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TETANUS (CLOSTRIDIUM TETANI); ITS STATUS, PATHOGENESIS, AND TREATMENT (VACCINATION): A DIGEST

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ABSTRACT

Clostridium tetani is the bacterium that causes tetanus, also referred to as lockjaw, which is characterized by muscle spasms. The most prevalent kind causes the jaw to tremble first, then the rest of the body. In 1884, tetanus was first created in animals by injecting them with pus from a fatal human tetanus case, even though clinical descriptions of the disease date back to documents from the 5th century B.C. Painful, uncontrollable jaw spasms are frequently the initial symptoms of widespread tetanus. Ten days on average after the pathogen enters your body, tetanus symptoms appear. However, they may begin three days after infection or three weeks or longer later. Additional early signs of tetanus include: Additional signs of tetanus. Tetanus toxoid (TT), another name for the tetanus vaccine, is a toxoid vaccination that is used to prevent tetanus. Crystal Bae; Bourget, Daniele. Current Date of Update: May 31, 2023. Lockjaw, commonly known as trismus, and muscle spasms are symptoms of tetanus. Clostridium tetani produces toxins that are in charge of the distinctive appearance. During the 1990s, tetanus infection rates in many Asian and African nations exceeded 5 cases per 100,000 years. Several nations have tetanus infection rates of more than 20 per 100,000 inhabitants, including Somalia, India, Pakistan, and Chad. However, by 2019, many countries had seen a decrease in infection rates, and only a few nations had annual tetanus infection rates of more than 5 per 100,000 people. In this article, we assess tetanus's present state, possible therapies, and underlying causes.

KEYWORDS: Tetanus (Clostridium Tetani), Epidemiology, Etiology, Pathophysiology, Treatment.

INTRODUCTION

Spores of the bacteria Clostridium tetani are the cause of the acute infectious disease tetanus. The spores are present in many parts of the environment, although they are more prevalent in soil, ash, animal and human intestines excrement, skin, and rusty objects like nails, needles, barbed wire, etc. A medical condition known as tetanus is typified by widespread hypertonia, which can cause excruciating jaw and neck muscle spasms. The sickness primarily affects older people with declining immunity or those who have not received a vaccination. Worldwide, tetanus incidence and prevalence have currently declined as a result of immunization initiatives. Tetanus can cause spasms that begin in the face and spread to the rest of the body, lasting anywhere from a few minutes to many weeks. The bacterium Clostridium tetani produces toxins that induce symptoms. There are four primary forms of tetanus based on clinical characteristics: cerebral, localized, neonatal, and generalized tetanus. Most frequently, infections happen when germs get into the body through wounds to the skin or mucous membranes. In the contaminated wound, the causal agent grows and reproduces if anaerobic conditions are reached, producing an exotoxin that results in illness symptoms. If there is little oxygen present in the wounded tissue, tetanus may develop from little or even undetectable wounds. The term "tetanus" refers to a bacterial infection caused by the necessary anaerobic gram-positive bacillus Clostridium tetani. Spores can enter the body through a cut or other wound and manifest in soil or faeces. As it were, expansion occurs in tissue that is not adequately oxygenated, leading to localized contamination and the production of two toxins: tetanospasmin and tetanolysin. The former causes systemic symptoms, while the latter damages nearby tissue, which promotes further bacterial growth. Individuals cannot contract tetanus from one another. Through the engine conclusion plates, cell bodies, and unavoidably the presynaptic terminals, tetanospasmin enters the circulation system and spreads to the anxious framework. All neurons are affected, but the inhibitory pathways that regulate the release of glycine in the spinal

cord and γ-aminobutyric acid (GABA) in the brain are the most affected. The most effective preventive measure is tetanus vaccination. The vaccine, which was developed in 1923, consists of a benign byproduct of the toxin that triggers the body to produce antitoxic antibodies. Beginning at two to three months of age, the vaccination consists of four subsequent infusions spaced out over time. After the instant of infusion, resistance begins. For ongoing resistance, adults should receive a booster infusion every ten years. Old records from the 5th century BC contain clinical descriptions of tetanus. Nicolaier created tetanus in animals in 1884 by injecting them with soil samples. In 1889, Kitasato isolated the organism from a human tetanus patient and reported that some antibodies neutralised the toxin. December first described tetanus toxoid in 1924, and it was successfully employed throughout World War II. Around 18 cases of tetanus occur for every 100,000 people worldwide each year, with a 20–50% case fatality rate. While the prevalence of this disease has significantly decreased over time in places like the USA, it is still commonly detected in poorer nations.[1,2] There is no specific laboratory test to validate the clinical diagnosis of tetanus. Antibiotic medication, neuromuscular inhibition, tetanus immunoglobulin, and supportive care for breathing issues, autonomic instability, and muscle spasms are all part of the treatment. Following recovery from the illness, a complete tetanus vaccination is necessary. Survivors have experienced long-term consequences.[3-6]

