

Botulism, *the silent killer*

Botulism, regarded by many as a form of food poisoning due to spoiled meat is seen relatively frequently in equine patients at New Bolton Center. "We see about 50 botulism cases annually, more than are seen by any other veterinary teaching hospital in the country," said Dr. Robert H. Whitlock, professor of medicine at the University of Pennsylvania's School of Veterinary Medicine. "In addition we investigate 20 to 30 additional outbreaks, several of which are referred to us by the Communicable Disease Center in Atlanta because they are not permitted to work on animal diseases." The number of botulism outbreaks isn't surprising because the spores of the bacillus *Clostridium botulinum* are found in about 20 percent of soil samples from the Middle Atlantic states and Kentucky. These spores are dormant in the soil but under the right conditions they become vegetative and produce a toxin so potent that a tiny amount can cause death. The organism only grows in anaerobic conditions. The intestines of the young, puncture wounds, improperly canned foods and forage material incorrectly ensiled may provide the right environment in which the spores can become vegetative and produce toxin. The spores themselves are relatively harmless and do not produce toxin unless the conditions are exactly correct.

Botulism strikes all mammals, particularly young ones. It is implicated in some cases of Sudden Infant Death Syndrome. Botulism can develop because of ingestion of preformed toxins. People are exposed to the toxin primarily through improperly canned foods. Animals come into contact with the toxin through spoiled silage or spoiled meat. Botulism can also occur when a wound is contaminated with the spores and heals over, providing an anaerobic environment for the organism to flourish. The third way to develop the disease is to ingest the spores which then become vegetative in the intestinal tract if the right conditions exist. Toxin thus produced is absorbed into the body. It is thought that this is the most likely way by which foals contract the disease.

The study of botulism at New Bolton Center began in 1981 when 25 horses at a racetrack were diagnosed with the disease. The mortality rate was nearly 75 percent. "We obtained some antitoxin late in the course of the outbreak from Canada," explained Dr. Whitlock. "But we could save only a small percentage of the animals. Today the chances of survival are better as we have developed an antitoxin at New Bolton Center. It is readily available and is given to the patient within an hour after admission to the hospital."

When botulism is suspected the veterinarian or physician cannot order a battery of tests to confirm the diagnosis. Only rarely can the toxin be found in the bloodstream. The patient has no fever nor will the blood picture be abnormal. A tentative diagnosis is made by clinical symptoms only. These are muscular weakness, inability to swallow normally and exercise intolerance. Such signs can also be associated with other disorders and tests must be performed to rule out other diseases. The clinical signs of botulism progress depending on the amount of toxin present in the body and the amount of muscular exertion. Animals and people with rapidly progressing signs have a poorer prognosis than those with gradual onset.

It has been found that the horse is extremely susceptible to botulism toxin. It only takes a small amount to cause symptoms. The toxin prevents release and production of acetylcholine, a chemical transmitter of impulses to the muscles. Toxin attaches itself to motor end plates and this prevents the transmission of nerve impulses and flacid paralysis results (muscle weakness).



A mare and her "shaker" foal being cared for at New Bolton Center.

Young foals are most prone to botulism caused by the ingestion of spores. As the animal gets older, it appears that the intestinal environment changes and no longer is favorable for the spores to produce toxin; they pass through without harm. It is thought that most cases of the disease occurring in older horses are due to ingestion of toxins or large numbers of spores present by chance in the feed. Dr. Whitlock stressed that mature horses seen with the disease came from well-managed farms and that it is extremely difficult to trace the origin of the toxin.



A three-week old foal with botulism on the way to recovery.

After the outbreak in 1981 researchers at New Bolton Center began to produce antitoxin for

Clostridium botulinum infection. The organism causing the disease was type B. There are several different toxin types; for example in Europe horses are affected by type C botulinum. The antitoxin is a gammaglobulin derived from horses with a high antibody titer against botulism. These horses are injected with a toxoid, toxin rendered harmless. Repeated injections of toxoid stimulate antibody production over a period of months. Then the animal is challenged with the toxin, this results in still higher numbers of antibodies which then are removed and stored for use in affected animals.

"Since we have been giving the antitoxin we have been able to reduce the mortality rate to about 20 percent," said Dr. Whitlock.

"The prognosis is better if the animal is not recumbent; this is particularly true for older animals. Once an adult horse is down it is more difficult to treat effectively. Pneumonia develops and fluid can accumulate in the chest. Foals on the other hand are easier to handle and the prognosis is pretty good even though the foal is down." Nevertheless, even for the young animals a great deal of intensive nursing care is required. They may need a respirator to assist with breathing. Intravenous feeding may be required and the veterinarian has to look for ways to prevent pressure sores. These animals require prolonged intensive care and antitoxin therapy.

"The antitoxin does not cure the disease," Dr. Whitlock explained. "It prevents further spread of the toxin in the body. It does not remove the toxin from the already affected motor end plates but it binds the circulating toxin, preventing it from attacking more sites." Affected animals have to be kept very quiet with a minimum of physical activity. "A lot of thrashing and struggling just aggravates the condition," he said. An animal or person with botulism will not remain paralyzed. The body develops new motor end plates at the affected sites and gradually the function of muscles returns. This healing process can take anywhere from one to three weeks depending on the severity of the disease. "It is an expensive proposition," Dr. Whitlock said.

