

Clinical findings and response to treatment of 17 cases of tetanus in horses (2012–2021)

Achados clínicos e resposta ao tratamento de 17 casos de tétano em equinos (2012-2021)

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Abstract

Tetanus is a distressing and often fatal disease caused by exotoxins released by the bacterium *Clostridium tetani*. *Clostridium tetani* is a commensal of the gastrointestinal tract of humans and domestic animals, and its spores are highly resistant to environmental changes, acid, and alkali and may persist in the soil for many years. The disease is characterized by generalized muscular rigidity and spasms, hyperesthesia, convulsions, respiratory arrest, and death. Horses are the most susceptible domestic animals. Treatment is typically directed towards elimination of the source of the toxin, neutralization of any unbound toxin, establishment of antitoxin immunity, control of neuromuscular derangements, and relief of pain. This study described the clinical findings and therapeutic protocols of 17 horses with tetanus, treated between March 2012 and December 2021. The diagnosis of tetanus was based on the history and clinical examination findings of the animals. All horses received a treatment pattern composed of the administration of tetanus serum (50,000 UI, intravenously, followed by three injections of the same dose at 48-h intervals), procaine penicillin (25,000 UI/kg, intramuscularly, BID, for 10 days), and muscle relaxant (acepromazine 0.02–0.05 mg/kg, intramuscularly, BID, for 8 days). Support therapy based on hydroelectrolytic replacements, feeding via a nasogastric tube, and assistance in the maintenance of the quadrupedal position were performed when needed. The mortality rate observed in this report was 23.52%. Early diagnosis associated with the instituted treatment contributed the most to the animal recovery.

Keywords: *Clostridium tetani*, hyperesthesia, tetanus antitoxin, tetanospasmin.

Resumo

O tétano é uma doença angustiante e frequentemente fatal, causada por exotoxinas liberadas pela bactéria *Clostridium tetani*. *Clostridium tetani* é um microrganismo comensal do trato gastrointestinal do homem e de animais domésticos, e seus esporos são altamente resistentes às mudanças ambientais, ácidas e alcalinas, podendo persistir no solo por muitos anos. A doença é caracterizada por rigidez muscular generalizada e espasmos, hiperestesia, convulsões, parada respiratória e morte. O cavalo é a espécie de animal doméstico mais suscetível. O tratamento é tipicamente direcionado à eliminação da fonte da toxina, neutralização de qualquer toxina não ligada, estabelecimento de imunidade à antitoxina, controle de distúrbios neuromusculares e alívio da dor. Os achados clínicos e protocolos terapêuticos de 17 cavalos com tétano tratados durante o período de março de 2012 a dezembro de 2021 são descritos. O diagnóstico de tétano baseou-se na história e nos achados do exame clínico dos animais. Todos os cavalos receberam padrão de tratamento, composto pela administração de soro tetânico (50.000UI, por via intravenosa, seguido de três outras aplicações da mesma dose em intervalos de 48 horas), penicilina procaina (25.000UI/kg, intramuscular, BID, por 10 dias) e relaxante muscular (acepromazina 0,02-0,05 mg/kg, por via intramuscular, BID, por oito dias). Foram realizadas terapia de suporte baseada em reposições hidroeletrólíticas, alimentação por sonda nasogástrica e auxílio na manutenção da posição quadrúpede, quando necessário. A mortalidade observada neste estudo foi de 23,52%. O diagnóstico precoce associado ao tratamento instituído foram os fatores que mais contribuíram para a recuperação dos animais.

Palavras-chave: *Clostridium tetani*, hiperestesia, antitoxina tetânica, tetanopasma.

Introduction

Tetanus is an acute and fatal nervous system disorder caused by the neurotoxin *Clostridium tetani*, and it affects humans, domestic animals, and wildlife. Although prevention is possible with vaccination, it continues to be a life-threatening problem in livestock (Altıparmak et al.,



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2018; Ribeiro et al., 2018; Oliveira et al., 2020). The fatality rates for tetanus vary widely among regions (Ribeiro et al., 2018).

