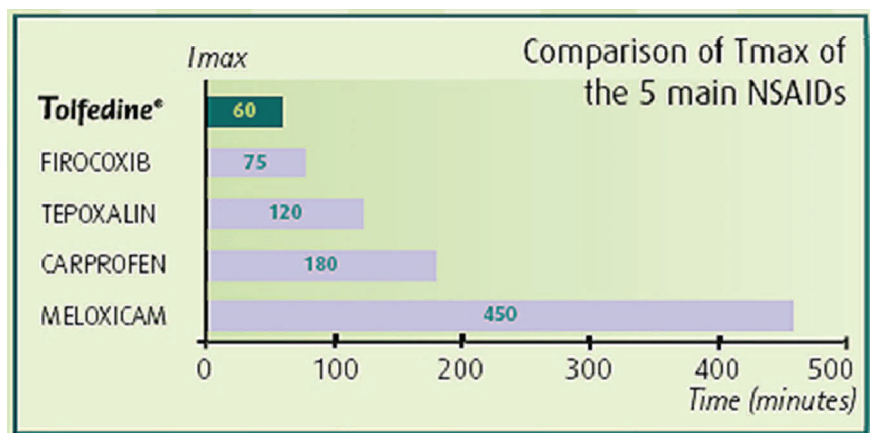
There are, of course other considerations, and a major one is the therapeutic window.

Therapeutic Window

Why are opiates used instead of NSAIDs during surgery? To lessen the risk of renal damage due to the low renal flow rate induced by anaesthetic agents and/or dehydration. In other words opiates have a better therapeutic window, a wider margin between therapeutic and toxic doses.

Different NSAIDs also have different therapeutic windows. Why does the dose of Meloxicam in cats have to be reduced to about 1/3 of the dog dose in mg/kg? Because it is not as safe in cats. Why is there no alteration in dosage for cats and dogs with tolafenamic acid? Because the safety is there, i.e. tolafenamic

(Continued on page 6)



Paddy Died

His will provided £40,000 for an elaborate funeral.

As the last guests departed the affair, his wife Colleen turned to her oldest and dearest friend. "Ah well, Paddy would be pleased," she said.

"You're right," replied Mary, who lowered her voice and leaned in close.

"So how much did this really cost?"

"All of it," said Colleen. "Forty thousand."

"Aw No!" Mary exclaimed, "I mean, it was very grand, but £40,000?!!!"

Colleen answered, "The funeral was £6,500. I donated £500 to church.

The whiskey, wine and snacks were another £500. The rest went for the Memorial Stone."

Mary computed quickly. "For the love of God Colleen, £32,500 for a Memorial Stone? How big is it?"



Inside Story Headline

(Continued from page 5)

acid has as wide a therapeutic window in cats as in dogs.

A lower therapeutic window means a lower dose. Pharmacokinetically this means a reduced C_{max} , theoretically meaning a lower peak effect that may impinge upon efficacy. That is not the only striking effect however.

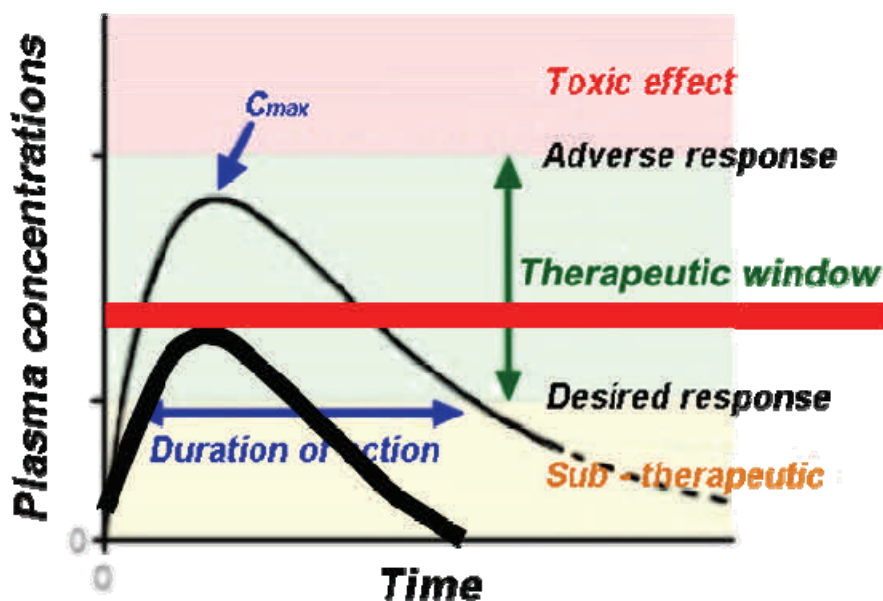
"The chains of habit are too weak to be felt until they are too strong to be broken."

When one looks at the graph alongside what is evident is that the lower decay curve is not only reduced in height but also dramatically reduced in length.

This means that duration of action is shortened considerably so that not only is onset of analgesia slower with meloxicam but also, with the reduced dosage in cats, the length of activity is curtailed.

Unfortunately, as they say, pain is silent so there is no good measure of the length of analgesia with such a lower response curve.

If rationalising really is to mean rational use, then tailoring rapidly acting, wide therapeutic window drugs for surgery or acute use is the answer. What is best for the inventory is not necessarily best practice.



Vétoquinol
Signe de Passion

Pain is silent.
That is not a reason to let it express itself.

The Munch-Bjerg Group - Adapt. Paris 2004

Call Centre

An Emergency Call Center worker in Sydney, has been fired, much to the dismay of her colleagues who are reportedly unhappy with her dismissal.

It seems a male caller dialed 000 from a mobile phone stating: "I am

depressed and lying here on a railway track.

