BAD BUG Basics

PARASITE PRIMER—PART 1

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It seems that every year, major equine publications take on a virtually impossible task. They publish an omnibus article on equine parasitology that attempts to describe the biology of everything from pinworms to stable flies, discuss the numerous ways in which parasites can harm equine hosts, list the multitude of drugs available for treating parasitic infections, and present a variety of control strategies, all in one user-friendly package.

Like most areas of applied science, equine parasitology is simply too broad and too complicated to be covered adequately in a single article. So in an effort to really do justice to the topic in comprehensive detail, we welcome you to the first of 12 monthly articles on parasite-related topics. To implement this project, *The Horse* has enlisted the aid of three recognized experts in equine parasitology.

Denny French, DVM, MS, Dipl. ABVP, currently is jointly appointed as a

ANNE EBERHARDT

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professor in veterinary clinical sciences at the Louisiana State University (LSU) School of Veterinary Medicine and professor of veterinary science at the Louisiana Agricultural Experiment Station, while maintaining an active role in equine research and ambulatory practice. French's primary research interests have been in the field of equine herd health, especially parasite control programs. Collaborating with Tom Klei, PhD of LSU, French has been involved with the development of numerous anthelmintics (dewormers) and has taken the research information directly into his practice.

Ray Kaplan, DVM, PhD, has been an assistant professor at the University of Georgia College of Veterinary Medicine since 1998. He teaches and does research in large animal parasitology. Kaplan earned his PhD in veterinary parasitology in 1995 at the University of Florida. The goals of his research are to measure, understand, and solve the problems presented by drug-resistant parasites and include three major areas of concentration: 1) Measuring the prevalence of drug resistance; 2) studying the molecular basis of drug resistance; and 3) studying and developing novel and sustainable approaches to parasite control. Much of this work is focused on equine parasites.

Craig Reinemeyer, DVM, PhD, is president of East Tennessee Clinical Research in Knoxville, Tenn. He earned his PhD in veterinary parasitology from The Ohio State University in 1984, and he was a faculty member of the University of Tennessee College of Veterinary Medicine from 1984 to 1998. His major research interests are clinical development of veterinary pharmaceuticals and strategic control of internal parasites of grazing animals.

Let's start by taking a look at how parasites differ from other infectious organisms that damage horses, and go on to explore the historical perspective on equine parasite control—where we've come from, and how far we've yet to go.

What Makes A Parasite?

The world of infectious diseases is inhabited by an incredibly diverse cast of characters, and the list seems to be growing every year. Organisms such as bacteria, viruses, fungi, roundworms, and lice are familiar to most readers. However, the modern list of infectious agents also includes the prions that are responsible for "mad cow" disease, protozoa that induce malaria and equine protozoal myeloencephalitis (EPM), and ehrlichia, which are spread by ticks and other vectors and cause numerous, severe diseases of pets and humans, including Potomac horse fever.

The field of parasitology focuses on those infectious organisms that are considered to be "animals," as opposed to "non-animals" (bacteria, rickettsia, and fungi), or viruses or prions, which are too simple to be either.

The list of generally recognized parasites includes protozoa; flatworms (tapeworms and flukes); nematodes (roundworms); a few rare, worm-like organisms; and a diverse group of arthropods that includes lice, fleas, flies, ticks, and mites.

ANNE EBERHARDT

Determining your horse's fecal egg counts (FEC), or number and type of parasite eggs in the feces, helps you determine what parasites infest him and how heavy his parasite load is.

There are three important ways in which most (but not all) parasitic worms differ from bacteria and viruses:

- Parasitic worms do not amplify their numbers within the host;
- Each generation of parasites must return to the environment to undergo essential changes; and
- Immunity to parasites is rarely absolute.

