Journal of Advances in Microbiology Research

E-ISSN: 2709-944X
P-ISSN: 2709-9431
JRM 2024; 5(1): 22-26

www.microbiojournal.com
Received: 02-12-2023
Accepted: 10-01-2024

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Animal and human tetanus: An overview on transmission, pathogenesis, epidemiology, diagnosis, and control

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Abstract
Tetanus is a bacterial environmental disease with neurological condition that affects both people and animals, causing spastic paralysis. The disease is prevalent in many countries of the world including India and Ethiopia. Neonatal tetanus is a killer disease that carries high mortality. It affects the people of active age. Source of infection is exogenous as soil and dust serve as a natural habitat of the bacterium. Agricultural workers are at special risk of acquiring the infection because of their contact with soil. The gram-positive, sporulating bacterium *Clostridium tetani*, which is soil-borne and environmental, produces the toxin that causes tetanus. The majority of the times, the soil contaminated by *Clostridium tetani* spores causes wound contamination, which produces the disease. Tetanus toxin can harm humans, horses, and sheep, but it can also cause injury to cattle, dogs, and cats. The cost and availability of high-quality protein for human consumption are directly impacted by illnesses that compromise the well-being and productivity of food animals. Diseases contribute to economic losses by diminishing meat, milk, or feed conversion, slowing weight gain, and lengthening the period an animal to stay on the farm before being marketed, in addition to the costs associated with treating sick animals and their deaths. Currently, there is no specific laboratory test available to unequivocally establish the diagnosis of tetanus. However, clinical symptoms, case history, wound presence, and disease development are typically used to make the diagnosis of tetanus in animals. It is frequently challenging to identify *Clostridium tetani* at the wound site. A formaldehyde-inactivated tetanus toxin vaccination is a method of medical prevention. For tetanus, there is not an effective medication for treatment of disease in animals. Active immunization with tetanus toxoid is considered the best preventive method in humans. Severe complications of disease can be life-threatening. This review focuses on pathogenesis, diagnosis, economic importance, and control of tetanus in animals and humans.

Keywords: *Clostridium tetani*, diagnosis, humans, pathogenesis, prevention, public health, tetanus

Introduction

Tetanus, also known as lockjaw, is a life-threatening bacterial disease of public and economic significance, and is characterized by spastic paralysis (Pal, 2007) [15]. It is a fatal disease of nervous system caused by toxins released by *Clostridium tetani* that is found in the soil. Tetanus toxin (TeNT), a neurotoxin, is the cause of tetanus. *Clostridium tetani* is an anaerobic, sporulating environmental soil bacterium that produces tetanus toxin. It is not possible to spread tetanus. Wound contamination with *Clostridium tetani* spores frequently leads to infection and subsequent clinical illness (Hassel, 2013) [10]. Usually, a cut, puncture, or other break in the skin caused by a contaminated object allows the bacteria to enter the body. They create poisons that prevent muscles from contracting, which cause the common symptoms (Vandelaer *et al*., 2003) [21].

The neurotoxins of *Clostridium tetani* cause tetanus, a severely lethal, non-infectious illness that affects all domestic animal species. The way that different animal species react to neurotoxins varies. The species that are most vulnerable are humans, horses, guinea pigs, monkeys, sheep, mice, goats, and carnivores like dogs and cats (Pal, 2007) [15]. The disease is also reported in elephant (Pal, 2007) [15]. The species that are most resilient are birds and poultry. The variation in sensitivity and resistance between species can be attributed to the differential difficulty of poisons penetrating and attaching themselves to nerves in various species (Acke *et al*., 2004) [1]. Sometimes, it is difficult to locate the tetanus wound since it can be extremely small. Injections, ear tagging, shearing, castration, and many other traumatic body procedures can also contaminate *C. tetani* (Lotfollahzadeh *et al*., 2019) [13].

It is commonly recognized that the soil polluted by animal feces and animal waste, especially horse dung; contain *C. tetani* organisms, whose spores can remain in the soil for many years. When bacterial spores from contamination get into injured or damaged tissue, the disease begins (Radostits *et al*., 2008) [16].

