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Taking Back

Alternative medicine is very good at taking ideas from science and adapting to their own ends.

With probiotics we have a case of science taking back the reins.

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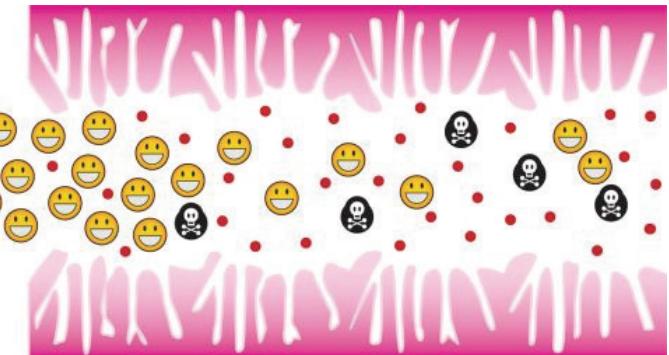
Heavily promoted to cure all sorts of ills probiotics, to many, have had a whiff of pseudoscience about them but that is not really the case.

The trillions of microflora that can be found in the gastrointestinal tract play an essential role in supporting and maintaining strong immune and digestive systems, so having the optimum balance of these beneficial bacteria is important.

A number of factors can compromise this balance, including antibiotic therapy, infection, stress, travel or a period of unhealthy nutrition or lifestyle.

An effective solution is to supplement the microflora by taking a multi-strain probiotic supplement to restore the balance.

So there are compelling reasons to use probiotics



and one of the latest, to give them in conjunction with antibiotics is not as oxymoronic as it sounds.

One issue with antimicrobial therapy, especially when given orally, is that beneficial bacteria in the gut may also be inhibited, or even wiped out, as well as the pathogens.

Thus problems such as antibiotic associated diarrhoea are quite common.

TV ads urge us to swallow copious amounts of probiotics when taking antibiotics.

The obvious question is, would not the antibiotics kill the bacteria in the probiotics?

The short answer is yes, although one could expound upon things like pharmacodynamics, etc.

The solution is much more simple than that; it is a matter of timing.

Much like the fact that the recommendation for amoxicillin/clavulanic acid combination is to take it with food, even though efficacy is better on an empty stomach.

This is because the clavulanic acid can induce nausea and this effect is nullified on a full stomach.

Similarly with taking probiotics, any concurrent antibiotic use must have some effect but this is minimized by following the general rule of administering the probiotics either two hours before or two hours after the antibiotics.

And Protexin certainly has the science to prove that this is effective.



Prostaglandin Dose and Recent Corpora Lutea

Most recommendations for treating non cycling cows are herd recommendations based on the 'typical' non cycler. However there are always those stubborn ones, those at the bottom of the chain that need something extra.

The two biggest issues are corpora lutea being too recently formed, and so less responsive to prostaglandin stimulation, or nutritional status simply being too low for animals to respond well enough.

In the first instance the natural resistance of corpora lutea to exogenously administered luteolytic agents early in dioestrus has been widely studied in ruminants. This is may be due to the reduced availability of endothelin-1 and increased level of prostaglandin dehydrogenase in early corpora lutea compared with mature corpora lutea. Endothelin-1

is a proteinaceous vasoconstrictor agent and steroidogenic cell modulator produced from

endothelial cells after injection of PGF2 α that alters progesterone production in cattle, whereas prostaglandin dehydrogenase metabolizes PGF2 α to its inactive form, 15-keto-PGF2 α in ewes.

Therefore it is eminently feasible that variations in prostaglandin dosage could possibly overcome these mechanisms.

There has been work recently done by one company in New Zealand showing a 3% increase in pregnancy if their racemic cloprostenol dose is increased from 2 ml (500 μ g) to 3 ml (750 μ g) per cow. This tallies with other data from around the world showing that the response rate in cows with a partially sensitive (or refractory) corpora lutea aged between 2-5 days, when the sensitivity towards PG is questionable. This can be improved by either increasing the

dose rate or giving a second injection 24 hours later.

