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By Michael I. Lindinger, PhD

EQUINE LEAKY GUT SYNDROME

— part 3

IN THE THIRD PART OF THIS ARTICLE INVESTIGATING EQUINE LEAKY GUT SYNDROME (LGS), WE EXAMINE THE ROLE OF THE INTESTINAL MICROBIOME AND HOW PROBIOTICS AND PREBIOTICS HELP MAINTAIN BARRIER FUNCTION AND IMPROVE YOUR HORSE'S HEALTH.

The microbiome plays an important role in modifying how a horse's gastrointestinal tract (GIT) functions and responds to pathogenic challenges. In the third part of this article on equine leaky gut syndrome (LGS), we'll look at how the intestinal microbiome (see sidebar on page 42) may be manipulated, through diet and use of probiotics and prebiotics, to improve GIT health and barrier function.

FEEDING THE GIT

Bacteria and yeasts are used as microbial feed additives. If these additives are dead or inactivated, they are considered prebiotic and not probiotic. The most commonly-used genera for probiotics are *Lactobacillus*, *Bifidobacterium* and *Enterococci*. We will also consider a strain of *Bacillus subtilis*. The equine GIT does not naturally contain high levels of these genera. However, probiotics are not required to colonize the GIT in order to obtain beneficial effects. In many animals, the ability of probiotics to colonize the GIT is not host-specific. Therefore, strains are selected on the basis of their beneficial effects, and not their origin.

Good evidence-based research supports the positive effects of probiotics and prebiotics on intestinal barrier function and health in laboratory and production animals, but results obtained to date in healthy and diseased horses remain inconclusive – additional and improved research is needed.

Bifidobacterium, Lactobacillus and Bacillus subtilis

Different species of live *Bifidobacterium* and *Lactobacillus* have had positive effects on animal models with intestinal infection and inflammation. In several studies using mice, *Bifidobacteria* showed a range of beneficial effects, including enhanced intestinal immune system support, improved survival against pathogens, improved intestinal histology, and reduced inflammation and leakiness.

Bacillus subtilis is a naturally-occurring species of bacteria commonly found in soil, but also present in the GIT of many animals, including horses. In horses, the *Bacillus* species represent less than 1% of the microbiome, but they may play a larger role than their numbers indicate. The PB6 strain of *B. subtilis* was

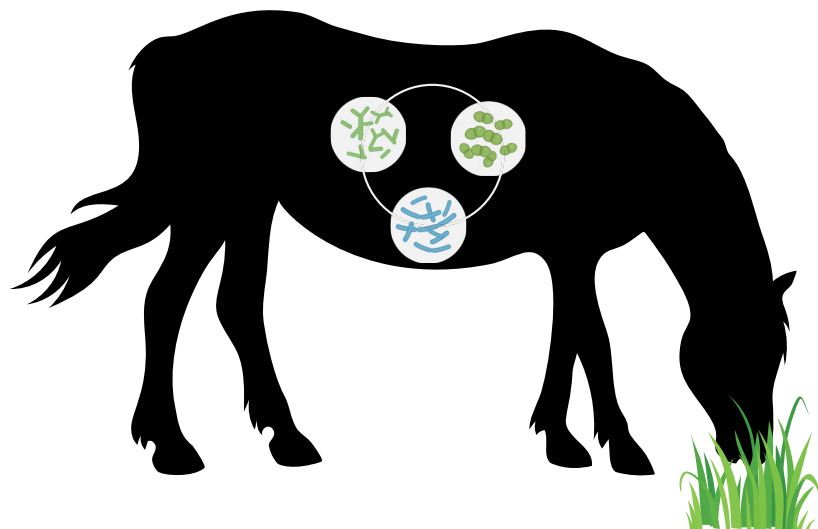
identified in the GIT of stressed poultry nearly 20 years ago, when found to be associated with increased survival rates of poultry suffering from the GIT disease necrotic enteritis. This strain has been developed and extensively tested for function and safety. PB6's mechanism of action appears to operate through its ability to produce and secrete an active molecule into the GIT that hinders the proliferation of *Clostridium* and other pathogenic species. PB6 has been used in research studies using poultry and pigs. The results included improved feed utilization, reduced number of pathogenic bacteria, improved IEC morphology, and improved tight junctions between IECs.

