Botulism Toxicosis of Cattle

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Summary

Botulism in cattle is occurring with greater frequency in North America, coincident with increased frequency of large plastic bags used to store forage and with the increased use of small grain (ryelage) haylage. The clinical signs of botulism in cattle are very characteristic, almost pathognomonic if epidemiological factors are considered. Nearly always multiple cattle in a herd, within a few days of each other, have clinical signs of progressive muscular weakness leading to recumbency over a 2-5 day period of time. Perhaps the most dramatic, characteristic, clinical sign is the loss of normal lingual tone, to the point that the tongue will hang out of the side of the mouth. However, in order to elicit this finding, the tongue needs to be grasped manually and then pulled out of the side of the mouth with the jaws closed. In normal cattle, the tongue will then be retracted back into the mouth. Abnormal tongue tone, as occurs with botulism, will be manifest by both loss of normal muscular tongue tone and lack of prompt response to retract the tongue into the mouth. A limp tongue is clearly abnormal and with loss of ability to swallow, suggests botulism. Types A, B and type C botulism occur in cattle in the USA, but type B predominates. Type B is associated with feeding improperly fermented forage where the pH has not reached 4.5 or lower. Acid pH inhibits sporulation preventing botulinum toxin from being produced. Type C botulism occurs with the accidental feeding of carrion (birds, cat or dog carcasses) in the ration to cattle. Definitive diagnosis is challenging, often requiring multiple samples of forage, rumen contents, and/or fecal samples to be tested for botulinum spores and toxin in a laboratory experienced in botulinum testing.

Introduction

Types of botulism

Botulism is caused by one of the most potent toxins known to man.[60] The toxin is produced by *C. botulinum* that may affect all mammals, birds and fish.[99] The organism is a strict spore forming anaerobic gram-positive rod. The potent exotoxin is produced during growth and autolysis. The 8 known types of the botulinum toxin include A, B, C_a, C_b, D, E, F, and G.[100] Each type is unique in its geographic distribution and species susceptibility.[91,100,101] For example, type E botulism occurs primarily in fish and secondarily in man that consumes the spoiled fish products.[13,46,47] Types F and G have only been reported in man. Cattle may be affected by types A, B, C and D. Types A, B and E are most common forms of botulism in man.[119]

Type A spores are common in the soil from regions of the USA west of the Rocky Mountains. Approximately 18% of soil samples contain spores of *Clostridium botulinum.*[101] Only rarely have Type A spores been associated with botulism in cattle.[88] Two horses in Utah and one in California were confirmed Type A.[118]

Type B spores are common in the soil in the mid-Atlantic states[101] and are responsible for most outbreaks of botulism in cattle in North America.[122] Type B botulism typically occurs in forages with a final forage pH above 4.5. If forage pH is lower than 4.5, as typically occurs with adequate fermentation, the botulism spores fail to germinate, therefore botulinum toxin will not be produced. Non-carrion associated botulism (forage poisoning) in cattle due to forages contaminated with *C. botulinum* Type B toxin has been reported in Europe.[12,36,42,43] A similar episode was reported in the United States associated with ingestion of contaminated silage but dead animals were not found, nor was the toxin type identified.[39] Outbreaks in the Netherlands were due to silage made from brewers grain and grass silage containing Type B toxin.[12,43,75,77] In each of these outbreaks Type B organisms were isolated from the silage which may have been improperly fermented. The key factor seemed to be the lack of adequate fermentation to reach a low pH, thus inhibiting sporulation and toxin production by *Clostridium botulinum.*

Botulism associated with the consumption of feed containing a carcass is most often Type C or D[33,34] while forage poisoning is typically Type B.[12,43,89] Type C botulinum intoxication in cattle is usually associated with a decomposing animal carcass, such as a cat,[10] dog or birds.[19,71] During life, the dog or cat may consume a bird

which may be a carrier of type C botulism spores.[38,84] Following death of the dog, cat or bird, the enteric botulinum spores vegetate in the protein rich anaerobic environment of the carcass, producing potent neurotoxin.[85,98] If cattle consume a forage product contaminated with the decomposing carcass containing botulinum toxin, the toxin is soon absorbed from the gastrointestinal tract leading to clinical signs of botulism in the new host, cattle.[56] Feeding poultry litter, especially litter containing chicken carcasses, has frequently been associated with outbreaks of botulism in beef cattle.[3,7,17,18,30,31,37,49,50,52,65,66,74,86,96]