So, when a blind treatment with hormones using a synchronisation programs is applied, since the ages of corpora lutea are not determined, the administration of a higher dose of prostaglandin could improve the positive results.

Whether or not to adopt the higher dose is a matter of benefit/cost ratio, considering the time spent for double injection and for the cost of a larger dose. However when we look at the work done by Montaser *et al* comparing racemic cloprostenol with dinoprost and d cloprostenol it appears that the pure potency of the d cloprostenol may make it more effective in the presence of prostaglandin dehydrogenase and so offer a more economical solution.

In addition Valldecabres-Torres *et al*, indicated that there is a farther increased benefit with an increased dose of d cloprostenol, 300 μ g in place of 150 μ g.

"the pure potency of the d cloprostenol may make it more effective in the presence of prostaglandin dehydrogenase"

Therefore, for a better response with refractory corpora lutea in a blind synchronisation program, the options are:

- 1) If using racemic d/l cloprostenol, or dinoprost, give an extra injection thus increasing the workload and the cost of treatment.
- 2) If using racemic d/l cloprostenol, or dinoprost, in-

Group	Follicular size (mm)	Days to heat	1st insemination pregnancy rate (%)
Dinoprost 25 mg	11.17±0.433	3.7± 0.26	10
d/l cloprostenol 500	11.53±0.33	3.3 ± 0.21	30
d cloprostenol 150 μg	15.5±0.82	3.6 ± 0.31	40

Note: generic names are substituted for the trade names used in the original article.



crease the dose and also the cost of treatment

- 3) Get similar results, with no cost increases, using a standard dose (150 μ g) of d cloprostenol (Dalmazin)
- 4) If cost is not the object get the best results using 300 μ g of d cloprostenol (Dalmazin)

References (available on request):

- 1) Meziane *et al*, A clinical study of metritis in dairy cows in the region of Batna (Algeria) and their treatments using different therapeutic protocols, Vet World 6(1):45-48.
- 2) Montaser and El-Desouky, Effect of Dinoprost Tromethamine, Cloprostenol and d-Cloprostenol on Progesterone Concentration and Pregnancy in Dairy Cattle, (Continued on page 3)

Prostaglandin Dose and Recent Corpora Lutea

(Continued from page 2)

Journal of Agriculture and Veterinary Science (IOSR-JAVS), Volume 9, Issue 2 Ver. I (Feb. 2016), PP 64-67

3) Pérez-Marín *et al*, Oestrus Synchronisation in Postpartum Dairy Cows Using Repetitive Prostaglandin Doses: Comparison between D-Cloprostenol and Dinoprost, Acta Veterinaria 2015 Mar; 63 (1): 79-88

- 4) Stevenson *et al*, "Luteolysis and pregnancy outcomes after change in dose delivery of prostaglandin F2 α in a 5-day timed artificial insemination program in dairy cows," Kansas Agricultural Experiment Station Research Reports: Vol. 0: Iss. 2.
- 5) Valdecabres-Torres *et al*, Effects of d-cloprostenol dose and corpus luteum age on ovulation, luteal function, and morphology in non-lactating dairy cows with early corpora lutea, J. Dairy Sci. 95 :4389-4395
- 6) Wiltbank *et al*, Effect of a second treatment with prostaglandin F α during the Ovsynch protocol on luteolysis and pregnancy in dairy cows, J. Dairy Sci. 98:8644-8654
- 7) Young, Evaluation of Prostaglandin dose for NZ non-cycling dairy cows. NZVA Conference 19-22 June 2018

A Meal in the Bush

A forest ranger, trekking through a remote campground area caught a whiff of something burning in the distance. Farther along the trail he found an old hermit making his evening meal.

"What are you cooking?" the ranger asked.

"Peregrine falcon," answered the hermit.

"Peregrine falcon!" the shocked conservationist shouted. "you can't cook that, it is on the endangered species list."

"How was I to know?" the hermit questioned, "I haven't had contact with the outside world for ages."

The ranger told him he would not prosecute him this time, but he wasn't to cook peregrine falcon ever again.