PB6 was therefore tested against strains of pathogenic bacteria common to horses. In many animals, *Clostridium* species are associated with gastrointestinal distress. *C. difficile* is common, and one of the most important causes of diarrhea and enterocolitis in foals and adult horses. These species produce toxins that break down the structural integrity of the mucosal barrier and IECs, resulting in LGS. In a lab study of five common equine pathogenic bacteria (*C. difficile*, *C. perfringens*, *R. equi*, *S. equi*, *Salmonella typhimurium*), PB6 resulted in the inhibition of growth of all pathogenic species. Routinely providing the PB6 strain of *B. subtilis* as part of the horse's diet may help prevent the occurrence of leaky gut, or reduce its severity.

PROBIOTIC AND PREBIOTIC YEASTS

Nonpathogenic *Saccharomyces cerevisiae* and *S. boulardii* of various strains are the primary probiotic and prebiotic yeasts used. Some inactivated yeast products also used as prebiotics include those that are rich in mannan oligosaccharides and/or beta glucans – both of which are associated with nutraceutical benefits in animals. Research under controlled conditions using laboratory animals provides good evidence for the efficacy of probiotic and prebiotic yeast supplements – including preservation of intestinal barrier integrity, improved intestinal morphology, reduced intestinal damage, stimulation of IgA production, improved inflammatory profile, reduced weight loss, and enhanced survival.

These positive results led to research in healthy horses and in those with gastrointestinal disease. In a randomized, blinded, placebo-controlled clinical trial, horses with acute colitis – but supplemented with *S. boulardii* – had a shorter duration of diarrhea compared to non-supplemented horses, although the duration of loose feces was similar in both groups. In other studies, a seeming lack of efficacy was attributed to difficulty in standardizing treatment, and a possible lack of colonization by *S. boulardii* in the GIT. It appears the beneficial effects of these yeasts may only



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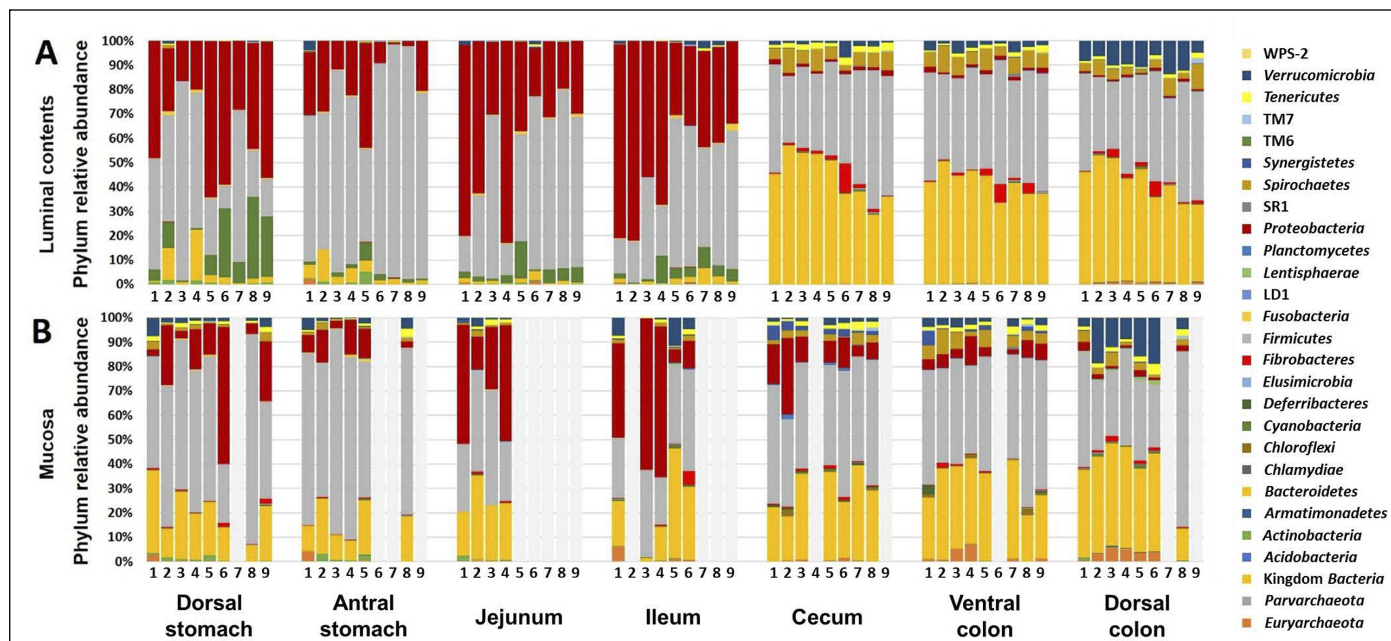
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A microbiome map of the phyla resident in the healthy equine GIT. The horse's GIT contains as many as 500 different species of microbiota from 27 different phyla.



