

Champions in the Fight Against Colic

Colic generally refers to intestinal injury or damage that manifests as abdominal pain. A horse with mild colic appears restless, uncomfortable and may paw, kick, or frequently look at its abdomen. Horses may exhibit mild abdominal discomfort after sudden changes in the type or quality of the diet, when feed becomes impacted in the intestine, and when portions of the intestine stop contracting (ileus). Horses may experience severe pain if the gut becomes twisted or displaced and may lie down and stand up repeatedly or roll and thrash on the ground. Their heart and respiratory rates increase and they may sweat. When the intestine twists, the blood supply is dramatically reduced or stopped (ischemia) and the affected tissue will die if the condition is not corrected.

Despite significant advances in the medical and surgical management of gastrointestinal disease, colic remains the leading cause of mortality and sickness in horses. Although some horses are fortunate enough to escape the fatal consequences, they are not exempt from the discomfort and pain that are all too characteristic of intestinal disease. The UC Davis Comparative Gastroenterology Laboratory develops strategies to prevent colic and minimize subsequent complications.

Since its inception in the early 1980's, the laboratory expanded tremendously from a single small office unit to a fully staffed laboratory complete with state-of-the-art equipment. Although the research focus is predominantly directed towards understanding equine gastrointestinal disease, the laboratory also collaborates with other specialties including the equine reproduction service and human specialists in the spirit of cooperation that makes UC Davis a strong research institute.

Dr. Jack R. Snyder, a worldwide authority on colic, directs the laboratory, combining basic scientific research and innovative laboratory design in an effort to solve the devastating problems associated with equine colic. Damage to the intestine, especially the small bowel, disrupts the delicate balance of cellular activity which promotes smooth coordinated contractile activity. This disruption leads to motility (intestinal movement) disturbances. The resulting loss of contraction is a serious and life threatening complication of colic, especially in the post-operative period which can persist for days and even weeks. As long as the intestine remains inactive, the horse requires intensive medical support and the hospital recovery period is prolonged and expensive.

HELPFUL TIPS

- Loss of appetite
- Depression and isolation from herd mates
- Sweating
- Lying down more than normal and may refuse to rise
- Rolling repeatedly

Colic Symptoms

- Crouching as if to lie down but remains standing
- Repeated stretching as if attempting to urinate
- Kicking and/or biting at flanks
- Abdominal distention

Over the last ten years, Dr. Snyder and his laboratory staff have investigated the factors which devitalize the intestine when colic and intestinal torsion (twists) occur. They discovered that when the intestine is twisted and its blood supply compromised, oxygen levels decline and metabolites

accumulate within the tissue and surrounding areas. The intestine releases toxins and other chemical agents which damage the gut even after the blood supply is restored. In fact, in some cases, restoring intestinal circulation by surgically untwisting the gut actually accentuates the toxins' negative effects. When the blood flow is restored, the oxygen interacts with the metabolites and forms toxic compounds that cause additional cellular damage.

To effectively investigate the factors that contribute to motility disturbances, researchers must study both the normal and abnormal function of the horse's intestine, as well as the possible effect of various medications on the gut. Once researchers identify the chemical agents that damage the intestine, then they can test other agents to block this damage and thus provide improved medical treatment before and after surgery.

Dr. Snyder realized that he could not humanely subject large numbers of horses to the experimental twisting and untwisting of their intestines, nor could he subject live animals to the unknown effects of many toxins and drugs, so he set out to find a better way. What he devised to study this problem is a credit to his ingenuity and his scientific expertise.

First, he and his team devised a system whereby small strips of intestine harvested from horses who had died are suspended in a bath-like solution. The intestinal strips are attached to strain gauges interfaced with a computer program which records and measures contractile activity. Within this bath, the intestinal fragments can be kept alive long enough to measure the effect of various chemicals on the intestinal wall and its muscular cuff. This investigative system led to the discovery of many natural and synthetic agents which positively or negatively affect the intestinal motility or action of the gut. The resulting information has contributed significantly toward guiding the medical treatment of colic.

The second investigative system developed by Dr. Snyder and his colleagues is known around the veterinary

Colic: before the vet arrives

- Walk the horse if it will safely tolerate activity, but don't force exercise.
- If the horse lays down and rests quietly, let it be. If it thrashes around, try to get the horse up and walk it, but not at the risk
- Minimize interaction with other horses and people.
- Be prepared to answer questions regarding previous history of colic, changes in diet or exercise, etc.

DONOR SUPPORT

In Appreciation

The following individuals and organizations have generously contributed funding to the UC Davis Comparative Gastroenterology Laboratory. Thanks to their support, our researchers are improving the treatment and prevention of colic and saving equine lives.

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school as the "Gut in the Box." Using this system, researchers can take a large section of the intestine and its attending blood vessels, attach them to a type of heart-lung machine, and maintain viability for an extended period of time. The "Gut in the Box" allows researchers to study the effects of various proposed medical treatments on the intestine and its vascular system. The "Gut in the Box" minimizes the manpower required to perform the studies (which would normally be conducted with the horse under general anesthesia), and more importantly, also reduces the number of animals required for research since multiple studies can be performed on the same tissue specimen outside of the body.

The Comparative Gastroenterology Laboratory not only utilizes innovative investigative systems to study the function of intact intestine, but also employs state-of-the-art equipment to study motility disturbances at the cellular level. In the past, researchers had limited information on the mechanisms involved at the cellular level in regulating intestinal motility. This deficit was partly due to the lack of appropriate tools and technology to study the individual intestinal cell. However, the Comparative Gastroenterology Laboratory devised an intracellular recording system as a means to overcome this hurdle. This delicate device allows the investigator to impale individual intestinal cells with microelectrodes and record the electrical activity across the cell membrane. Intestinal contractility is the summation of all the electrical activity initiated at the cellular level. By measuring the effects of various agents on individual cells, researchers can predict likely changes in motility. After researchers establish these baseline patterns, they can investigate the effects of compromised blood flow, endotoxins and other inflammatory mediators on the electrical activity of the cell.