"By the way," he asked, "what does it taste like."

"Well," replied the hermit, "I'd say it's somewhere between a dodo and a whooping crane."

Tapping

Late one night Nagy, taking a short cut through a cemetery, became frightened when he heard a tapping sound.

As he walked the tapping got louder and louder and his fright grew into terror..

Suddenly he came upon a man, crouched down, chiseling on a grave stone.

"Oh thank goodness," Nagy said with great relief, you frightened me half to death, I did not know what the noise was. What are you actually doing?"

The other man turned his face in the moonlight and said, "They spelt my name wrong."



Metabolase and Metabolase Forte Dosage

A common question with Metabolase has been, "how often should you give it?" In the past the answer has been rather empirical with allusions to extent of malaise, the convenience factor and maybe cost. However, thanks to support from Fatto we have some concrete recommendations that can be made.

First of all, while Metabolase and Metabolase Forte have been predominantly used for facial eczema cases



in NZ, and that is a very viable option, the major use in Europe is for cattle with ketosis, both clinical and subclinical. Ketosis can be very complex and there is often not one magic bullet that can fix it.

Propylene glycol based nutritional supplements, such as Acetol, have been the 'go to' remedies in New Zealand for decades and that is not about to change.

However such supplements alone are, more often than not, not enough for complete recovery and best results, here and abroad, are obtained with a multi-faceted approach.

In this vein there has been considerable research in Europe on the uses of creatinine and methionine together.

These have been far more effective given parenterally as they often do not survive being metabolised by rumen microorganisms when given orally.

Data show that it is not a case of either a propylene glycol based product or a methionine/creatinine based product but rather a situation where using both gives statistically better results.

Our pastoral farming and much larger herds make blanket treatments with either not practical from an economic point of view, hence the use of starter drenches as a preventative on a herd basis.

However there are always those cows at the bottom end that still suffer from subclinical, and even clinical ketosis. These are the targets for stronger therapy and the gold standard for them would be rigorous treatment with both a propylene glycol based product and a methionine/creatinine based product, i.e. Acetol and Metabolase.

As to a treatment regime it is now much simplified although slightly different for Metabolase as opposed to Metabolase Forte.

Metabolase itself has a few extra 'goodies' and is a more rounded therapy but has to be given in a 500 ml dose intravenously. This generally means veterinarian action, although many farmers are proficient at i/v injections.

Metabolase Forte has the essential ingredients in a much more concentrated form and must be given intramuscularly. Thus the dosing regimens are centred on convenience.

Jeong J-K et al, treated cows with 250ml Metabolase for three consecutive days after calving (plus oral propylene glycol) and found highly improved parameters and concluded, "Treatment of dairy cows with propylene glycol plus L-carnitine and methionine improved the chances of resolution of ketosis and increased

milk yield, while affecting neither the incidence of postpartum complications nor reproductive performance."

"Thus the dosing regimens are centred on convenience"

The trial work by Antanaitis, et al, showed significant benefits with one 500ml intravenous dose, plus oral propylene glycol, followed up by another seven days later.

Arslan et al got excellent results using Metabolase Forte, 5 ml/100 kg bodyweight, intramuscularly once per day for seven days, plus oral propylene glycol. This would suit a farmer situation better, whereas the Metabolase treatment would fit in well with veterinary administration.

When one looks at the trial work done it is quite evident that both Metabolase and Metabolase Forte in combination with propylene glycol give significantly better results than using propylene glycol alone, the only debate has been the dosage.



Good results were seen with two different Metabolase regimes, either 250 ml for three consecutive days or two injections of 500 ml, seven days

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Metabolase and Metabolase Forte Dosage

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apart. Similar results were seen with Metabolase Forte injected for seven consecutive days.

Hence for ketotic cows in the New Zealand pastoral situation it would be quite reasonable for the veterinarian to inject 500 ml of Metabolase intravenously then leave Metabolase Forte as a follow up treatment by the farmer for a few days.

All the benefits of correcting ketosis, including increased milk yield, should ensue.