From Ericsson et al. (2016) PLOS ONE 11(11): e0166523.

THE EQUINE MICROBIOME


The microbiome refers to the microbes living within the gastrointestinal tract (GIT). These living organisms include bacteria, yeasts, fungi and archaea. The microbiome within each horse is unique, but healthy horses show similar trends. *Bacteroidetes*, *Proteobacteria*, *Verrucomicrobia*, *Actinobacteria* and *Spirochaetes* contribute up to 15% each to the microbiome. With gastrointestinal diseases, however, microbiota dysbiosis (a microbial imbalance) is characterized by substantial shifts in the phyla. Many GIT diseases are characterized by an increased abundance of *Fusobacteria*, with little or no difference in the abundance of *Lactobacillales*.

In a healthy GIT, the populations of beneficial microbiota are high, which keeps the populations of pathogenic microbiota in check. These latter microbiota are called "pathogenic" because some of the products of their metabolism are toxic to IECs, immune cells, and to beneficial microbiota. High-starch diets, sudden changes in diet, medications, excessive stress and ingested pathogens can all result in increased populations of pathogenic microbiota and LGS.

One nutritional strategy, therefore, is to ensure the GIT is regularly provided with the kind of probiotics and prebiotics that can support the populations of beneficial microbiota, while suppressing the population of pathogenic microbiota. Probiotics (pro = good, biotic = alive) are simply living biological organisms, mainly bacteria and yeasts, that are good for GIT health. Prebiotics are compounds that provide nutritional substrates to support beneficial microbiota, resulting in the increased growth, proliferation and metabolism of beneficial microbiota. Beneficial microbiota will also produce molecules that combat pathogenic microbiota. Balance is key – it's not desirable for all pathogenic microbiota to be destroyed.

persist during the period of administration, and therefore consideration needs to be given to long-term feeding.

IN CONCLUSION...

Probiotics and prebiotics can be supplemented in a horse's normal diet with the goal of better maintaining or repairing GIT barrier functions. While more research in horses is needed, use is indicated from animal studies of intestinal disease. The safety of commercially-available probiotics and prebiotics is high, and large amounts and repeated dosing do not appear to have harmful effects. Most are considered safe by regulatory authorities when used as intended in horses and other animals. 

Michael Lindinger (PhD) is the president of the Nutraceutical Alliance. A former professor at the University of Guelph, he is involved in animal health research and nutraceutical product development. Correspondence: Dr. Mike Lindinger, email: michael@nutraceuticalalliance.ca