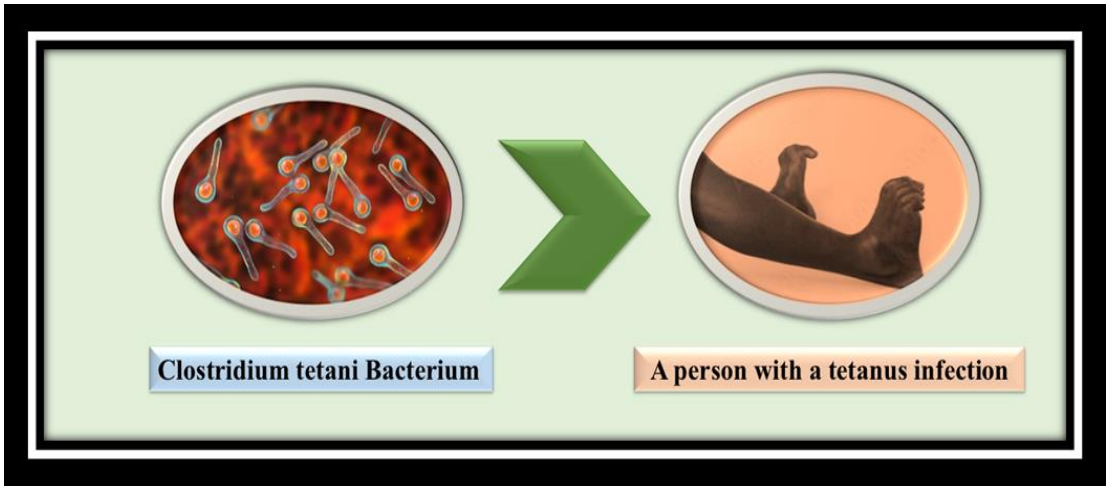

Fig. 1: Infection with tetanus.

Sign and Symptoms

For the majority of patients, tetanus manifests as trismus. Patients who have tetanus may initially seek dental care due to the masseter muscles' greater prominence in comparison to the opposing digastric and mylohyoid muscles. The distinctive appearance of risus sardonicus is caused by the rigidity of the facial muscles. Laryngeal muscular spasms can occur at any moment. In patients with undiagnosed tetanus, recalcitrant pharyngeal spasms following tracheal extubation have been observed. Pharyngeal muscular spasm may be the cause of dysphagia. Diaphragmatic and intercostal muscular spasms interfere with adequate ventilation. The opisthotonic position is caused by the lumbar and abdominal muscles' inability to bend. The tonic and clonic character of skeletal muscle spasms makes them extremely painful. Excessive skeletal muscle activity is linked to emotional increases in oxygen use, and hyperthermia may result from peripheral vasoconstriction. Generalized skeletal muscular spasms can be accelerated by external stimuli (such as abrupt exposure to bright light, startling noise, or tracheal suctioning), which can result in inadequate breathing and mortality. Myocarditis has been blamed for hypotension. Though more frequently this hyperactivity manifests as systemic hypertension, confined and inexplicable tachycardia may be an early indicator of hyperactivity of the mindful worried structure. Tachydysrhythmias and labile blood pressure are examples of too-dramatic responses to external stimuli brought on by the thoughtful anxious framework. In addition, diaphoresis and severe peripheral vasoconstriction are linked to excessively thoughtful anxious framework action.[2,7,8]

Complications with tetanus

Numerous issues that impact various bodily systems might result from tetanus: *Respiratory system* Apnea, hypoxia, respiratory failure, laryngeal spasm, aspiration pneumonitis, and atelectasis are among the potentially fatal side effects. Extended ventilation can lead to tracheostomy issues such as tracheal stenosis and ventilator-associated pneumonia (VAP). Muscle stiffness and vocal cord tightness cause breathing problems. *The renal and gastrointestinal systems* might develop complications such as high-output renal failure, oliguric renal failure brought on by rhabdomyolysis, gastric stasis, ileus, diarrhoea, bleeding, urinary tract infections, and urine stasis.