Type D botulinum occurs more commonly in South America and South Africa when phosphorous deficient cattle chew bones of decaying carcasses to restore their phosphorus stores.[24,51,83,109] Feeding poultry litter to cattle in Europe, Israel and Australia has been associated with type D botulism, often in massive outbreaks.[3,7,17,18,24,31,49,65,66,74,93,96,111] Our laboratory documented the first and only case of Type D in the United States (1988). Feeder cattle in West Virginia were being fed poultry litter mixed with corn. *Clostridium botulinum* Type D spores were isolated from the poultry litter.[118] Other cases of type D botulism in US cattle have been suspected but not proven.[1,40]

Type E botulism typically occurs in man following the consumption of fish, but has not been reported in cattle to the authors' knowledge. Most human cases in North America occur in the Pacific Northwest with the highest occurrence in Alaska - estimated to be 20-50 human cases/year.[13,91,92] Types F and G are extremely rare in man with only a few reports worldwide and none reported in cattle.

Route of Intoxication

Botulism intoxication may occur by one of three routes: a) ingestion of the preformed toxin, b) wound botulism, and c) toxicoinfectious botulism.[47,104,105] The ingestion of preformed toxin in feed materials, usually silage, is the most common source of exposure in cattle. The finding of a dead carcass in the water, such as a rat, and commercially prepared feed concentrates are rarely associated with botulism in cattle. Wound botulism may develop when the organism infects a wound, sporulates, and releases toxin under anaerobic conditions.[11,32,55,67,78] Wound botulism has been reported secondary to misuse of intravenous drugs in humans[63] and in castration infections in horses.[11] Toxicoinfectious botulism develops after spores are ingested and the toxin produced in the gastrointestinal tract is absorbed.[16,68] This form of botulism occurs in children less than 6 months of age as one cause of sudden infant death syndrome[4-6] and in foals up to 8 months of age.[104,105]

Confirmed toxicoinfectious botulism and wound botulism have not been reported in cattle.

Pathophysiology

Botulism is caused by the systemic absorption, most commonly from the gastrointestinal tract, of a potent neurotoxin elaborated by *Clostridium botulinum.*[94] The neurotoxin exerts its influence on the myoneural junction, resulting in impaired transmission of the electrical impulse from the nerve fiber to the adjacent muscle.[69,70,94,103] Following toxin absorption from the digestive tract, botulinum toxin circulates in the blood stream. However, the plasma toxin concentration is in extremely minute levels, far below those detectable using the most sensitive means of detection, the mouse bioassay test. Only in rare situations can botulinum toxin be detected in the serum or plasma of acutely infected cattle.

Botulinum toxin is preferentially taken up by specific endopeptidase receptors on the motor endplate.[44,69,70,87] Once attached to the receptor, the toxin is translocated within the cell, and finally bound to the acetylcholine vesicle preventing the electrical signal from reaching the myoneural junction. The process of initial attachment, translocation and final binding is toxin dose dependent and requires several hours. Thus, with relatively small doses of botulinum toxin, the clinical signs may not become apparent until 5 to 10 days or more after toxin ingestion. However, with massive doses of toxin (10^8 mouse lethal dose units) cattle may become recumbent and die within 18 to 24 hours following ingestion of toxin.

Botulism spores are relatively ubiquitous in the environment that may remain dormat, yet viable for years, even in harsh environmental conditions.[97,99] Ingestion of spores rarely leads to clinical botulism, as the spores do not elaborate toxin, unless in an anaerobic environment with appropriate nutrients and more neutral pH nutrients.[54,97,99,102] Botulism spores are very pH sensitive and will not form toxin when the pH is less than 4.5.[20] However, if forages are harvested too dry and fermentation is inadequate resulting in decreased acid production, toxin may be elaborated if the pH is above the critical pH of 4.5 and spores are present.