Clostridia are genera of anaerobic organisms comprising at least 209 species, and *C. tetani* is one of the most well-known exotoxin-producing pathogens within this category (George et al., 2021). However, not all strains of *C. tetani* are pathogenic. *C. tetani* is a spore-forming, saprophytic, obligate anaerobic, gram-positive bacillus (Oliveira et al., 2020; Almas et al., 2021).

The spores of *C. tetani* can withstand anaerobic and extreme temperature conditions in both indoor and outdoor environments and can be isolated from both human and animal fecal samples and/or from soil. It is well known that tetanus spores survive in the environment for various years and are resistant to heat and disinfectants/antiseptics, but can be destroyed by heating to 239°F (115°C) for 20 min (Hanif et al., 2015; Almas et al., 2021; George et al., 2021).

The transmission of *C. tetani* occurs via exposure of a tissue wound to spores present in soil or fecal matter from animals (e.g., horses, bulls, goats) or humans. The anaerobic conditions in necrotic tissue and/or infected wounds provide an ideal environment for the replication and growth of *C. tetani*. In some cases, tetanus may develop from burn injury, abscess following a surgical procedure, intravenous or intramuscular drug administration, or gangrene. In some cases, no clear portal of entry can be identified, and tetanus may develop after wound healing. The incubation period of *C. tetani* is approximately 7 days but ranges from 3 to 21 days (Hanif et al., 2015; Popoff, 2020; George et al., 2021).

Under anaerobic conditions, *C. tetani* spores germinate and produce three exotoxins: tetanolysin, tetanospasmin, and nonspasmogenic toxin. Reportedly, tetanolysin is capable of locally damaging viable tissue surrounding the infection and optimizing the conditions for bacterial multiplication (Cook et al., 2001). Tetanospasmin, a tetanus neurotoxin, affects the central nervous system and prevents presynaptic release of neurotransmitters that inhibit muscle contraction, leading to uncontrolled muscle contraction and clinical spasms. The role of nonspasmogenic toxins in the pathogenesis of tetanus is not fully understood, but it may involve blocking transmission in peripheral neuromuscular junctions (Hanif et al., 2015; Rhinesmith & Fu, 2018).

Clostridium tetani enters the body through wounds or the gastrointestinal tract, and clinical signs begin after the incubation period. The classical presentation of tetanus seen in patients begins with “locked jaw” or trismus due to spasms of the masseter muscle. The animals present with muscle spasticity, resulting in rigid movements of the limbs, reflex spasms, dyspnea, stiff neck, and difficulty in food prehension, mastication, and deglutition. Sensory stimulation can cause prolonged spasms. Generalized spasms are also accompanied by autonomic disturbances, such as alterations in blood pressure, arrhythmias, hyperpyrexia, and sweating (Reichmann et al., 2008; Rodrigo et al., 2014).

Ears stand immobile and erect, and the tail head is held elevated (“flag tail”). Other characteristic symptoms include hyperesthesia and prolapse of the nictitating membrane. In serious cases, horses adopt a sawhorse stance with severe dyspnea and maintain a recumbent position. The severity of infection is related to the incubation period, time between the onset of symptoms, and emergence of spasms. Death can occur due to laryngospasm or diaphragmatic spasms (Reichmann et al., 2008).

The diagnosis of tetanus is based on immunization history and historical and clinical findings, whereas less emphasis is placed on laboratory testing. Accurate identification can be challenging for clinicians who may never encounter a case over the course of their career (Rhinesmith & Fu, 2018).

Treatment of tetanus involves supportive care for the symptoms of muscle spasms and potential respiratory compromise, neutralization of the circulating toxin, and eradication of bacteria at the wound site. Patients should receive minimal stimulation to avoid reflex spasms. Wound care, including cleaning and debridement of necrotic tissue, is essential for limiting bacterial growth after infection. Antibiotics, particularly penicillin and metronidazole, may prevent disease progression by killing tetanus bacilli, thereby preventing the creation of more tetanospasmin. Infection with *C. tetani* does not provide immunity; thus, all patients diagnosed with tetanus should receive immunization with tetanus toxoid as soon as possible (Rhinesmith & Fu, 2018; George et al., 2021).