There are additional reports of thromboembolism and skin disintegration. There have been reports of temporomandibular and shoulder joint dislocations. As the illness worsens, numerous organ failures may accompany sepsis. *Cardiovascular System*: Autonomic

dysfunction is the cause of some of the most dangerous complications. These include cardiac failure, asystole, tachycardia, hypertension, myocardial ischemia, hypotension, and different arrhythmias, including bradyarrhythmias and tachyarrhythmias. High levels of catecholamines in the bloodstream are a contributing factor to certain heart-related symptoms. *Musculoskeletal System:* Problems like tendon rupture, joint dislocation, and bone fractures can result from muscle spasms and rigidity. *Nervous System:* Seizures, coma, and neurological impairments are among the central nervous system symptoms that tetanus can induce. If not treated quickly and efficiently, tetanus-related complications can lead to extended hospital stays, incapacity, and even death.

Given the possible seriousness of these side effects, early detection and aggressive tetanus treatment are crucial to reducing negative effects and enhancing patient outcomes. This emphasizes how crucial it is to vaccinate against tetanus and treat wounds as soon as possible to keep susceptible people from becoming infected.[9,10]

Epidemiology

Essentially tetanus affects people of all ages; nonetheless, the highest occurrence is noted in babies and young persons. The World Health Organization (WHO) notes that intensive immunization initiatives in recent years have contributed to an improvement in tetanus fatality rates. According to WHO estimates, there were around 275,000 tetanus deaths worldwide in 1997, with better rates of 14,132 cases in 2011. Nonetheless, tetanus fatality rates range from 20% to 45%, and the prevalence of the infection is still disproportionately greater (some studies indicate 135 times higher) in low-resource settings compared to rates in rich countries. The availability of resources, particularly early treatment, invasive blood pressure monitoring, and mechanical ventilation, affects mortality rates. Worldwide, systematic vaccination, in conjunction with other vaccinations, pertussis, and diphtheria (DPT), is reducing the prevalence of newborn tetanus. The primary cause of neonatal tetanus is the infant's insufficient immunization. Around 84% of children under 12 months old got tetanus coverage globally in 2013. People who are not inoculated or who are elderly and have weakened immunity over time are at risk of contracting tetanus in high-resource nations like the United States. Contaminated needles or drugs can potentially pose a concern to intravenous drug users. One of the diseases of the developing world is tetanus. It is more prevalent in warm climates, among males, and in regions where the soil is farmed. Additionally, neonates and infants in nations without an immunization regimen are more likely to have it. Tetanus deaths in India reached 7,093 in 2020, or 0.08% of all deaths, according to the most recent WHO data. India is ranked #51 in the world with an age-adjusted death rate of 0.43 per 100,000 inhabitants. Tetanus cases are still common in India, most likely as a result of poor environmental hygiene and basic health education, insufficient vaccination (including booster shots), persistently unsanitary ritual practices (such as nose and ear pricks and head shaving, particularly in newborns), septic abortion, inadequate wound care after injuries, and the contamination of nearly all roads and fields with animal excrement (cow dung).[10,13]

Etiology

The bacteria Clostridium tetani, which can be found in dust, soil, or animal excrement, is the cause of tetanus. It is an obligatory anaerobic bacillus that is gram-positive and forms spores. Although this bacterium and its spores are found all over the world, they are more common in hot, humid areas with abundant soil organic matter. Through insect bites, lacerations, wound punctures, skin fractures, or inoculation with an infected syringe, C. tetani can enter the human body. The most frequent cause of infection is an injury that is frequently insignificant and could go unrecognized, like a small cut from a thorn or a splinter made of metal or wood. Immunocompromised individuals, intravenous drug users, and unvaccinated individuals are high-risk groups. Additional sources of infection have been reported from dog bites, open fractures, intramuscular injections, dental infections, and surgical operations. In some settings, tetanus spores can endure for extended periods due to their durability. Most of the time, a wound from a small injury is the source of infection. Immunization failure is a common cause of tetanus. As people age, even those who have received vaccinations lose their immunity. Additionally, gangrene and abscesses are chronic illnesses that might result in tetanus. Additionally, the infection can spread to people who have had burns or are having surgery. People who are not inoculated, either partially immunized or fully immunized but not receiving enough booster doses are typically at risk for tetanus.