With the advent of plastic wrapped large round bales (dry hay or haylage) the frequency of outbreaks of botulism in cattle has increased. In plastic wrapped haylage each bale acts as its own fermentation compartment, resulting in large bale to bale differences in fermentation and quality of the forage. Additionally, once the plastic seal is broken, spoilage occurs which may lead to anaerobic conditions and production of botulinum toxin as occurred in one outbreak.[123]

History of a Typical Clinical Case

Most clinical cases of botulism in cattle occur as a herd outbreak compared to horses which most frequently

occur a single cases. In cattle, the referring veterinarian is called to evaluate multiple down cows that may have initially responded to treatment for hypocalcemia, but relapsed.[117,120] These downer cows are often not associated with recent parturition, but may be more prevalent in higher producing cattle. Thus, multiple cattle in a herd with clinical signs similar to milk fever and evidence of progressive muscular weakness typifies many outbreaks of botulism.

Further investigation of the herd outbreak usually finds a potential point source of botulinum toxin.[39] Recent feeding of small grain silage (such as ryelage) stored in large plastic bags in the past 3-4 days or a storm that necessitated feeding of spoiled silage typify the history. Clearly ryelage and grass silage stored in plastic bags or in plastic tubes are major risk factors for botulism in cattle.[123] Baled silage is often harvested and stored in individual plastic bags (~750 lb) or in long tubular plastic sacks up to 300 ft. long, containing as much as 100 tons of silage. On some occasions in botulism outbreaks you may find evidence of damage to the plastic, allowing mold and spoilage to occur, which may lead to anaerobic conditions with botulism spores producing toxin.[123]

The incorporation of an animal carcass in the silage making process may lead to an outbreak of botulism. Cats, dogs and poultry carcasses are typical villains which lead to type C botulism. In one recent outbreak in California, cat carcass contaminated TMR was responsible for the death of more than 420 adult cattle over a one week time period (Galey, 1998). Poultry litter containing decomposing chicken carcasses predispose to either type C or D botulism. Repeated occurrences of botulism in beef cattle have occurred in West Virginia, Arkansas and other states associated with feeding poultry litter based rations.

Clinical Signs

In cattle, the clinical signs of botulism toxicosis include progressive muscular weakness leading to recumbency.[118,120] Partial dysphagia becomes complete as cattle become recumbent due to botulism. Perhaps the most specific and sensitive clinical sign for botulism in cattle is loss of lingual or tongue tone.

Tongue tone

Tongue tone is best assessed by grasping the tongue from the interdental space with your fingers. With the tongue still in the mouth, one can assess the muscular tone of the base of the tongue by reaching back in the mouth and putting pressure on the base of the tongue. Normally the tongue is firm with muscular tone. When the tongue is pulled out of the side of the mouth with the jaws closed, most cows quickly retract the tongue back into the mouth. Reduced tongue tone is best assessed by comparing it to the tongue tone of a normal cow. First, the normal tongue is more difficult to grasp and retract out the side of the mouth and has firm muscular tone in the base of the tongue. Second, when pulling the tongue out of the mouth, normal cows will retract it very quickly. If the tongue hangs limply from the lip and is not retracted quickly, this clinical finding is very suggestive of botulism. In cattle with botulism, the tongue is retracted slowly into the mouth, if at all. Tongue weakness is not specific for botulism, but is characteristic. Decreased lingual tone may occur with listeriosis and other causes of hypoglossal nerve injury. However, in cases of botulism, the weakness is symmetrical, associated with dysphagia, progressive muscle weakness and several animals are typically involved.

Jaw movement and muscle tone

In addition to tongue weakness, one should also assess the masseter muscle tone or strength by lateral movement of the of the mandible. The mandible has more lateral movement in cattle with botulism compared to normal cattle. Lateral movement or motion is best assessed by grasping the mandible in the area of the symphysis, then move in back and forth to determine muscular tone of the masseter muscles. In cattle affected with botulism, little resistance is encountered and the jaw seems very loose. Similarity, both the upper eyelid and tail tone are limp in cattle with botulism compared to normal cattle.