Animal tetanus is often diagnosed based on clinical symptoms, case history, wound presence, and disease progression. Tetanus must be identified based on distinctive clinical indicators because there is no reliable ante-mortem testing for the disease. The diagnosis is facilitated by the recent history of injury, muscle spasms, and third eyelid prolapse (Radostits *et al*., 2008) [16]. The indications and symptoms that are present are what make a diagnosis. People do not contract the sickness from one another. Muscle spasms are a symptom of tetanus, commonly referred to as lockjaw. The most prevalent kind starts with jaw spasms and spreads to the body's other parts. For three to four weeks, there will be regular spasms that typically last a few minutes each (Atkinson, 2006) [4]. Severe spasms have the potential to break bones. Fever, perspiration, headaches, difficulty swallowing, elevated blood pressure, and a rapid heartbeat are possible additional symptoms. Usually, the symptoms appear 3 to 21 days after the infection. Months could pass before an individual recover. It is mentioned that 10% of afflicted individuals pass away (Atkinson, 2006) [4].

The bacteria *C. tetani's* spores are the source of the acute infectious illness tetanus. The illness is still a major concern in many parts of the world, but it is particularly prevalent in low-income nations with low vaccination rates and unhygienic birth practices. The diagnosis and treatment of tetanus is challenging. Therefore, the objective of this communication is to review tetanus in farm animals and humans with particular reference to pathogenesis, diagnosis, economic importance, and control.

Etiology

The bacillus form of *C. tetani* is the pathogen responsible for tetanus. *Clostridium tetani* spores are widely dispersed throughout the environment, and have a long lifespan (WHO, 2017) [23]. These spores can become tetanus bacilli under the right anaerobic conditions, which will then cause them to create tetanus toxins. Despite this resistance, the spores can be decontaminated in a number of ways. The most prevalent cause of infection is spore contamination of the wound, even in cases where medical intervention was not considered urgent (WHO, 2010) [22].

Mode of transmission

The spores *Clostridium tetani* from the earth and animal and human excrement are directly transferred to wounds and cuts, causing tetanus. It is not passed from one person to another. Tetanus risk factors in unvaccinated or partially vaccinated populations include contaminated puncture wounds, compound fractures, burns, frostbites, ulcers, gangrene, unclean births, and unsanitary cord care procedures. With a median of seven days, the interval between tetanus spore injection and the onset of symptoms might vary from one day to one month. Neonatal tetanus has an incubation period (age at first symptom) that spans the first 3–14 days of life, with days 6–8 being the most common (ECDC, 2023) [8]. In animals, shearing, dehorning, castration, and tail docking may give opportunities to infection (Pal, 2007) [15]. Ear tagging in sheep resulted in an outbreak of tetanus in sheep (Lotfollahzadeh *et al.*, 2019) [13]. In few cases, the bite from dogs has also resulted tetanus (Pal, 2007) [15].

Pathogenesis

An anaerobe with terminal spherical spores, *Clostridium tetani*, is found in intestinal tracts and soil, particularly cultivated soil. Most of the time, wounds-especially deep punctures wounds that offer an appropriate anaerobic environment-are how they enter the tissues. In healthy tissue or even in wounds, *C. tetani* spores cannot proliferate provided the tissue maintains the usual oxidation-reduction potential of the circulating blood. Tissue necrosis brought on by a small quantity of dirt or an alien object creates ideal circumstances for multiplication. The germs continue to grow and remain concentrated in the necrotic tissue at the injection site. Strong neurotoxins are released during the autolysis of bacterial cells. The zinc-binding protease known as neurotoxin cleaves the membrane protein synaptobrevin, which is connected to vesicles. Toxin is usually absorbed by the local motor nerves and moves up the nerve tract retrogradely to the spinal cord, where it results in ascending tetanus (MVM, 2021) [14].