The following are among the risk factors for newborn tetanus: mother without vaccinations, home birth, Neonatal tetanus in a prior child, and septic severing of the umbilical cord. Infectious materials—such as mud, animal faeces, or other similar materials—are applied on the umbilical stump. The gram-positive, obligate anaerobe, spore-forming bacillus Clostridium tetani has a distinctive drumstick or tennis racket-like look. The bacterium is found in soil, the intestines of cattle, sheep, horses, dogs, cats, rats, chickens, and about 10% of people. Additionally, the spores are present on skin surfaces and in pollution. The organism may be present in a sizable portion of adult humans in agricultural regions like ours. The spores are particularly resistant to heat, common antiseptics, and chemical agents, but they are destroyed by autoclaving at 120°C for 15 minutes or boiling for at least 4 hours. This is in contrast to the vegetative forms of the organism, which are vulnerable to heat and oxygen. The vegetative form yields "tetanospasmin," a strong neurotoxin that causes the clinical symptoms and is the second most potent microbial toxin known, behind botulinum toxin.[14,17]

Pathophysiology

The toxins tetanospasmin and tetanolysin, which are secreted by C. tetani, cause the distinctive "tetanic spasm," which is a widespread contraction of agonist and antagonistic muscles. The clinical syndrome of rigidity, muscular spasms, and autonomic instability is specifically brought on by tetanospasmin's effects on the nerve and muscle motor endplate interaction. Conversely, tetanolysin causes tissue injury. Tetanus spores enter the body at the site of inoculation and start to grow in the wound. Certain anaerobic conditions are necessary for germination, such as devitalized and dead tissue with a low oxidation-reduction potential. Tetanospasmin is released into the circulation following germination. A vesicular synaptic membrane protein is destroyed by this toxin when it enters the presynaptic terminals in the neuromuscular endplate of motor neurons. This deactivates inhibitory neurotransmission, which typically inhibits motor neuron and muscle activity. Muscle fibres are paralyzed as a result. About two to fourteen days after inoculation, this toxin then makes its way to neurons in the central nervous system via retrograde axonal transport, where it likewise prevents the release of neurotransmitters. A tetanic spasm results from cells' inability to suppress the motor reflex response to sensory stimuli because glycine and GABA are important inhibitory neurotransmitters. Bone fractures and muscle rips may result from this strong, unopposed muscular contraction and activity. Although it can range from one to sixty days, the incubation period typically lasts seven to ten days. The distance from the central nervous system affects the severity of the symptoms; shorter incubation times are linked to more severe symptoms. Autonomic dysfunction happens once the neurotoxin penetrates the brainstem, usually within the second week of the onset of symptoms. Patients may exhibit diaphoresis, bradyarrhythmias, cardiac arrest, and labile blood pressure and heart rate due to a loss of autonomic control. The fatality rate for individuals who are infected is 10%, and it is significantly higher for those who have never been vaccinated. Symptoms can last for weeks to months. Although many survivors fully recover, there have been several long-term neuropsychiatric and motor difficulties,[18,20]

Diagnosis

There is no specific laboratory test needed to diagnose tetanus; it is a clinical diagnosis. In just 30% of situations, providers may discover a positive wound culture and the organism's isolation. Acute onset and muscle contractures with widespread spasms that have no apparent medical explanation are important characteristics to look for when diagnosing tetanus. A history of damage may be remembered by some patients but not by others. Although it is not easily accessible, an antitoxin-level assay could be useful in ruling out tetanus. It is commonly believed that a serum antitoxin level of 0.01 IU/mL or greater is protective and reduces the risk of tetanus. For the clinical diagnosis of tetanus, the previously established spatula test exhibits great specificity and sensitivity. This entails touching the posterior pharyngeal wall with a soft-tipped tool. A positive test result is indicated if this causes an involuntary jaw contraction rather than the typical gag reflex. It is crucial to remember that infections can happen to those who lack immunity or have low serum anti-tetanus antibody levels. Aspiration-related pneumonia, laryngospasm, rhabdomyolysis, upper gastrointestinal bleeding, cardiovascular instability (e.g., transient cardiac arrest, tachycardia, or bradycardia), arrhythmias, hypertension, acute renal failure, and secondary wound infections are among the potentially fatal consequences of tetanus. Autonomic dysfunction-related respiratory failure and cardiovascular collapse are the infection's main causes of death.[21,23]