Pupillary response and dysphagia

Pupils tend to be dilated and poorly responsive to light in cattle with botulism. Botulism affected cattle may drool small amounts of saliva because of their inability to swallow. Often botulism affected cattle appear to prehend hay or grass, chew and then swallow. However, on closer examination, the affected bovine continually chews the same cud for hours at a time without swallowing. Examination of the pharynx or oral cavity may show evidence of chewed hay or forage due to the inability to swallow.

Animals with botulism look dull, depressed, lethargic and often become dehydrated because of inability to drink. They very closely resemble cattle with milk fever except with botulism multiple animals are involved at the same time. Animals may show muscle tremors and truncal ataxia, even to the point of dribbling urine, before becoming recumbent. As a recumbent cow, they remain in sternal recumbency in the initial phases and in the more advanced stages become laterally recumbent with more evidence of respiratory failure.

Bradycardia and hyperglycemia

Occasionally affected cattle will have a prominent bradycardia (40-50 beats/minute). This is not a specific

sign for botulism, but may occur with any acute decrease in feed intake.[64] Rumen contractions are usually reduced in rate and decreased in the strength of the contractions. Some animals may have glucose in the urine along with evidence of hyperglycemia or high blood glucose. The hypergylcemia is simply a stress phenonom as frequently occurs in any bovine affected with a severe life threatening disease process.

Clinical course

The progression of clinical signs following ingestion of toxin contaminated forage is toxin dose dependent. High or massive concentrations of toxin may lead to clinical signs within 12-24 hours of ingestion of the toxin (an unusual event), whereas low toxin concentrations may not yield any clinical signs for 7 to 10 days or longer following ingestion. Typically cattle that absorb a moderate amount of botulinum toxin exhibit some evidence of weakness for 24 to 48 hrs prior to becoming recumbent, then are unable to get up for 2 to 3 days before death. The extent of physical activity has a major influence on the progression of clinical signs. More physically active cattle or cattle that are stimulated to walk some distance are more likely to be affected by low doses of toxin. The physical activity results in depletion of acetylcholine reserves and then muscle weakness (downer).

Most cattle that become recumbent following botulinum toxin absorption die of respiratory failure, dehydration and complications of being down. Cattle with a more gradual progression of clinical signs that become recumbent are often able to eat and drink, maintaining homeostatic mechanisms and may recover.[21] Typically, botulism affected down-cattle that recover will be down for 5 to 10 days, then gradually regain muscular strength to be able to rise again. Recovery from botulism is mainly by the sprouting of new motor end-plates.[29] In the authors' experience, in a typical herd outbreak, many cattle will have sub-clinical signs, such as a weak tongue and decreased jaw tone, possibly mild dysphagia and never become recumbent. These animals should have a detectable antibody response to botulinum toxin 3 to 4 weeks following recovery from subclinical botulism. The clinical course ranges from 2 to 30 days, depending on the dose of toxin absorbed and treatment provided.

Prognosis

Rapidly progressive clinical signs over 12 to 36 hrs is indicative of greater amounts of toxin absorption into circulation, and therefore have a poorer prognosis for survival. Cattle that are able to stand,but mildly dysphagic with muscle weakness have a fair to good prognosis if treated with botulinum antitoxin. Once botulism affected cattle are recumbent and dysphagic, the prognosis for survival is grave despite any treatment provided.[23,72]

Diagnostic Rule-outs

The differential diagnosis for botulism includes any disease that results in progressive muscle weakness and recumbency. Early in the clinical course of bovine botulism, the vital signs, hematologic and biochemical parameters are close to normal, which helps to rule out infectious diseases. Bovine botulism almost always involves multiple animals in various stages of lactation and gestation. Nervousness, apprehension and unilateral neurological signs are not features of botulism, which help rule-out diseases such as listeriosis, hypomagnesemia, nervous ketosis and rabies.

1. Hypocalcemia

Botulinum toxin reduces gastrointestinal motility which may diminish calcium absorption from the small intestine, leading to decreased plasma calcium concentration and clinical "milk fever". Some of these cattle may respond to the first therapeutic dose of intravenous calcium and soon stand, but then relapse after several hours and are not able to stand after the second dose of parenteral calcium.

