



Horse Care

Endotoxemia And Colic

by HEATHER SMITH THOMAS

Colic is a leading cause of death in horses. Colic itself is simply abdominal pain, but can be caused by a variety of factors, some of which are quite dangerous for the horse. One of the reasons colic can be fatal is development of endotoxemia in a high percentage of cases. Endotoxemia is the same villain that can make some cases of laminitis, retained placenta, Potomac Horse Fever or septicemia deadly.

What Is Endotoxemia?

Endotoxins (the term itself means inner poisons) are toxic components of gram negative bacteria that reside in the intestines of all animals. The endotoxins are part of the outer cell wall of these bacteria. As explained by Dr. James N. Moore, DVM, PhD, University of Georgia, "The bacteria are necessary for normal gut function and digestion. As bacterial populations turn over (as they grow and then die) the cell walls break up, releasing the toxins. These toxins are always present, contained within the lumen of the intestine."

The intestinal wall provides a safe barrier so toxins do not have access to the rest of the body. Under normal conditions, they have no ill effects on the animal, says Moore. In the healthy gut there is always a mix of gram positive and gram negative bacteria, working together to ferment and break down the horse's feed.

If something happens to compromise the gut wall, however, such as the blood supply being interrupted by intestinal displacements or twists, or the intestinal wall becoming inflamed, the mucosal barrier very rapidly breaks down, and the bacterial toxins can get out of the intestine and into the blood circulation, he explains. If the harmony of bacterial action in the tract is disrupted by a drastic change in feed, the bacterial balance can also change. Large numbers of gram negative bacteria may die off at once, releasing an unmanageable amount of endotoxin.

There are a number of things that can damage the intestinal lining, allowing endotoxins to enter the bloodstream. Condi-

tions that cause inflammatory response in the gut wall include enteritis, colitis and certain bacterial diseases. If the inflammatory and immune systems then over-respond to the presence of the toxins, endotoxemia is the result. Various cells in the body release inflammatory substances to help fight the invasion. This response, in moderation, is necessary for destroying bacteria that cause disease. But if the horse's immune system over-reacts (which happens in endotoxemia), the result is tissue destruction, endotoxic shock and possible death of the horse.

The body frantically unleashes all its weapons. Clotting occurs in small blood vessels and the tissues they serve become starved of vital nutrients. The endotoxins stimulate production of chemicals that cause the cells lining the capillaries to contract, leaving "holes" for plasma to seep through. This leads to edema (fluid in the tissues) and subsequent decrease in total circulating blood volume, low blood pressure and reduced blood flow back to the heart. As the blood volume falls, the progressive lack of oxygen to the tissues results in shock, collapsed blood vessels, kidney failure and death, unless the condition is quickly reversed.

Signs of endotoxic shock are increased heart rate, weak pulse pressure, dehydration, cold feet and ears (due to circulatory failure), darkening of the gums and other mucous membranes and increased respiratory rate (fast and shallow). As the condition worsens, respiratory rate slows and the animal slips into a coma. The farther this condition progresses, the harder it is to reverse it, and the animal may die.

Research At University Of Georgia

The University of Georgia has pursued several aspects of endotoxemia, particularly as it pertains to colic. Dr. Cynthia Trim, the anesthesiologist at Georgia, has been working with colic surgery cases for 30 years and says endotoxins are already in the bloodstream of 25 to 40 percent of the horses with colic who come to university clinics for surgery.

Horses have a better chance of survival if they are not suffering from severe endotoxemia at the time of surgery. Trim says there is a higher success rate with colic surgery now, partly because people are bringing horses in sooner—they are not so ill yet. Her study shed more light on the status of the horses as they come into surgery, to help detect the ones who need special treatment to help counteract the effects of endotoxins.

Dr. Trim also did a two year study testing horses' blood before and during surgery, checking blood samples for endotoxin levels. She found that some horses become much worse during surgery; some with very low levels of endotoxin at the beginning surge massively during the operation. She is convinced that manipulation and handling of the intestine during colic surgery increases the risks of endotoxemia, promoting more movement of harmful endotoxins.



A horse in endotoxic shock with the typical symptoms of being very dull and depressed

“When we anesthetize horses, we often see a change in the animal while the surgeon is operating. I wanted to find out if there was, in fact, further endotoxin release during the surgeon’s manipulations. There’s been work done to show that the presence of endotoxins before surgery makes quite a difference in how well the horses do afterward. I was sampling the horses before the surgeon started, and every 30 minutes during the surgery. I was surprised how few were endotoxemic at the first, but endotoxin is very short-lived in the body. Once it’s there, however, it has set off the train of events that is harmful to the horse,” she says.