References (available on request)

- 1) Antanaitis, et al, Effects Of Metabolase® On Several Blood Indices, And Productivity In Fresh Dairy Cows, Veterinaria Ir Zootechnica (Vet Med Zoot). T. 71 (93). 2015
- 2) Arslan et al. Effects of Combination of Asetylmethionine, L-
- 3) Jeong J-K et al, Effect of two treatment protocols for ketosis on the resolution, postpartum health, milk yield, and reproductive outcomes of dairy cows, Theriogenology 106 (2018) 53-59

Nutrition and Non Cyclers

A major reason for non-cycling in cows after calving is low nutrition. The follicle used at the first round of AI is developing in the transition period so any metabolic insult at transition can be detrimental to follicular development.

Subclinical metabolic disease can be insidious and not apparent until that time an animal is expected to be in season.

Nutrition is a major factor and so those cows that are not putting on condition or thriving are more likely to be among the non-responders when synchronisation programmes are instituted.

Some veterinarians in practice have claimed great response in low nutri-

tion non cyclers with the use of parenteral nutrition in the form of the EA product Hemoplex, an injectable vitamin and mineral mix.

While anecdotally very effective there is even better rationale for using another EA product in Metabolase Forte, contain creatinine and methionine.

It is not a label claim and controlled clinical trials have not been done with either product but it just makes pharmacological sense.

There is one interesting piece of work in sheep reproduction showing that the effect of using Metabolase on the male effect of ovulatory stimulation in prepubertal ewes. In short using Metabolase, at the same time

Carnitine, Vitamin E and Vitamin B12 on Some Clinical, Haematological and Biochemical Parameters in Cattle YYÜ VET FAK DERG (2008) 19(1): 9-14 (Abstract only)

Jeong J-K et al, Effect of two treatment protocols for ketosis on the resolution, postpartum health, milk yield, and reproductive outcomes of dairy cows, Theriogenology 106 (2018) 53-59

as introducing the rams, improves the ovulation rate, influences the response to the presentation of the preovulatory LH peak as well as the ovulation percentage.

While not conclusive proof, and it was Metabolase not Metabolase Forte used, it makes practical sense to try Metabolase Forte on those cows not cycling because their level of nutrition is low.

Reference:

Hernández-Marín et al, Ovulation Induction with Male Effect and a Commercial Energy Tonic in Prepubertal Pelibuey Ewes, Agrociencia 50: 811-823. 2016.

The Legacy

The miserly millionaire called a family conference.

"I'm placing a box of money in the attic," he said. "When I die I intend to grab it on my way up to heaven. See to it that no one touches it until it's my time to go."

The family respected his wishes. After his death his wife looked in the attic. The box was still there.

"The fool," she said, "I told him he should have left it down in the basement."



Biological Worm Control



Now for something completely different, Biological Worm Control. BioWorma has been dubbed a game-changer in worm control. It is a biological worm control product, which has the potential to save graziers and horse owners time and money, both through limiting stock losses and also reducing the need for chemical drenches for cattle, sheep, goats and horses.

After more than 20 years of research and development this new product has been approved by the Australian Pesticides and Veterinary Medicines Authority (APVMA) and now also by ACVM in NZ.

BioWorma uses a natural strain of fungus - Duddingtonia flagrans - which seeks out and 'traps' the larvae of many of the parasites that are common in horses and other grazing animals, including strongyles.

It acts by substantially reducing the numbers of infective worm larvae, including multi-resistant larvae, emerging from manure onto pasture. It will be of most benefit to pasture grazing animals and works best with rotational grazing systems.

Duddingtonia flagrans is a nematophagous fungus. It is found on pasture (rarely in soil) or in manure where it builds a microscopic net that traps, paralyses and consumes the juvenile stages (larvae) of parasitic worms and is highly host specific, only targeting parasitic nematodes.

Animals become infected when they eat pasture which has been contaminated with the larvae. The worms mature inside the animal and they reproduce by producing eggs, which are shed into the manure of the infected animals.