2. Hypokalemia

Some animals with profound low blood potassium will show evidence of muscle weakness. Hypokalemia may result in muscle weakness, but rarely is dysphagia a major clinical sign. Hypokalemia associated with steroid usage typically results in very weak neck muscles, to the point where the head 'flops' or swings from side to side, suggesting profound weakness of the cervical muscles.[90] Recently, 20-plus adult cattle had died in a 900 cow dairy herd in northern Vermont. Affected cows became weak, wobbly, ataxic and then recumbent over a period of 1-3 days. Affected animals were in the early periparturient period, often with a history of ketosis. Plasma potassium and phosphorus concentrations were very low (< 2.0 mEq/l for both), suggesting steroid associated myopathy. Several affected recumbent animals had very weak neck muscles, which typifies hypokalemic myopathy, but not botulism.

3. Myopathy

Plants such as *Cassia sp* or coffee weed, if consumed, may produce evidence of muscle weakness but usually occurs in younger animals or animals where coffee weed plants are present.[48,79] Nutritional deficiencies, especially vitamin E/selenium deficiency, may show evidence of muscle weakness but occurance is usually in younger animals in specific geographic areas with low selenium levels.[62,73,112] Ionophorous antibiotics such as monensin, narasin, lasalocid, and salinomycin which are used as coccidiostats and growth promotants in animal feeds, if included at high concentrations, may re-

sult in muscle weakness due to myocyte injury.[119] If the outbreak is associated with recent feeding of a new delivery of feed, these types of compounds needs to be investigated with a toxicological analysis.

4. Organophosphate toxicosis

Salivation with hyper-excitability and constricted pupils characterize organophosphate toxicosis whereas animals with botulism will have dilated pupils[8] and are not hyperexcitable. Weak tongues and decreased jaw tone are not typical of organophosphate poisoning. Cattle with tri-ortho-cresyl phosphate toxicity have spinal cord demyelination which may mimic myasthenia leading to recumbency and death, but should have normal tongue tone and are not dysphagic.[8,27,75,81,122]

5. Spinal cord disease

Cattle with spinal cord disease may also resemble botulism but evidence of weakness will be in the rear limbs compared to animals with botulism which would be weak in all limbs and have a weak tongue. Spinal cord diseases such as lymphosarcoma and vertebral body abscess affect only one animal, almost never presenting as herd problem.[82]

Diagnostic Approach

The diagnostic approach to botulism begins with the herd history and includes elucidation of typical clinical signs of botulism in affected animals. Identification of preformed botulinum toxin in partially consumed feed materials or rumen contents provides a definitive diagnosis of botulism. Identification of *Clostridium botulinum* spores in the rumen contents and/or feed materials and ruling out other possible diagnoses provides strong evidence for a presumptive diagnosis of botulism.

Demonstration of preformed botulinum toxin in the serum, feed material or rumen contents remains the gold standard diagnosis for botulism.[45,46] If serum or plasma is submitted as a diagnostic specimen, it must be taken from the affected animal early in the stage of the disease, preferrably soon after onset of clinical signs. A minimum of 10-20 mls is needed because each of two mice should receive 0.5 to 1 ml of serum and, if a mouse shows evidence of wasp-waisting and dies, the test is positive. However, another group of four mice need to be tested with more serum to demonstrate that specific botulinum antitoxin will protect two mice, while the toxin remains lethal for the two unprotected mice. A negative mouse assay does not eliminate botulism, only that if toxin were present it was below the threshhold of detection using the mouse bioassay. Rumen contents and fecal samples may also be tested for preformed toxin but must be kept frozen until tested in the laboratory. Rumen microbes have been shown to degrade botulinum toxin, which may be a partial explanation why cattle are more resistant to botulinum toxin than horses.[2] Toxin is rarely detected in peripheral blood or serum except in very peracute cases that show clinical signs and die within a period of 6-18 hours. Animals with a more gradual onset of clinical signs, over 24-48 hours, rarely have adequate toxin in the circulation to be detectable by the mouse assay, the current gold standard for detection of botulinum toxin by most laboratories in the world.