The laboratory's investigative systems and techniques have contributed much to the colic research and will continue to do so. As a result of this work, veterinarians more thoroughly understand how intestinal motility or function is maintained and how to

restore that function once it has been compromised. Dr. Snyder's investigative systems simulate the intestine's natural state outside the horse's body in the laboratory which allows for rapid advancements in knowledge to occur without unnecessary animal sacrifice. Using innovative techniques and the available resources, Dr. Snyder's Comparative Gastroenterology Laboratory is making great strides in understanding and minimizing the devastating consequences of intestinal disease and thereby improving the quality of equine life.

For more information on the Comparative Gastroenterology Laboratory and its research, contact Dr. Jack Snyder, Comparative Gastroenterology Laboratory, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California Davis, One Shields Avenue, Davis, CA 95616, phone (530) 752-3599, or visit its Web site at www.vsr.vetmed.ucdavis.edu/vsr/labs/gastrolab/gastrolab.html.

Some of the Comparative Gastroenterology Laboratory's Current Research

1) Nitric Oxide's Role in Motility Patterns of the Large Colon

HELPFUL TIPS

Colic Prevention

Providing passive exercise and grazing 24 hours a day or consistent multiple feedings is the best way to prevent colic. Unfortunately, this may not be possible for most horse owners, therefore:

- Maintain a regular deworming and vaccination program
- Always provide good quality feed and fresh clean water
- Avoid drastic changes in diet and/or exercise
- Maintain regular dental checkups
- Provide cool water in freezing weather

Researchers must understand the mechanisms that regulate normal gut motility before they can develop treatment strategies to minimize complications associated with intestinal disorders. In a previous study, scientists determined that nitric oxide inhibits the small intestine's ability to contract, which can slow down or even stop the passage of feed through the gut. They also found that the motility could be restored using inhibitors of nitric oxide synthesis. Presently, the Comparative Gastroenterology Laboratory's researchers are studying nitric oxide's effect on the large colon using the mechanical testing apparatus that records contractile activity.

2) Prostaglandins' Role in Healthy Intestinal Tissue

In all mammalian tissues, prostaglandins are produced from the metabolism of lipids found in cell membranes. These compounds regulate various functions including smooth muscle contraction or relaxation, the regulation of vascular tone, and with certain prostaglandins, the mediation of inflammatory response. In the horse, there is little information concerning prostaglandins' role in intestinal contractile activity. The Comparative Gastroenterology Laboratory is conducting investigations to determine prostaglandins' role in colic. Once researchers determine prostaglandins' definitive function, then they may be able to develop appropriate pharmacological therapy for post-operative ileus (the lack of intestinal contractions following surgery).

3) Nonsteroidal Anti-Inflammatory Agents' Effect on Colon Motility
Nonsteroidal anti-inflammatory drugs (NSAIDs) such as phenylbutazone ("bute") and banamine are associated with large intestinal impactions. NSAIDs are frequently used to ease colic discomfort due to their potent analgesic and anti-inflammatory effects. However, their effect on intestinal motility is controversial. Recently, the Comparative Gastroenterology Laboratory's researchers determined that NSAIDs decreased muscle contractions in one part of the intestine. Currently, they are investigating the effect of these compounds on other areas of the colon.

HELPFUL TIPS

Colic in Pregnant Mares

Last Trimester:

Maintain consistent feeding schedules with good quality feed, fresh water and regular exercise.

Mild signs of abdominal discomfort are normal, however, watch closely to see if the discomfort becomes more severe, indicative of colic.

Colon torsions may occur in broodmares 30 days prior to foaling, most likely due to changes in abdominal space and colonic motility towards the end of gestation. Surgery may be necessary, but there is a risk to the foal and later, of the midline incision breaking during foaling.

Uterine torsions (part of the uterus twists) most often occur in the last trimester. The mare shows mild to moderate signs of abdominal pain like colic, but the pain is persistent. Surgical correction is necessary and there are several methods that can be used. Most mares foal normally following surgery.

After Foaling:

Colon torsions are most common in broodmares 60 days after foaling and again, are most likely due to changes in abdominal space and motility.

4) Distention's Effect on Small Intestinal Motility

Horses with small intestinal obstructions exhibit pain when the intestine becomes dilated with

accumulated fluid, feed and gas. Although distention always occurs as a complication of intestinal obstructions, its effect on intestinal motility changes has not been investigated. Using the Comparative Gastroenterology Laboratory's Gut-in-the-Box apparatus, researchers artificially distend a length of small intestine by filling it with water to a predetermined pressure. After a period of distention, researchers characterize the contractile activity of the intestine using the mechanical testing system.

5) Motility Drugs' Effect on Normal and Distended Small Intestine

In humans, several drugs are used to increase intestinal motility. In horses, unfortunately, information is lacking regarding their use. Using the Gut-in-the-Box apparatus and the mechanical testing system, the Comparative Gastroenterology Laboratory's researchers are testing these drugs' effects on normal and artificially distended intestine.

6) Development of Perfusion Solutions to Reduce Tissue Injury

Ischemia refers to when the intestine's blood supply is dramatically reduced or stopped. Reperfusion refers to when the blood supply is returned to damaged intestine. Ischemia and reperfusion often result in subsequent tissue damage. The Comparative Gastroenterology Laboratory's researchers are developing and testing perfusion solutions using data acquired from motility/Gut-in-the-Box studies.

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