This article reports the clinical findings and therapeutic results of 17 cases of tetanus in horses.

Case description

The clinical findings and therapeutic protocols of 17 horses with tetanus, treated between March 2012 and December 2021, are described. The diagnosis of tetanus was based on the history and clinical examination findings of the animals (Table 1).

Table 1. Main clinical and epidemiological findings of 17 cases of tetanus in horses.

Case	Age (years)	Sex	Breed	Injury history	Immunization history	Outcome
1	5	Stallion	Quarter Horse	Castration	Yes	Recovered
2	6	Female	Quarter Horse	Unknown	No	Recovered
3	5	Gelding	Quarter Horse	Unknown	Yes	Recovered
4	2	Stallion	Quarter Horse	Castration	Yes	Recovered
5	7	Female	Quarter Horse	Unknown	Yes	Recovered
6	6	Gelding	Quarter Horse	Unknown	No	Death
7	6	Stallion	Pônei	Castration	Yes	Death
8	12	Gelding	SRD	Unknown	No	Death
9	8	Female	Quarter Horse	Unknown	No	Recovered
10	2	Gelding	Quarter Horse	Unknown	Yes	Recovered
11	6	Gelding	Quarter Horse	Unknown	Yes	Recovered
12	11	Gelding	SRD	Unknown	No	Death
13	4	Female	Quarter Horse	Unknown	No	Recovered
14	1	Foal	Quarter Horse	Hernia surgery	No	Recovered
15	10	Female	M. Marchador	Unknown	Yes	Recovered
16	3	Gelding	M. Marchador	Unknown	Yes	Recovered
17	6	Female	Quarter Horse	Unknown	Yes	Recovered

Hyperesthesia, limb spasticity, hyperexcitability, third eyelid protrusion, “flag tail,” cervical stiffness, tetanic spasms, tachycardia/tachypnea, standing/immobile ears, dysphagia, and restriction of jaw movements were the main signs observed during the first clinical examination of all horses in this study (Figure 1). “Easel” position, drooling, and bruxism were also observed.



Figure 1. Horse showing clinical characteristic signs of tetanus.

All horses received treatment that comprised administration of tetanus serum (50,000 UI, intravenously, followed by three other applications of the same dose at 48-h intervals), penicillin G (20,000 UI/kg, intramuscularly, BID, for 10 days), and muscle relaxant (acepromazine 0.02–0.05 mg/kg, intramuscularly, BID, for 8 days). Support therapy based on hydroelectrolytic replacements, feeding via a nasogastric tube, and assistance in the maintenance of the quadrupedal position were performed, when needed. In all animals, cotton was placed in the ears as part of the therapy to reduce responses to sound stimuli, and direct sunlight was avoided. Clinical monitoring was performed daily until remission of clinical signs.

The ages of the animals ranged from 1 to 12 years. Twelve animals were of the Quarter Horse breed and used for athletic or reproductive purposes. The remaining five animals (one pony, two Mangalarga, and two mixed breeds) were used for weekend recreation. All animals evaluated had a regular nutritional status. Ten of the 17 animals had a history of tetanus vaccination before clinical examination.

In only four of the animals evaluated, it was possible to identify a tissue lesion (three surgical castration wounds and one umbilical hernia closure). Two animals that underwent castration surgery received tetanus antitoxin (10,000 IU, intramuscularly, single dose) in the immediate postsurgery period and had been immunized against tetanus 6 months prior. In the three animals subjected to castration, the clinical signs of tetanus began to manifest 30 days after the procedure.

The mortality rate observed in this report was 23.52%.

Discussion

The observation of the involvement of animals of different sexes and ages corroborates the findings of previous studies (Reichmann et al. 2008; Di Filippo et al., 2016), which demonstrated that there is no predilection for sex, breed, or age. Although 12 animals in this case series were Quarter Horses, this finding reflects only the most representative breed in the study region.