I am waiting for the train to come so I can finally meet God."

Apparently, "Remain calm and stay on the line," was not considered to be an appropriate response.....



Penicillin In The Car

There are two ways that horses can react to procaine penicillin, one is anaphylaxis and requires prior sensitisation. While possible this is not common. The other way is reaction to procaine itself. This requires procaine absorption into the blood stream which can result in locomotor and behavioural changes.

"the claim that "we have always done it this way," would be no defence."

Individual injection technique can be a factor, especially with dynamilled penicillin, which is much more rapidly bioavailable. It became fashionable for many equine practitioners to inject horses in the pectoral muscle rather than the neck, as the blood supply was much greater there than in the neck region leaving less risk of injection site reactions. However this is not universally popular as there is no drainage in this area in the advent of an injection site reaction. (The best of both worlds is the rump injection, easier than it looks and gives both good absorption and drainage.)

Is it really necessary to inject in regions of high blood supply for better absorption, something that is not necessary with a dynamilled product? This may inadvertently increase the risk of elevated procaine arising in the bloodstream.

However the greatest risk of free procaine in penicillin preparations is the storage of the product. From time immemorial veterinarians have had bottles of antibiotics rolling around in the backs of cars, winter and summer.

A very interesting paper was published in 2000 by G. E. S. Summerhays entitled Monitoring of temperature in cars with regard to the pharmaceutical precautions of medicine storage (Equine vet. Educ. (2000) 12 (6) 307-311). There were some relevant quotes.

"Recommended storage temperatures fall into 2 main groups: below 25°C (Cool) and between 2 and 8°C (Cold). These temperatures are used by the manufacturers as a standard, to form the basis of shelf life estimation. If medicines are not stored at the appropriate temperature they may degrade, and nullify the 'use-by' date."

"There is some evidence to suggest that, when veterinary preparations of procaine penicillin G are heated to temperatures similar to those which may prevail in car boots, the concentration of procaine increases significantly, such that a standard dose given i.m. could be sufficient to produce plasma concentrations in excess of those necessary to produce central nervous system excitation (Chapman et al. 1992; McCann 1995)."

The author proceeded to measure temperature recordings in various

receptacles in the car, from battery fridges to a cabinet with drawers. Temperatures up to 40°C were regularly recorded, well above recommended storage for most drugs. By using Styrofoam in some of the drawers, such as vaccine storage drawers, he kept temperatures down and it did matter where in the wooden cabinet the drawer was (the lower the better).

This information is really thought provoking and even more so when one realises the trial was done in South East England, where ambient temperatures do not rise above 22°C even in the peak of summer.

When ambient temperatures in most of New Zealand at this time of year can regularly get to around the 30°C mark then it is anybody's guess as to what the temperature is inside the car or back of an enclosed truck.

Not only is the risk of free procaine dramatically increased the question also arises as to what effect this has on the kinetics of the drug. Is the penicillin above the MIC for the whole time it is in the body? Probably not. Therefore there are not only risks to toxicity but also to efficacy.

With information like this available since 2000 the claim that "we have always done it this way," would be no defence.

Thanks to Alec Jorgensen, Hamilton Vets for the above paper.

The New Clerk

The bank manager notices the new clerk is terrible when it comes to counting money and adding up figures.

"Where did you get your financial education?" he asks.

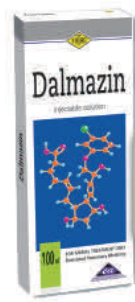
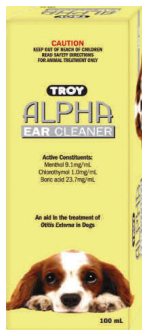
"Yale," replies the lad. The manager is sure he's misheard the man, so he asks his question again and the man again responds "Yale."

That can't be right, thinks the manager. He decides he's going to check

out the new clerk's credentials online.

"And what's your full name again?" asks the manager.

"Yim Yohnston."



3 Holy Men and 3 Bears

A Catholic Priest, a Baptist preacher and a Rabbi all served as Chaplains to the students of Northern Michigan University. They would get together two or three times a week for coffee and to talk shop.

One day, someone made the comment that preaching to people isn't really all that hard, a real challenge would be to preach to a bear.

One thing led to another, and they decided to do an experiment.

They would all go out into the woods, find a bear, preach to it, and attempt to convert it to their religion

Seven days later, they all came together to discuss their experiences.

Father Flannery, who had his arm in a sling, went first.

'Well,' he said, 'I went into the woods to find me a bear and when I found him, I began to read to him from the Catechism. Well, that bear wanted nothing to do with me and began to slap me around.

So I quickly grabbed my holy water, sprinkled him and, Holy Mary Mother of God, he became as gentle as a lamb. The Bishop is coming out next week to give him first communion and confirmation.'

Reverend Billy Bob the Baptist, spoke next. He had one arm and both legs in casts.

In his best fire-and-brimstone oratory, he exclaimed, 'WELL, brothers, you KNOW that we Baptists don't sprinkle I went out and I FOUND me a bear. And then I began to read to my bear from God's HOLY WORD ! But that bear

wanted nothing to do with me. So I took HOLD of him and we began to wrestle.

We wrestled down one hill, UP another and DOWN another until we came to a creek. So I quickly DUNKED him and BAPTIZED his hairy soul. And just like you said, he became as gentle as a lamb. We spent the rest of the day praising Jesus. Hallelujah !'

The Priest and the Reverend both looked down at the Rabbi, who was lying in a hospital bed. He had broken arms and legs, was in a body cast and traction, with IVs and monitors running in and out of him. He was in really bad shape.

The Rabbi looked up and said: "Looking back on it, circumcision may not have been the best way to start."