What do we mean by "no amplification?" Bacteria and viruses are able to increase their numbers exponentially within a host animal. When a young horse ingests the bacterial agent of strangles (*Streptococcus equi*) from a contaminated water bucket, for example, clinical signs do not develop until after those bacteria go through numerous divisions and increase their numbers by millions. Influenza viruses infect cells in the respiratory tract and similarly induce the production of multiple copies, each of which will infect a new cell and do the same thing. In both cases, disease results when sufficient numbers of cells have been damaged to cause clinical signs.

In contrast, when a horse swallows one ascarid (roundworm) egg, one and only one adult ascarid will become established as a consequence of that exposure. The same rule applies for pinworms, strongyles, bots, and most common internal parasites of horses.

Parasitic Disease

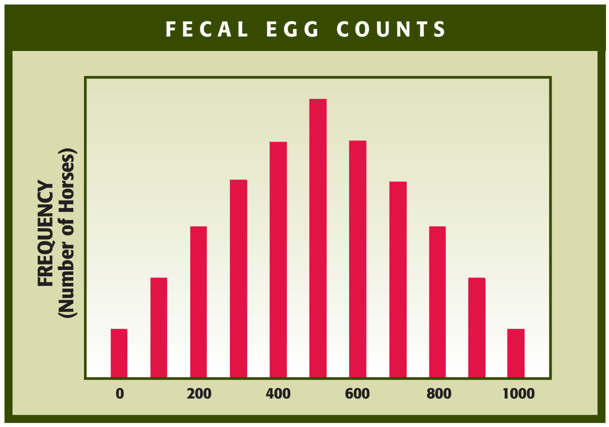
Just as with bacteria and viruses, clinical parasitic disease results only when the numbers of infectious organisms reach critical levels. With agents that can amplify within the host, it's simply a matter of time. With non-amplifying parasites, however, numbers (and thus disease) are directly related to the level of exposure. Horses in clean environments pick up few parasites and stay healthy, while horses in contaminated environments acquire more parasites and are at greater risk of disease. (This is the magic key to parasite control and will be discussed in great detail later in the series.)

In contrast, protozoal parasites, which are tiny single-celled organisms, can amplify their numbers within the host. The protozoal agent of EPM *(Sarcocystis neurona)* is a good example, but even this critter conforms to the second general characteristic of parasites—it must return to the environment to undergo essential changes, rather than being transmitted directly from horse to horse.

The word "contagious" implies that a disease can be transmitted directly from one infected animal to another. Thus, a horse with influenza might be directly responsible for infecting others in the herd through droplet spray from a cough or nasal discharge. But not all infectious organisms are contagious. In the case of the vast majority of parasitic infections, a susceptible horse could be housed in the same stall with one harboring any number of parasites without the slightest risk of becoming infected.

Each parasite generation must return to the environment for some essential change or developmental step, a process traditionally termed a "life cycle." Female strongyles (bloodworms), for instance, lay eggs within the gut of the horse, and these eggs pass into the outside environment with the manure. Under conditions of suitable temperature and humidity, strongyle eggs hatch and go through three development stages before they are able to infect another horse. The timing of the life cycle is specific and absolutely essential for the development of the parasite.

One exception to this rule is lice, which lay eggs, hatch babies, grow old, and die, all on the same animal without returning to the environment between generations. This exclusive association is so critical to lice that most species have claws that help them to hang onto the hair shafts of the host.



Horses differ in their ability to handle parasite infestation; in general, a few horses will have high fecal egg counts (FEC), a few will have low or zero FEC, and the majority will be grouped around the average.

Immunity

The final unique characteristic of parasitic infections is that host immunity is rarely absolute or entirely protective, unlike many bacterial or viral diseases.

When your horse is vaccinated with tetanus toxoid, for instance, you can be quite confident that any contaminated puncture he might acquire over the next year will not result in a fatal case of lockjaw. Have you ever wondered why we don't have a vaccine for small strongyles? It's because few horses in nature ever develop effective immunity against these parasites.