Routine diagnosis of equine tetanus is based on typical clinical signs, presence of wounds, or history of surgical procedures that may predispose to disease (Di Filippo et al., 2016; Ribeiro et al., 2018). Likewise, the diagnosis of tetanus in horses in the current study was based on compatible clinical signs, presence of wounds, and history of surgical procedures.

In studies by Steinman et al. (2000), Reichmann et al. (2008), and Di Filippo et al. (2016), clinical signs similar to those obtained in this series of cases have been described, despite differences in occurrence and severity. Clinical signs of tetanus, characteristic of the disease, and epidemiological data allowed the diagnosis of the condition in this case series. The same approach has been reported by Reichmann et al. (2008), Di Filippo et al. (2016), and Ribeiro et al. (2018).

Thirteen horses examined in the current study did not show visible wounds or previous surgical procedures. These data are in agreement with those of several retrospective studies involving equine tetanus, in which lesions or history of surgical procedures that may predispose to disease were not observed or identified (Reichmann et al. 2008; Gračner et al. 2015; Di Filippo et al., 2016; Ribeiro et al., 2018). Ribeiro et al. (2018) alerts to the fact that the absence of visible wounds at the initial clinical examination, so-called idiopathic tetanus, occur occasionally in herbivores associated with consumption of fibrous or rough feed, possibly leading to toxin production in the wounds located in the mouth or intestinal tract.

Unlike other studies demonstrating that most horses affected by tetanus had no history of immunization at diagnosis (Di Filippo et al., 2016; Ribeiro et al., 2018), in this case series, 58.82% (10/17) of the animals had been immunized for a maximum of 365 days, whereas 41.18% (7/10) had no history of immunization in the last 365 days or had never been immunized.

Immunization against tetanus is part of routine veterinary care for horses, but recommendations for best practice vary between countries. For example, the American Association of Equine Practitioners (AAEP) guidelines recommend annual boosters after basic immunization, but state that protective titers may persist for longer. In Sweden, tetanus vaccination is administered once every 3 years, whereas in the UK, it is generally recommended to give the booster every 2 years, and in New Zealand, tetanus vaccines are registered for boosters at 5-year intervals after basic immunization (Kendall et al., 2016). In Brazil, the general recommendation for immunization against tetanus is to carry out a primary vaccination course followed by a booster dose after 21 to 30 days. After this basic immunization, annual booster doses are recommended.

The mortality rate observed in this study was 23.52%, in contrast to previous reports by Di Filippo et al. (2016) and Ribeiro et al. (2018) who reported death rates of 80%, 72.9%, and 76.3%. However, in these studies, the evaluated population was composed of nonimmunized animals, which is different from that of the present study. When only animals without a history of vaccination were considered, the mortality rate increased to 57.12%.

High mortality caused by tetanus in horses has been attributed to the dose of clostridia inoculation and toxin production, poor body condition and immune status of animals, lack or improper vaccination, therapeutic procedures and veterinary assistance only long after the onset of clinical signs, high susceptibility of horses to tetanus toxin, inappropriate horse care, and nursing care limitations in affected horses (Ribeiro et al., 2018).

Of the animals with an identified tissue lesion as a likely entry point for *C. tetani*, only one died. These findings are similar to those described by Reichmann et al. (2008) and Ribeiro et al. (2018) who did not observe any statistically significant association between the outcome and the presence of wounds or previous surgical procedures. However, in a retrospective study carried out in Croatia, the presence of obvious wounds has a statistically significant effect on mortality (Gračner et al. 2015).

The clinical course and prognosis for survival depend on the immune and vaccination status of the host, dose of clostridial inoculation, and duration and availability of aggressive treatment and supportive care. The prognosis is best for horses that have been vaccinated with toxoids within 1 year (Green et al., 1994).

Although there is a belief among horse owners and some veterinarians that tetanus immunization prevents its occurrence, our study and the study by Green et al. (1994) demonstrated that tetanus can occur in previously immunized animals. Indeed, individual horses vary in their immune response to the tetanus toxoid.