Options for treating clostridium tetani or tetanus

Human tetanus immune globulin is used to neutralize circulating toxin, and antibiotics (penicillin or metronidazole) are used to reduce toxin generation. To prevent aspiration and laryngeal stridor, early elective tracheostomy is frequently recommended in moderate to severe cases, and nasogastric tube insertion is crucial for feeding and medicine administration. Benzodiazepines are essential for lowering autonomic dysfunction, stiffness, and spasms. Diazepam is usually given by nasogastric tube at high dosages (0.2–1 mg/kg/h). For refractory spasms, mechanical ventilation and neuromuscular blocking medications are used. Tetanospasmin toxin that has been released is eliminated by HTIG, a first-line treatment; however, the toxin that is already attached to the central nervous system is unaffected. Additionally, HTIG shortens the duration of the sickness and may lessen its severity. 500 U administered intramuscularly or intravenously is just as effective as higher dosages. Particularly in situations of cerebral tetanus, HTIG is administered intrathecally. Therapeutic doses (3000-6000 U) are also advised in cases of widespread tetanus. The source of toxin generation will be controlled by wound debridement. Metronidazole has been demonstrated to decrease the disease's course, even though toxins are the primary cause of illness. It has also been demonstrated that metronidazole reduces mortality. After learning that penicillin may have synergistic effects with tetanospasmin, it is no longer advised for usage as a therapy. Depending on the clinical situation, antispasmodics such as propofol, vecuronium, pancuronium, baclofen, and benzodiazepines have been employed. Baclofen is useful in reducing muscular rigidity and can also be administered intrathecally. Patients with more severe tetanus are probably admitted to the intensive care unit (ICU) for sedation and mechanical ventilation, which may have an impact on long-term consequences and death. Due to the possibility that endotracheal tubes could trigger muscle spasms, tracheostomy is recommended. Additionally, tracheostomy is recommended when intubation is necessary for longer than ten days. Diazepam is the most researched and used medication in this area.

Benzodiazepines are thought to be a cornerstone treatment for tetanus symptoms. In addition to lowering anxiety, it also relaxes muscles and induces drowsiness, which helps to avoid fatal respiratory issues. It has been demonstrated that intravenous magnesium can avoid muscular spasms. GABA-agonist benzodiazepines, such as midazolam or diazepam, are administered continuously to avoid cardiovascular or respiratory problems. IV diazepam (10–40 mg every 1–8 hours) should be used to avoid spasms lasting longer than 5–10 seconds. The intravenous dose of midazolam is 5–15 mg/h. Supportive treatment must also be given by providers, particularly to individuals who have autonomic instability (hyperpyrexia, hypothermia, labile blood pressure). Benzodiazepines and magnesium are frequently used together to treat these side effects. It should be administered intravenously as a 5 g bolus, then continuously at a rate of 2-3 g/hour until the spasm is under control. The patellar reflex must be watched during magnesium infusion; if areflexia occurs, the dosage should be lowered. High blood pressure is frequently treated with morphine. Death and hypotension are possible side effects of beta-blockers. Small doses of esmolol can be taken under close supervision. It's also critical to provide high-calorie foods to offset the higher metabolic demand brought on by muscle contractions. Survival depends on controlling cardiovascular issues, autonomic dysfunction, and respiratory state. Furthermore, having the infection does not confer immunity in the future; all patients need to have a complete tetanus toxoid vaccination upon recovery.[9,24,32]

DISCUSSION AND CONCLUSION

A summary of tetanus is included in our review articles, including its epidemiology, pathophysiology, diagnostics, alternative therapies, and many causes. Although tetanus can be treated with drugs (vaccination) and other treatments, our research suggests that more clinical trials are required for tetanus due to its complexity. The treatment of tetanus requires more randomised controlled studies. In the future, we intend to conduct a preliminary tetanus investigation. With our colleagues' help, counseling-based research in our state or nation will evaluate patients' physical and mental health and give more precise information about tetanus and its treatment in the future.

Ethical statement

Be sincere and maintain a high standard of conduct in all of our dealings and activities about our jobs. Let us be honest in our words and actions.

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Conflict of interest

The authors attest that they are free of any known financial or personal conflicts of interest that could taint this study's findings.

Informed consent

Using websites, review articles, and other sources to produce research content.

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