That isn't to say that immunity doesn't occur, but it's probably revealed in less obvious ways. One school of thought holds that immunity against parasites is manifested as protection against disease rather than against infection. Thus, if a 10-year-old mare and a yearling filly were exposed to the same parasite challenge, both would become infected, but the older, experienced horse would be less likely to suffer weight loss, colic, and other side-effects of a parasitic infection because she was somewhat protected as a result of prior exposure.

Individual horses clearly differ in their ability to handle parasitic infections, as exemplified by strongyle fecal egg counts (FEC). If one examines the fecal egg counts of a herd of horses that has not been dewormed for several months, those egg counts will assume an overdispersed distribution (see "Fecal Egg Counts" below). This means that parasites are not evenly distributed among the herd, but rather, most parasites congregate in a small percentage of the herd. In general a few horses will have high FEC, a few will have low or zero FEC, and the majority will be grouped around the average of all counts. The few horses with high FEC will actually be producing the majority of all eggs contaminating the pastures.

If egg count measurements are repeated the following year, one would find that most horses occupied their similar, prior rankings. In other words, the few horses with low counts in 2002 would likely occupy the lower end of the curve again in 2003 (in the absence of treatment). The individual differences in egg counts are considered to be manifestations of differences in immunity.

Horses develop nearly absolute acquired immunity to two parasites: *Strongyloides westeri* (threadworms) and *Parascaris equorum* (ascarids or roundworms). Both of these are rarely seen in horses after six months and two years of age, respectively. These are exceptions to the rule, however; few other domestic animals are able to control their parasites as effectively as horses manage these two.

Because horses apparently don't develop effective immunity against more harmful parasites such as large and small strongyles, controlling these parasites becomes a lifelong challenge for horse owners. Stay with us over the course of this series for some detailed information about how this can be accomplished.

A Short History of Deworming

Mankind has been aware of the impact of parasites almost as long as we've practiced animal husbandry. But for many centuries, efforts to tackle the problem were at best ineffective, and at worst life-threatening for the horse as well as the worms!

A 1999 paper in the journal *Veterinary Parasitology* by Gene Lyons, PhD, and Sharon Tolliver, BS, of the Gluck Equine Research Center at the University of Kentucky; and Hal Drudge, DVM, professor emeritus of the University of Kentucky, took a look at equine parasite control from a historical perspective and described several rather questionable early "cures" for worms.

Back in 1610, veterinary surgeons were inclined to use bloodletting—drawn from the horse's palate—to address parasites, with the notion that making the horse drink the blood afterward "would kill the worms and help most inward maladies." (How exactly one induces a horse to drink its own blood is not described, which is perhaps a mercy!)

Other alleged anthelmintics in history include chicken eggs, chicken dung, human feces, the guts of young hens or pigeons, black (carbolic) soap, aniseed, aloe, antimony, licorice, linseed (flaxseed), and even quicksilver (mercury). Horse owners were cautioned not to use some of these treatments in pregnant mares because they often triggered "violent purges."

Tobacco was another popular home remedy for internal parasites, and one that some horses readily ate. But although nicotine does have some anthelmintic properties, Kaplan notes that it's extremely toxic in the doses needed to kill worms. "Just giving a plug of tobacco isn't going to do anything, and the correct dose would make a horse quite sick," he says.

There are a number of herbs to which anthelmintic properties have been attributed, but they tend to have the same problem—what's poisonous to the worms is also

DOROTHY WOODWARD

Prior to the 1960s, horse owners had no set deworming routine. They just tended to administer an anthelmintic when they noticed signs of a heavy parasite load, such as a dull coat, a pot belly, frequent colic, or weight loss. Nowadays, most farms use deworming as preventive rather than treatment.

poisonous to the horse. Wormwood (artemisia) was named for its antiparasitic qualities, but it is also the basis of the "tonic" absinthe, much abused in Victorian times (and responsible for some cases of brain damage and death among its devotees). Wormseed, a.k.a. *Chenopodium anthelminticum*, is another plant long pressed into service (the oil pressed from its seeds was used to dose horses and other livestock). There is documentation from the early 1900s indicating that oil of *Chenopodium* was a popular deworming treatment for both horses and humans, but it has also been described as causing terrible side-effects.