Inside the manure pats or piles on the pasture, the eggs hatch and the larvae develop through several stages into the infective larvae, which migrate out onto the nearby pasture. When this pasture is grazed by an animal, the infection is spread. In this way, the population of worms in the animal is maintained.

It has been estimated, at any one time, about 90% of the worms on a farm are present as larvae on the pasture and only 10% are living inside the animals.

The Duddingtonia flagrans spores pass through the digestive system and into the manure, and are activated when parasitic worm larvae become active.

When fed to animals, the thick-walled fungal spores remain inert (having no effect within the host animal) and resist digestion, passing through into the manure. There, they germinate and form trapping organs that capture, paralyse and consume emerging infective worm larvae, including multi-resistant larvae.

The good news is that BioWorma is not just another chemical dewormer, which worms can become resistant to. It's Duddingtonia flagrans, a natural fungus that actually eats the worm larvae in manure.

Larvae can become resistant to chemicals but not to being eaten.

Because this fungus is a very picky eater, it does not upset the balance of anything else in the environment, such as earthworms or soil nematodes. The fungus only consumes roundworm larvae in manure of grazing animals, so it won't work with poultry.

The spores have been thoroughly tested and are considered safe, non-toxic and residue-free.

Drenches currently used to fight intestinal parasites will be supported by BioWorma in reducing re-infestation onto pasture. It does more than just Barber's Pole, and it does more than just sheep... It's in a new class."

"Larvae can become resistant to chemicals but not to being eaten."

Breaking the parasitic worms' lifecycle will also reduce the need for chemical anthelmintic treatments which, in turn, will help slow down the spread of resistance to the available drugs.

Work over two decades involved 19 trials and three different safety studies - testing for everything from environmental effects, toxicology and residues, through to the simple questions of how to harvest thousands of tonnes of Duddingtonia flagrans spores and how to feed it to the livestock in a known dosage to then test the manure for the number of larvae remaining.

Given that BioWorma works through interrupting the crucial re-infestation stage of the parasites' lifecycle and reducing the amount of re-infection from contaminated pasture it works best when the livestock are moved onto fresh pasture.

The product works particularly well within a rotational grazing system.

It's also important to understand that the fungus does not consume 100% of the larvae, so things like pasture rotation are still important. Animals have lived with parasites inside their bodies since the beginning of time, and a natural refugia is vital in the reduction of resistance to chemical drenches.

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Biological Worm Control

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The fungus reduced the worm load enough that animals did not need chemical deworming.

BioWorma is registered in Australia and New Zealand by International Animal Health and is marketed and distributed to New Zealand veterinarians by Ethical Agents Veterinary Marketing Ltd.

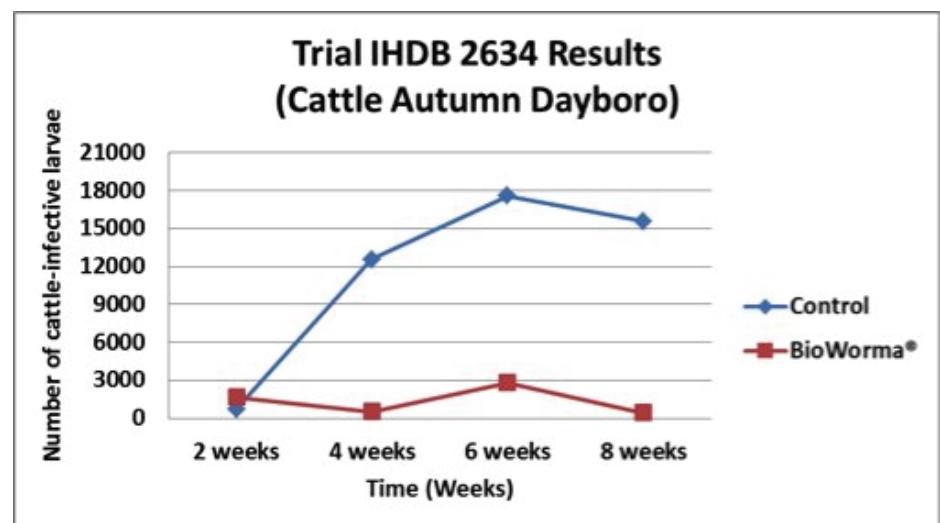
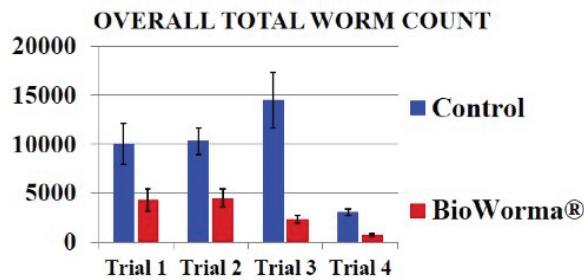
Sheep trials