An anaerobic laboratory, specifically set up to assay samples for botulism, should use precise techniques, have mice available, have appropriate antitoxin standards, including trained, vaccinated personnel working with toxin. Botulism is a toxin dose related disease, where a high dose of toxin (10^8-10^9 $IPMLD_{50}$) will produce death in 12-24 hours. A moderate dose of toxin, such as 10^6-10^7 $IPMLD_{50}$ may cause illness in 24-48 hours and death by 68-96 hours. A lower dose of toxin, 10^3-10^5 $IPMLD_{50}$, may produce only mild clinical signs and some cattle may recover. Botulism toxin may be demonstrated by several techniques including a mouse assay which is the most specific test. An ELISA assay has been developed for type C and D toxin.[41,53,61,110] More recently an ELISA assay coupled with a sensitive coagulation assay improved the sensitivty of toxin detection for types A, B and E toxin to the mouse bio-assay[25,26]. Both the ELISA and mouse assay may fail to detect toxin in many animals suspect for botulism or that actually have botulism because the amount of toxin in the sample is below the detection level of the detection systems. The sensitivity of the initial ELISA assay was about 70% as compared to the mouse assay. Specificity was 96%. Use of a purified antibody increased the sensitivity to about 95%.[41]

In addition to demonstration of preformed botulinum toxin, one should attempt to isolate botulinum spores from rumen, gut or fecal contents. Diagnostic samples should be kept frozen prior to submission to the laboratory. Suspect feed sources such as animal feeds, animal carcass or parts in the feeds, such as bone or flesh should be examined, if found, for botulism spores. Microscopic analysis of feed samples, a diagnostic service available in specialized laboratories, has been invaluable to demonstrate animal parts such as fur or bone parts in the suspect feed.

The media used for botulism culture of spores is a chopped meat glucose broth which may require 3-5 days of incubation.[22,28] After incubation, the broth supernatant is tested in mice for evidence of toxin. If toxic, the supernatant needs to be neutralized with specific antitoxin in the same manner as with the preformed toxin. Alternatively, a sub-sample of the chopped meath broth should be transferred to an egg yolk agar medium using cyclosporine sulfamethoxazole and trimethoprim. If lipase positive colonies are detected following incuba-

tion in an anaerobic chamber, the colonies could be either *Clostridium sporagenes* or *Clostridium botulinum*. Differentiation of these lipase positive colonies is by bioassay of the re-cultured organism chopped meat glucose broth and the supernatant tested in mice for toxin. The mouse toxin assay is sensitive enough to detect 10 picograms of toxin, which is equivalent to 1 g in 1 million tons. At minimum, this is a 4 day test for the mice to show evidence of toxicity. The mice used should be ICR Swiss Webster mice that weigh between 18-24 grams. The time required for detection of botulinum spores is 5-10 days, if the samples are processed soon after receipt in the laboratory.

Another approach to the diagnosis of botulism is the evaluation of antibody titer in animals recovered from botulism. In most species there is relatively little or no circulating botulinum antibody in normal animals, unless they were vaccinated or recently recovered from botulism.[80] Recent reports indicate cattle recovered from botulism may have antibody to type C or type D botulism. Similar findings have been reported in human infants following recovery from type A or type B botulism. PCR has been used to detect botulinum neurotoxin genes in suspect materials and may serve as an alternative diagnostic test for botulism.[106,107,108]

The most common approach to the diagnosis of botulism is to exclude other diseases and having clinical signs compatible with botulism. Additionally, affected cattle should have normal hematologic and biochemistry findings, negative findings at necropsy and multiple animals involved. At this time, the gold standard for diagnosis of botulism is identification of preformed botulinum toxin in the serum or intestinal contents of the suspect animal. Detection of botulinum spores supports the botulism diagnosis but is not definitive. The presence of compatible clinical signs of botulism with the detection of clostridium botulinum spores in the absence of other disease with non-specific pathological lesions is highly suggestive of botulism. In our experience, botulinum spores are rarely found in the rumen contents or fecal samples of normal cattle not at risk for botulism.