Colonel Floyd Sager, an equine practitioner who wrote a book reflecting on his almost 60 years as a veterinarian, recalled that horses dosed with oil of *Chenopodium* often would not eat or drink for three to four days afterward and dropped significant amounts of weight.

Tobacco was a popular home remedy for internal parasites in the past, and one that some horses readily ate. But although nicotine does have some anthelmintic properties, it's extremely toxic in the doses needed to kill worms.

The first "chemical" cures for worms came in the form of carbon tetrachloride and carbon disulfide, both in regular use by the early 1900s for eliminating ascarids and bots. They had some effect, but were quite toxic. It wasn't until the 1940s that the modern age of deworming began with the introduction of phenothiazine.

"It wasn't a great drug, either," says Kaplan, "as it was pretty toxic. But it represents the first of a string of anthelmintic drugs introduced to the market at the rate of about one a decade from then on."

Phenothiazine did have the virtue of being the first drug active against strongyles (bloodworms), the most destructive class of equine parasites. It continued to be used into the early 1960s, by which time strongyle resistance to it was documented both in the United States and England. It was also the first drug to be made available as a daily dewormer when top-dressed on the feed. This low-level administration didn't remove strongyle infestations, but it did block or reduce transmission of the worms by affecting their reproduction.

Piperazine, which arrived in the 1950s, was the first medication with broad-spectrum activity (meaning it was effective against more than one type of equine worm). Useful in combating ascarids, small strongyles, and pinworms, it still wasn't effective against large strongyles. A mixture of piperazine, carbon disulfide, and phenothiazine made available in the 1950s and 1960s addressed the problem of toxicity to some degree by reducing the amount of each drug needed. This deworming "cocktail" had to be administered as a large-volume drench given by nasogastric tube, an unpleasant and slightly risky procedure that required a visit from the veterinarian.

Organophosphates—including trichlorfon and dichlorvos—showed up on the market in the early 1970s, along with levamisole, a drug which, while useful for some other types of livestock, quickly proved to be too toxic for horses. Organophosphates, which are pesticides, were useful against bots, pinworms, and ascarids, but not strongyles. So, they also were mixed with piperazine and phenothiazine to attack more worm species. But with a very narrow safety margin, and extreme toxicity when other species (such as birds) were exposed, these drugs were tricky to use at best.

The 1960s and 1970s saw parasite control take a giant leap forward with the discovery of the benzimidazoles, a class of drug that had unparalleled broad-spectrum action and could be delivered at a much lower dose rate, with a much wider margin of safety, than anything previously available. Thiabendazole was the first of these drugs to hit the market, followed quickly by cambendazole, fenbendazole, mebendazole, oxfendazole, and oxibendazole. Many of these remain available today.

The 1970s also took deworming out of the exclusive province of the veterinarian. With the introduction of convenient paste formulations, horse owners could administer dewormers themselves.

Pyrantel (known to most of us as Strongid) was the next class of drug to surface in the 1970s. It provided an alternative to the benzimidazoles when resistance began to be a problem, and it had a broad margin of safety. It also earned a reputation for being effective against tapeworms when given in a double or triple dose, although it was never officially labeled for that use.

But the real "silver bullet" in parasite control was ivermectin, introduced in the early 1980s. The first drug to kill migrating larval stages of worms, as well as the adults, in a regular dosage, it was (and remains) extraordinarily safe and dramatically effective against virtually every class of nematode and arthropod, including external parasites. Ivermectin would quickly come to dominate the market, particularly once it became available in an easy-to-use paste formulation (it was originally introduced as an injectable, which proved not to be the ideal format for horses).