Although frequently cited in literature, regardless of the presence of dysphagia, aspiration pneumonia was not observed in any case in this study, corroborating the findings of Reichmann et al. (2008).

The major principles of treatment include elimination of the causal agent, neutralization of tetanus antitoxin, maintenance of hydroelectrolytic balance, cleaning and antiseptic care of wounds, administration of muscle relaxants, and maintenance of the animal in a quiet and comfortable environment (Ribeiro et al., 2018). Although therapy with anti-tetanus serum, antimicrobials, and myorelaxants constitutes the standard protocol for the treatment of tetanus, there are differences in the doses used, intervals between administrations, and drugs used between various case reports, as well as within the same report describing several cases (Reichmann et al. 2008; Di Filippo et al., 2016; Ribeiro et al., 2018; Pereira et al., 2019; Silva et al., 2020).

The administration of variable doses of the tetanus antitoxin for the treatment of clinical cases of tetanus or after tissue injury (Di Filippo et al., 2016) aims to neutralize the circulating toxin outside the nervous system, because the tetanus antitoxin cannot cross the blood-brain barrier or combine with toxins that are in route to the central nervous system via retrograde axonal migration (Green et al., 1994).

In contrast to previous reports (Reichmann et al. 2008; Di Filippo et al., 2016; Ribeiro et al., 2018; Pereira et al., 2019; Silva et al., 2020), in the present case series, 50,000 IU of tetanus toxin was administered intramuscularly every 48 h, totaling four doses. Although the concentration of circulating unbound toxins is likely low, some patients may have overwhelming amounts of circulating toxins. The rapid catabolism of passively acquired anti-tetanus antibodies may justify repeated treatment or large doses of tetanus antitoxin when aggressive wound debridement is not possible or when treatment has been delayed for several hours or days (Green et al., 1994).

Di Filippo et al. (2016) stated that better results were achieved when the tetanus antitoxin was administered early in the course of the disease, that is, even before muscle stiffness, spasms, and decubitus ulcers occur, goals were rarely achieved due to the late referral of the animal. In the present study, some animals already presented stiffness and muscle spasms at the time of the clinical examination, and although it was not possible to apply any statistics, the clinical impression obtained was that in the surviving animals, the administration of a tetanus antitoxin was effective even in cases with the most advanced clinical symptoms.

Penicillin G was used to eliminate the etiological agent of tetanus. Historically, penicillin has been recommended in veterinary literature at dosages of up to 50,000 IU/kg. The chemical structure of penicillin is similar to that of GABA, an important inhibitory neurotransmitter. Penicillin may act as a competitive antagonist. In tetanus, this potential side effect of penicillin may act synergistically with the toxin to block GABA neuronal activity and worsen the clinical signs in some cases. However, in none of the animals was worsening of the clinical signs observed with the administration of penicillin G. Other antibiotics of value include metronidazole, erythromycin, doxycycline, and chloramphenicol (Furr, 2015).

Antimicrobial treatment should be continued for at least 10 days, with the ultimate goal of ensuring the death of the spore-forming bacteria in tissues (Furr, 2015). However, although resistance is rare, the bacteria may not be universally sensitive to first-line antibiotics for tetanus (Rodrigo et al., 2014).

The clinical follow-up period for surviving animals was 15 days. Despite the remission of clinical signs, these animals showed a time deficit in locomotion and proprioception, neck stiffness, and heightened sensitivity to noises that disappeared over 30–60 days, corroborating the findings of Di Filippo et al. (2016).

Conclusion

Despite being vaccine-preventable, tetanus is still a relatively common disease in horses. The most important factor that determines the outcome of tetanus is the quality of supportive care and the rapidity of treatment initiation after a diagnosis has been made. The established therapeutic protocol proved to be effective in reversing clinical symptoms.

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Ethics statement

All procedures were consented by the animal owner.

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the preparation of this manuscript.

Authors' contributions

UPM, CF - Writing, Review and Editing manuscript.

Availability of complementary results

None.

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