“A proportion of horses did have endotoxin after the surgeon started manipulating the bowel; a horse can have no endotoxin in the blood just before surgery, but moving the bowel around can cause endotoxin release into the circulation,” says Trim.

“Regarding cardiovascular deterioration during surgery (which is one of the problems with endotoxemia), we can now detect this as it starts and deal with it. In the last 15 years, there have been many new drugs available that we can use to improve cardiovascular function. Drugs like dopamine, dobutamine and blood expanders like hypertonic saline are useful to bolster the cardiovascular system, counteract the ill effects of endotoxemia and keep horses from going into shock,” she says.

“Endotoxin sets off a cascade of events; if more is released into the circulation, the horse is potentially at greater risk. Other drugs, however, like the non-steroidals Banamine, will counteract this to a large extent. Since most horses already have this on board before going to surgery, it acts as one kind of blocker, even though more endotoxin is being released,” she says.

“Many of the horses get dobutamine and hypertonic saline right from the beginning of anesthesia, so we are fending off some problems before they start. Still, we occasionally see an animal that has trouble during surgery, especially if the underlying problem involved the colon. When the surgeon untwists the colon, the horse’s condition can deteriorate in front of your eyes, even though you are doing everything you can to counteract shock. Blood flow to the bowel has been interrupted and when the surgeons untwist it and restore circulation to the bowel, toxic substances, including endotoxin, can enter the circulation,” she says.

“This doesn’t happen so often now; you are less likely to have to stand there and watch a horse fade away in front of you—we can usually do something more about it. Success rate for colic surgery is improving; 20 years ago it was about 60 percent survival, but our most recent figures show 90 percent of horses survive colic surgery and go home.”

Dr. Trim says, “Our work has made me realize that the horse’s condition through surgery is an ongoing process. We get the horse in the best shape we can before the surgery—we give fluids, all these drugs and antibiotics—but we are not dealing with that condition entirely. It’s a dynamic process. Other things are being released in the body during the surgery, so we have to be constantly adjusting our treatment and our anesthesia to take care of this.” The

endotoxins are a big factor. “Things are happening throughout the surgery that we have to be aware of and it may change our technique. Not all horses are the same. The large colon twists seem to be worse than the small intestine ones, as far as endotoxin release during surgery,” says Trim.

Molecular Research

“For 20 years, we have studied how the toxins cause their ill effects. During this time, we’ve progressed from looking at the effects of toxins on cells isolated from the horse’s blood, to where we are now studying the process at the molecular level. Our aim is to identify how the cellular receptors for the toxins respond, and how to turn off or control the inflammatory response,” says Moore.

Michel Vandenplas, PhD, molecular biologist, has been working with the research group in Georgia for four years, performing studies on horse cells. Endotoxins activate certain white blood cells that have receptors on their surfaces that are specific for endotoxin. These receptors may be the key—turning on the white blood cell to create the inflammatory mediators that cause the horse to go into shock. Vandenplas has cloned and expressed the primary receptors that exist on the horse’s white blood cells.

“Our research team, under the leadership of Dr. Moore, is investigating a few avenues to prevent the deleterious effects of endotoxin in the horse, by targeting these processes,” says Vandenplas. Substances have been isolated (from bacteria that live in root nodes of certain plants) that can reduce the endotoxin-induced production of pro-inflammatory mediators by human white blood cells, and Vandenplas is now doing studies to see if they work on horse cells.

A Possible Treatment For Endotoxemia

Another researcher in the group, Dr. Michelle Henry Barton, has completed a study that holds promise for treatment, using polymyxin B, a polypeptide (compound containing more than two amino acids—part of the make-up of a protein) that has bactericidal activity against many gram negative bacteria. Polymyxin B also binds to endotoxin, preventing interaction of endotoxin with white blood cells, thus heading off the damaging effects of that reaction.

Barton says polymyxin B is effective treatment for endotoxemia in horses, but the drug has detrimental side effects; it can damage the kidneys and nervous system. Her study found that when given at lower doses than used for killing bacteria, it still has endotoxin-binding properties, without the adverse effects. “Even when used hours after the onset of endotoxemia, it reduces synthesis of damaging inflammatory mediators and improves survival rates. It is an affordable alternative to endotoxin antiserum for treatment in horses with carbohydrate engorgement (colic caused by grain overload), or given prior to surgery in patients with strangulated bowel,” she says. Studies are now looking into formulations with fewer side effects when given at the higher doses.

The future may bring us better treatments for endotoxemia and colic, thanks to the efforts of this research and the development of new techniques that help us combat the life-threatening effects of the horse’s “inner poisons.”