Antitoxin is not the only weapon against this disease. The Laboratory of the Department of Public Health, Lansing, MI, developed a vaccine (toxoid) against botulism type B for use in horses. This vaccine was tested at New Bolton Center and found to be effective. In studies conducted by Dr. Whitlock and his group horses were injected three times at monthly intervals with the vaccine. Two weeks after the last injection they were challenged with high doses of toxin. They did not develop the disease. It was found that these horses had protection for more than 100 days after the last vaccination even though their antibody titers against botulism were quite low by then.

The vaccine has also been used for pregnant mares in Kentucky. The mares developed antibodies which were passed to the foals passively through the colostrum giving protection at the most critical time for the young animal. Unfortunately, because of legal concerns, this vaccine is not available for general distribution outside of Michigan and Kentucky. The vaccine is only available in states where the state government has signed a waiver stating that Michigan cannot be held responsible for any complications due to the usage of the vaccine. To date only Kentucky has signed such document and the state there

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maintains strict control on who uses the vaccine. Farm managers and horse owners in that state are required to sign a waiver absolving Kentucky from any responsibilities should complications develop.

Dr. Whitlock feels the vaccine is safe and that its use would prevent the disease in the highest risk group, the foals. "After the initial three shot series, mares need an annual booster to keep up the protection," he said. "Botulism, like tetanus, can produce clinical disease, yet recovery is not

associated with any immunity. The amount of toxin necessary to cause disease is so small it will not stimulate an antibody response.

Botulism studies continue at New Bolton Center. Dr. Whitlock's team is in search of better diagnostic methods and a test which can confirm the presence of the toxin quickly as time is of the essence when treating a patient with the disease.

"Botulism is a disease of man and animals we have to be aware of," he said. "It is costly and better means of diagnosis will facilitate earlier treatment, helping to save lives. While the largest number of patients here are horses, we also see it in other animals. Recently we treated a herd of

cattle and managed to save some animals by giving the horse antitoxin to the cattle. This will only work once. If those cattle get botulism again they cannot be treated in the same manner because of immune reactions," Dr. Whitlock's group recently helped the owner of a pack of hounds which had botulism.

While botulism is of concern in this country, it is of greater frequency in Third World countries where it affects livestock contributing to the loss of valuable food resources.

The vaccination study at New Bolton Center was funded by the Equine Medicine Research Fund at New Bolton Center.

H.W.

Symposium for the Biomedical and Agricultural Industries

Representatives of 24 biomedical and agricultural companies attended the first symposium held at the School on April 16 on this topic. An overview of the research work at the School was given by 28 faculty members. The object of the program was to foster relations between the research enterprise in the School and industry. Short papers in medical genetics, oncology and virology, development and metabolism, cardiology and hypertension, respiration and sleep, cellular immunology, epidemiology and parasitology were given to acquaint the symposium participants with the scope of work in progress. The program was received well and the chairmen of the event, Dr. Leon Weiss and Dr. Kenneth Bovee, hope to organize another such symposium in 1987.



The Grand Champion Award for Sama Gertrudis at the Houston Livestock Show and Rodeo was presented by Dean Robert Marshak. He and Mrs. Marshak are shown here with the winning entry.

Sheltie Skin Syndrome

Shetland sheepdog clubs from coast to coast have contributed about \$5,000 for a study of "Sheltie Skin Disease" here at the School.

"Shetland sheepdogs, as a breed, have skin conditions which have not been diagnosed," said Dr. William Miller, Jr., assistant professor of dermatology. "These conditions really should not be called 'Sheltie Skin Disease', rather they should be termed Sheltie Skin Syndrome.

"Shelties, like other breeds, can have skin problems such as mange, ringworm, and conditions caused by allergies. But frequently they have a condition which still has to be identified. The dog has crusty, scaly patches around the face,

tail and feet and the severity of the disease varies from animal to animal."

Dr. Miller explained that three major diseases are thought to be the cause of Sheltie Skin Syndrome: lupus, dermatomyositis and epidermolysis bullosa. All three have a gross similarity of symptoms and at first glance appear to be the same disorder. However, they are different. Epidermolysis bullosa and dermatomyositis occur when the dog is between age eight weeks and one year. Manifestation of symptoms varies; some animals just show a few crusty, scaly patches while others have a multitude of sores. Lupus, which has the same symptoms, should appear when the animal is older.

"We want to find the frequency of Sheltie Skin

Syndrome and determine which disease we are dealing with," said Dr. Miller. "We also want to develop a test so that animals can be identified quickly and treatment can be instituted." He explained that dermatomyositis and epidermolysis bullosa are thought to be genetic. "There is a similar syndrome in the collie which has been proven to be dermatomyositis. In that breed it is a dominant trait with varied expressivity."

Dr. Miller is looking for severely affected dogs for the study and development of tests. "We have some of the funding for the study but lack the animals to do the study with," he said. "The work is important because if these are genetic diseases the frequency of occurrence can only be controlled through selective breeding."



Mrs. James H. Higgins of Sewickley, PA, has been elected to a three-year term on the Board of Overseers of the School of Veterinary Medicine. Mrs. Higgins, here with Overseers Chairman Charles S. Wolf of York, PA, is the delegate of the Pembroke Welsh Corgi Club of America to the American Kennel Club. She is a graduate of Sarah Lawrence College and is active in civic affairs in Pittsburgh.

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