Ivermectin would prove almost *too* good. Thanks in part to throttled-back research and development programs, it would be another 20 years before any new anthelmintics came down the pike. Moxidectin, in the same drug "family" as ivermectin, was developed as a horse dewormer in the late 1990s. It is the first drug shown to be effective at a single dose in killing the encysted larval stages of small strongyles hiding in the horse's intestinal wall, but has a narrower safety margin than ivermectin. Kaplan notes that "there are no reports of toxicity with moxidectin when administered at a correct dose."

The Evolution of Rotation

Prior to the 1960s, Kaplan says, horse owners had no set deworming routine. They just tended to administer an anthelmintic when they noticed signs of a heavy parasite load, such as a dull coat, a pot belly, frequent colic, or weight loss. An article published in the *Journal of the American Veterinary Medical Association* (JAVMA) in 1966 changed all that. In it, parasitologists Lyons and Drudge looked at worm biology, egg output, and worm epidemiology in horses, and they recommended a deworming routine of every six to eight weeks with thiabendazole (together with other various drugs in combination) to minimize egg shedding on pasture. Preventing the pasture from becoming heavily re-infected with worms was a new idea, and it became deeply embedded as a parasite control routine.

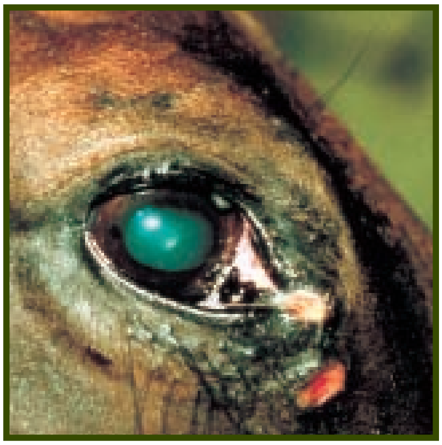
But as Kaplan points out, "That protocol was designed at a time when horses were loaded with all sorts of worms. Ninety percent of equine colics at the time were related to large strongyles. The deworming routine proved extraordinarily successful, and colic incidence dropped dramatically. It was a chemical assault which changed worm populations in domestic horses forever.

"Then ivermectin came along in the 1980s, killing all stages of worms rather than just the adults," Kaplan continued. "Parasites in horses became much less common. With a diligent routine, you could totally prevent large strongyle egg shedding onto pastures. As a result, *Strongylus vulgaris*, once the most common and important species of large strongyle, has become an endangered species in managed horses. And other problems, such as the summer sores caused by *Habronema spp.*, are far less common than they used to be."

However, with these changes have come new problems. Small strongyles are now recognized as the most important equine parasites, and drug resistance is making it increasingly difficult to adequately control these worms.

With resistance to phenathiazine first recognized in the late 1950s, and to thiabendazole just a few years after that, the idea of rotating different chemical classes of drugs was introduced. It also was eagerly accepted, and fiercely adhered to over the following decades.

"Rotation has become accepted as what you have to do," says Kaplan, "and the concept is important, historically. But over the years, resistance has become so prevalent-except against ivermectin, which remains a bit of a mystery—that rotation now means you're often failing to adequately control parasites even when you treat frequently. We've studied farms that follow the most common protocol, which is every eight weeks with a different drug, and found that the horses on many farms using such a program essentially only get two effective dewormings a year. Those are the times they're dosed with ivermectin. The rest of the treatments do little to control small strongyles, leading us to believe that traditional rotation is no longer the best approach."



COURTESY DR. DENNIS BROOKS

With regular deworming, problems such as the summer sores caused by *Habronema spp.*, are far less common than they used to be.

Several factors are continuing to contribute to drug resistance, which brings us to something of a 21st Century crossroads in parasite control. Should we depend on the now tried-and-true ivermectin and moxidectin and let older drugs fall by the wayside? Or will putting all of our eggs in one basket prove to be a massive mistake?

One thing is certain—it's time for a major re-evaluation of our parasite control routines. Stay tuned as we take the series in-depth over the next 11 issues and explore the best options for our horses' health.