Therapy

The initial therapeutic objective should be the neutralization of circulating toxin with specific monovalvent or multivalent antitoxin.[57,58] The antitoxin has no beneficial effect on botulinum toxin after it has been translocated in the cells.[94] Thus, treatment with antitoxin will not reverse clinical signs of muscle weakness or dysphia. At best, the antitoxin will stabilize the patient so that further progression of clincal signs ceases with gradual recovery over the next 5-10 days. After the specific antitoxin is administered, continued absorption from the intestine should have minimal or no additional effect on the clinical condition. The half life of equine origin botulinum antitoxin is about 8 days in cattle. Therefore, only a single dose of antitoxin containing approximately 10,000 IU antitoxin is needed. Since most available antitoxin is of equine origin, veterinarians need to anticipate the likely occurance of acute allergic and anaphylactic reactions.

Little improvement will be apparent for 2-4 days, then gradual regaining of muscle strength should be apparent over the next several days. The patient should have muscular activities restricted and be observed closely for signs of respiratory failure. Antimicrobics may be given for specific secondary complications (i.e., aspiration pneumonia). Antimicrobics have not been effective in eradicating the organism from the intestinal flora. If antimicrobics are used to prevent secondary infections, such as inhalation pneumonia, those that may potentiate neuromuscular weakness should be avoided, i.e., aminoglycosides, tetracyclines, and procaine penicillin.[59,115] Cathartics are often recommended because of the ileus. Magnesium products should be avoided, as these may potentiate the neuromuscular weakness. Mineral oil or sodium sulfate are more appropriate as they do not potentiate muscle weakness. Parasympathomimetics, although they may provide temporary improvement in clinical signs, have been shown to increase mortality in humans. Metronidazole, commonly used in anaerobic infections in humans and animals, does not reduce botulinum spores in the gastrointestinal tract and may enhance their growth in laboratory animals.[114] Germine, guanidine and aminopyridines have been used in the treatment of botulism with minimal beneficial effect and may exacerbate the disease.[14,15,35] Adherence to general principles of good nursing care and nutrition are of utmost importance because of the prolonged time required for recovery. Recovered patients are thought to regain normal nervous and muscular function.

Mildly affected, slowly progressive cases can survive without antitoxin. The patient should have muscular activities restricted as much as possible (confined to a stall).

Since the majority of patients cannot swallow, supportive alimentation is required. A high protein, low residue slurry of alfalfa meal, dextrose, and electrolytes has been used for up to a month to feed horses. Since most animals continue to eat, muzzling may be necessary to prevent aspiration of food or bedding.

Demonstration of toxin in the patient's serum is rarely possible, as the circulating levels of toxin are below the limit of detection with the mouse bio-assay. Occasionally this is possible in man, which as a species is more resistant to the toxin than cattle or horses, which are exquisitely sensitive to the toxin. A near definitive diagnosis can be made by demonstration of the botuli-

num spores and preformed toxin in feedstuffs which have been recently consumed and finding clinical signs typical for botulism.

Botulinum organisms were also isolated from the rumen contents and feces of affected cattle which help confirm the diagnosis because normal cattle do not have botulinum organisms in the gastrointestinal contents. The exception to this is the animal at risk, i.e., exposed to a herd outbreak but not showing clinical signs. Botulism does occur sporadically and the practitioner needs to be kept aware of that possibility.

Botulinum Toxin in Milk and or Meat?

During an outbreak of botulism in dairy or beef cattle, questions often arise about the advisibility of using the milk or meat from affected cattle for human consumption. Clearly cattle with clinical botulism have absorbed botulinum toxin from the gastrointestinal tract into the blood and peripheral circulation.

Therefore, it seems probable that toxin will be present in meat and possibly secreted into the mamary gland to be present in milk.

If botulinum toxin is in the milk or meat of affected cattle, how long should milk or meat be withheld from the marketplace? The author is unaware of any reports of finding botulinum toxin in the milk of cattle with botulism. However,in one report involving axenic rats experimentally dosed with *C. botulinum* spores, low levels of botulinum toxin was demonstrated in the gastrointestinal contents of 2 to 3 day old pups that nursed affected dams (Moberg, 1980).

Prevention

A toxoid Bot Tox B for *Clostridium botulinum* Type B is available from Neogen Corporation, Lansing, Michigan. No botulism vaccine is approved for cattle in the United States at this time. In horses, the recommended interval between the three doses of toxoid is 30 days. A type C and D toxoid is available for cattle and sheep in Australia which has been used to prevent outbreaks of botulism in sheep and cattle.[8]

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