Because it interferes with presynaptic nerve endings' ability to produce inhibitory neurotransmitters, the toxin causes spasmodic, tonic contractions of the voluntary muscles. If the infection site releases more poison than the surrounding nerves can absorb, the extra toxin is transported by the lymph to the circulation and eventually the central nervous system, where it results in descending tetanus. Tetanic muscle spasms are characterized by their ability to be triggered by even mild stimulation of the affected animal. Bone fractures could result from the spasm's extreme severity. Respiratory failure is caused by spasms that affect the diaphragm, intercostal muscles, and larynx. Chest tachycardia, hypertension, and cardiac arrhythmias are the outcomes of autonomic nervous system involvement (MVM, 2021) [14].

Epidemiology

Tetanus is a bacterial disease of humans and animals, and is reported from many nations of the world. However, the disease is more common in tropics than temperate climates (Pal, 2007) [15]. Infection is acquired by contamination of wounds with spores of the bacterium (Pal, 2007) [15]. *Clostridium tetani* primarily lives in soil, although a variety of animals, including omnivores and herbivores, carry the bacilli in their intestines, and expel the spores in their feces. Global dispersion characterizes tetanus spores, and a population's incidence of tetanus mostly indicates how well its immunization program is working. Countries with low prenatal care attendance, dangerous traditional cord care practices, and insufficient vaccine coverage continue to have high rates of tetanus (ECDC, 2023) [8]. People who work with soil, sewage, and manures are more likely to get the infection. The incidence of disease is higher in rural areas as compared to urban region. Disease in the new born is called as 'neonatal tetanus' as they acquire the infection at birth when umbilical cord is cut with unclean instrument. Most cases occur in poor and remote areas where unhygienic obstetric and post-natal practices are prevailed. Disease is not communicable from animals to humans and vice- versa (Pal, 2007) [15].

Clinical spectrum

Animals

Clinical signs of tetanus in cattle are varied and range from mild to severe on presentation (De Lahunta nd Drivers, 2008) [6]. The first detectable clinical signs of tetanus in cattle are usually generalized stiffness and reluctance to move (Andrews *et al*., 2004) [3]. As the disease progresses, a change in gait is detected; a stiff, stilted walk is classic for tetanus in cattle. A "sawhorse" stance is typical in affected cattle due to extensor muscle rigidity. On further physical examination, the practitioner will frequently note while taking a rectal temperature that the animal's tail is stiff and raised away from the perineum (De Lahunta, and Drivers, 2008) [6]. This "pump-handle" tail is frequently seen in cattle due to the involvement of the coccygeal muscles (Rings, 2004) [17].

Cattle that are affected may show signs of anxiety, including held-open eyelids, upright ears drawn toward the poll, and stretched heads with flared nostrils. It is common to observe prolapse of the nictitans, which is caused by the retractor oculi muscles spasming, pushing the globe into the bony orbit, and permitting passive prolapse of the nictitans. The jaws become extremely tight when trying to open the mouth because the muscles involved in mastication may be affected. Cattle that are affected typically become increasingly dehydrated as a result of losing their ability to drink and feed. As the illness worsens, rumen contractions are typically weak or nonexistent. Due to eructation failure, cattle often bloat (De Lahunta and Drivers, 2008) [6]. External stimuli, such as loud noises or handling the animal can cause tetanic convulsions, but in more severe situations, the convulsions may happen on their own (Andrews et al., 2004) [3]. When cattle contract tetanus, they may die from aspiration pneumonia caused by bloat or from respiratory failure brought on by exercise. Moreover, euthanasia might be required in cases of musculoskeletal ailments such as hip luxations or long bone fractures (De Lahunta and Drivers, 2008) [6].

Humans

The normal duration of disease is four to six weeks. The tightening of jaw muscles is recognized as the earliest sign of tetanus (Pal, 2007) [15]. The painful spasms (clonic and tonic) of masseter muscles (trismus) and neck muscles, rigidity of abdominal muscle, constipation, urine retention, paralysis, and death are observed in the affected patients (Pal,2007) [15].