These typically took place over a 4-month period and the supplement containing the fungus was fed on a group basis, rather than individual feeding. They demonstrated an average reduction of about 70% ($P<0.05$) in worm burdens in the tracer lambs that were used to measure the infectivity of the pasture (Healey, Lawlor et al., 2018a). A summary of the results is shown in the Figure below (worm burdens in the tracers at the end of each trial)

Cattle trials

In these trials, efficacy was measured by direct counting of infective larvae on pasture surrounding faecal pats obtained from control and BioWorma-treated cattle over an 8-week period. Typical results are shown below. Over all four trials the reduction in larval numbers due to treatment averaged 81% ($P<0.01$) (Healey, Lawlor et al., 2018b).

TOTAL WORM COUNTS OF TRACER SHEEP AT END OF EACH TRIAL



References (Available on request)

- 1) Healy *et al*, Field evaluation of *Duddingtonia flagrans* IAH 1297 for the reduction of worm burden in grazing animals: Tracer studies in sheep Veterinary Parasitology 253 (2018) 48–54

2) Healey *et al*, Field evaluation of *Duddingtonia flagrans* IAH 1297 for the reduction of worm burden in grazing animals: Pasture larval studies in horses, cattle and goats Veterinary Parasitology 258 (2018) 124–132

Three Wishes

A despondent woman was walking along the beach when she saw a bottle in the sand. She picked it up and Whoosh! A big puff of smoke appeared.

"You have released me from my prison," the genie told her. "To show my thanks I will grant you three wishes, but take care, for each wish your mate will receive double of what you request."

"Why, that bum left me for another woman."

"That it how it is written." said the genie.

The woman shrugged and asked for a million dollars. There was a flash of light and a million dollars appeared at her feet. At the same instant in a far off place her wayward husband looked down to see twice that amount at his feet.

And your second wish?"

"Genie, I want the world's most expensive diamond necklace." Another flash of light and she was holding the precious treasure and her far off husband was looking for a gem buyer for his latest bonanza."

"Now for my last wish," she said, "scare me half to death!"



Top 10 jokes from the 2018 Edinburgh fringe

- 1) Working at the job centre has to be a tense job – knowing that if you get fired, you still have to come in the next day. Adam Rowe
- 2) I had a job drilling holes for water – it was well boring. Leo Kearse
- 3) I took out a loan to pay for an exorcism. If I don't pay it back, I'm going to get repossessed. Olaf Falafel
- 4) In my last relationship I hated being treated like a piece of meat. She was a vegan and refused to touch me. Daniel Audritt
- 5) What do colour-blind people do when they are told to eat their greens? Flo & Joan
- 6) I've got a new job collecting all the jumpers left in the park at
- 7) the weekends, but it's not easy. They keep moving the goalposts. Darren Walsh
- 8) Trump said he'd build a wall but he hasn't even picked up a brick. He's just another middle-aged man failing on a DIY project. Justin Moorhouse
- 9) I lost a friend after we had an argument about the Tardis. I thought it was a little thing, but it seemed much bigger once we got into it. Adele Cliff
- 10) Why are they calling it Brexit and not The Great British Break Off? Alex Edelman
- I think love is like central heating. You turn it on before guests arrive and pretend it's like this all the time. Laura Lexx