Diagnosis

In animals, the existence of a wound, the course of the illness, the clinical indicators, and the case history all play a role in the diagnosis of tetanus. Severe muscle rigidity and spastic paralysis are hallmarks of tetanus. Sometimes a lengthy incubation period makes a wound invisible. Due to particular culture conditions and low bacterial numbers, the identification of *Clostridium tetani* in contaminated wounds is highly problematic. According to rigorous anaerobic culture conditions, *C. tetani* must be cultivated on certain media (Greene, 2006; Pal, 2007) [9, 16]. Tetanospasmin detection has diagnostic applications. Tetanospasmin can be identified via ELISA using certain polyclonal or monoclonal antibodies (Huang *et al*., 2013) [11].

Tetanus toxin is typically undetectable in biological samples and is frequently difficult to identify. Animals must have very low TeNT levels in order to exhibit tetanus symptoms. Seldom is it reported that TeNT can be found in serum samples from tetanus-stricken humans or animals (Delbrassinne and Vanderpas, 2015) [7]. There is minimal *Clostridium tetani* isolation from infected wounds. It is mentioned by Smith and George (2002) [19] that there is a lack of dependable clinicopathologic assays to validate a tetanus diagnosis, and there has been minimal endeavor to create an immunodiagnostic test. Although TeNT is so potent that detection at the picogram level would be required for it to be therapeutically helpful, an ELISA test was developed to detect TeNT at a level of l.2 ng/ml (Rings, 2004) [17].

Detection of Clostridium tetani in contaminated wounds

Isolation of *C. tetani* at the point of entry consists of enrichment culture from tissues or exudate from the suspected wound. Enrichment cultures are performed in rich medium for anaerobic bacteria such as TGY (trypticase, 30 g/L; glucose, 5 g/L; yeast extract, 20 g/L; cysteine HCl, 0.5 g/L; pH 7.5) or fortified cooked meat medium (FCMM; 12.5% cooked meat medium (Difco, Detroit, MI), 0.5% calcium carbonate, 1% ammonium sulfate, 1% yeast extract, 0.8% glucose, 0.5% soluble starch, and 0.1% cysteine-HCl, pH 7.6) (Takeda *et al*., 2005) [20]. Optionally, inoculated enrichment media are heated at 60°C for 30 min for spore selection. After 1–5-day incubation at 37°C in anaerobic conditions, *C. tetani* can be detected either by identification of TeNT in the enrichment culture supernatant or by detection of tent-containing clostridia. It is noteworthy that the detection of *Clostridium tetani* in suspected wounds is often problematic. For example, clostridia were cultured in only 4 of 2 wound samples from dogs with clinical signs of tetanus (Shea *et al*., 2018) [18].

Identification of tetanus toxin in culture supernatant

Tetanus toxin can be detected in the culture supernatant by the mouse bioassay. Culture supernatant (0.2 ml) is injected intramuscularly in mice, and the animals are observed for typical spastic paralysis for 1–4 days. Tetanus toxin can be detected by ELISA with specific polyclonal or monoclonal antibodies (Kiessig *et al*., 1991) [12].

Economic importance

Tetanus is a bacterial zoonosis, which is significant from public health as well as economic point of view (Pal, 2007) [15]. Diseases that affect the health and productivity of food animals directly impact the cost and supply of high-quality protein available for human consumption. In addition to the expense resulting from animal treatments and death, diseases also cause economic losses by decreasing meat, milk, or feed conversion, slowing weight gain, and increasing the time the animal must remain on the farm before marketing. Tetanus affects all ruminant animals including cattle and sheep. The clinical manifestations of disease begin as muscle stiffness and tremors, which progress to convulsion and death (Aiello and Mays, 1998) [2].

Treatment

The therapy of tetanus is challenging as no specific chemotherapeutic agent is available that is very effective in treating the disease. However, administration of tetanus antitoxin, antibiotics, wound debridement, and supportive care are advised.

Patients should be admitted in the hospitals for starting immediate treatment to save the life. Supportive treatment consists administration of muscle relaxants to control spasms, provision of quiet environment, and maintenance of airways by tracheostomy. Antibacterial therapy with penicillin or metronidazole should be started immediately and continued for 7 to 14 days. It is advised that patients recovering from tetanus should receive full course of active immunization (Pal, 2007) [15].

Prevention and control

Immunization with TeNT inactivated with formaldehyde is a method of medical prevention. There is no particular therapy for tetanus. Antitoxin antibodies cannot access poisons that have entered neuronal cells, whereas TeNT antibodies stop free TeNT from entering neurons through the serum (CDC, 2015) [5]. Although it has been noted that cattle are less likely than other farm animals to contract tetanus, it is nevertheless crucial to lower the possibility of wounds or necrotic areas where *C. tetani* spores could sprout on cattle. Dehorning, band castration, nose ring installation, tail docking, and ear tag implantation are examples of elective operations that may result in open wounds (Smith and George, 2002) [19]. Every procedure requires surgeons to utilize sterile tools and maintain hygienic surgical circumstances. Tetanus in neonates is mostly preventable with basic hygiene techniques, most notably the cleaning of the umbilicus. Surgical procedures (tail docking and castration) have to be carried out in hygienic settings and with sterile supplies (Acke *et al*., 2004) [1].

In this context, Smith and George (2002) [19] have mentioned that cattle are not regularly immunized against tetanus, and the majority of multi-clostridial vaccinations do not offer particular protection against *Clostridium tetani*. Cattle can be readily and affordably immunized with tetanus toxoid on farms or in regions where tetanus is a concern (De Lahunta and Drivers, 2008) [6]. After the initial series booster injection, protective antibody levels often develop two weeks later. If clinical tetanus is anticipated in exposed animals, tetanus antitoxin should be administered as soon as possible (De Lahunta and Drivers, 2008) [6].

In humans, certain measures like active immunization with tetanus toxoid, thorough washing of wound with soap and water and proper cleaning, complete removal of foreign material and debridement of necrotic tissues, application of antiseptics to surgical wound, use of aseptic condition in all surgical operations, proper autoclaving of instruments and dressings, and administration of tetanus antitoxin to unimmunized persons with a deep wound will certainly help to minimize the incidence of tetanus (Pal, 2007) [15]. The person who receives penetrating injury on the skin must immediately seek medical advice.

Conclusion and recommendations

Tetanus is a serious disease of humans and domestic farm animals with high morbidity and mortality. The disease is more prevalent in the developing countries, warm climate and in rural areas. The illness almost invariably results in death if treatment or prevention is not received. Although cattle, sheep, goats, and pigs are less susceptible, horses are the most vulnerable. Anaerobic environments, or those with no oxygen, are necessary for the growth of *Clostridium tetani*. A deep penetrating wound, an umbilical or post-partum uterine infection, a serious skin laceration, or a post-castration or post-tail docking treatment (particularly linked to banding) are the main entry points for bacterium into an animal's body. In humans, bacterium can enter the body through surgery, injection, burn therapy, umbilical stump, and induced abortion. Clinical signs in humans may help in making the tentative diagnosis. Isolation of the pathogen can be attempted anaerobically by culturing material from deep wound. Supportive treatment is given immediately to minimize the sufferings of the patient.

On the basis of the aforementioned conclusions, the following suggestions are made:

- It is emphasized that all traumatic injuries/ wounds must receive immediate medical treatment as it is the most efficient strategy to prevent tetanus.
- To help avoid *Clostridium tetani*, wounds should be properly cleansed, as this may help with the mechanical removal of spores. Additionally, antibiotics should be used in these situations.
- Tetanus toxoid injections can be used to achieve active immunization.
- The highest level of aseptic technique should be used during every surgical procedure.
- It is advised that patient should be immediately admitted to the hospital to reduce the morbidity and mortality.
- A person whose immunization is out of date and receive a traumatic injury, must receive booster within 48 hours of an injury.

Acknowledgements

The authors are thankful to Prof. R.K. Narayan for going through the manuscript and Yashvardhan for computer help. This paper is dedicated to the Scientists who made outstanding contribution in the field of tetanus.

Contribution of authors

All the authors contributed equally.

Conflict of interest

There was no conflict of interest among the authors.

Financial support

No financial support was received from any organization.

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How to Cite This Article
Pal M, Rebuma T, Regassa M, Tariku F. Animal and human tetanus: An overview on transmission, pathogenesis, epidemiology, diagnosis, and control. Journal of Advances in Microbiology Research. 2022;5(4):01-03.