Tetanus Vaccination 2020 and Collateral Protections against Pertussis and Diphtheria

ALEXANDRE KHOURY, MD; JOHN D. CAHILL, MD

ABSTRACT

Tetanus is a life-threatening but vaccine-preventable disease caused by the toxin of the bacterium *Clostridium tetani* and is characterized by muscle spasms and autonomic nervous system dysfunction. It is prevented through vaccination with tetanus toxoid, but because the causative agent is widespread in the environment, eradication is impossible. Therefore, efforts to reduce incidence are aimed at reaching elimination, rather than eradication. This article reviews the pathogenesis, clinical manifestation and treatment of tetanus, and summarizes all recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) regarding prevention and control of tetanus in the United States.

KEYWORDS: tetanus, tetanus vaccine, tetanus prophylaxis, tetanus immunoglobulin

INTRODUCTION

Tetanus is a serious and often fatal infection that affects the nervous system. It is characterized by generalized painful muscle spasms particularly in unvaccinated or incompletely vaccinated people. The disease is caused by a toxin-producing gram-positive anaerobic bacteria, *Clostridium tetani*, which is widely present in the surrounding environment, particularly in soil, dirt, and dust.

Tetanus is still prevalent in many developing countries. The disease can be prevented through vaccination but because the *C. tetani* spores are ubiquitous, it can never be eradicated. Due to the success of the US tetanus immunization program diphtheria – a disease of the upper respiratory tract and sometimes skin due to toxigenic strains of Corynebacterium diphtheriae biotype mitis, gravis, intermedius or belfanti – is nearly unheard of in the US, although the disease continues to cause illness globally and there have been outbreaks reported in recent years.

PERTUSSIS

Pertussis – "whooping cough" due to Bordetella pertussis – can be a life-threatening disease in infants with small airways and is endemic worldwide, including the US and other countries, with high vaccination rates. Disease in adults presents as a protracted cough with paroxysms that may be followed by vomiting. Coughing paroxysms may eventually become less intense but may recur with subsequent respiratory infections. Childhood vaccinations given since the 1940s helped to reduce infant mortality but would wear off by adulthood.

ELIMINATION STRATEGIES

The primary strategy to control and prevent these diseases is through elimination instead of eradication. The vaccination schedule is based on the tetanus component.

Tetanus is a leading cause for neonatal death in the developing world.[1]

The tetanus toxoid (TT) vaccines were first introduced in the United States in the mid-1940s. After that, the incidence of reported tetanus declined by >98%, from 0.39 per 100,000 population in 1947, when national reporting began, to 0.01 per 100,000 population by 2016.[2] The CDC reported 264 cases of tetanus in the United States between 2009 and 2017, 23% were in patients ≥65 years of age and only 13% were individuals younger than 20 years. The majority of new cases of tetanus occur in resource-limited countries with an estimated 48,000 to 80,000 deaths occurring from tetanus worldwide in 2016.[3]

PATHOPHYSIOLOGY

Humans become infected through wound contamination with *C. tetani* spores, which are durable and can survive for prolonged periods and germinate under the right environment (i.e. less vascularized necrotic tissue) to toxin-producing bacteria. The toxin is extremely potent and even deadly in small amounts. Once tetanus toxin invades the nerve cell, it can no longer be neutralized by the toxoid. The toxin can then move via retrograde axonal transport into the spinal cord and brain, where it accumulates and prevents the release of inhibitory neurotransmitters, resulting in overexcitation of the nervous system. This clinically manifests as painful muscle spasm and rigidity, increased muscle tone, and widespread autonomic instability.

Tetanus is a non-communicable disease and it is safe to come in close contact with someone that is affected by tetanus.

Tetanus is commonly acquired through septic burn wounds, animal bites and scratches, fractures, contaminated surgical instruments, lacerations, eye injuries, gunshot wounds, piercings and other puncture wounds. All of the above mechanisms have common predisposing factors, which include devitalized and dead tissue, foreign bodies and localized ischemia.

Tetanus can also manifest through the same pathophysiology in neonates from infected umbilical stump, obstetric patients after septic abortions, post-surgical patients with bowel necrosis, infected diabetic foot ulcer patients, and IV drug users.

The incubation period of tetanus is approximately 8 days but ranges from 3 to 21 days.

The most common and severe clinical form of tetanus is generalized tetanus. Rarely, tetanus presents with tonic and spastic muscle contractions in one extremity or body region which is localized tetanus. Patients with injuries to the head or neck may present with cephalic tetanus, involving initially only cranial nerves. Neonatal tetanus occurs as a result of the failure to use aseptic techniques in managing the umbilical stump in offspring of mothers who are poorly immunized. Severity of disease can range from grade 1 (mild trismus and/or general spasticity), to grade 2 (moderate trismus and general spasticity, with dysphagia and respiratory embarrassment), to grade 3 (severe trismus, severe and prolonged spasms, respiratory difficulties and sympathetic overdrive).

MANAGEMENT

Unfortunately, little evidence exists to support any particular therapeutic intervention in tetanus. Management includes early wound debridement, halting the toxin production, neutralization of the unbound toxin through post-exposure vaccination, control of muscle spasms, and general supportive care including airway management. Antibiotics are universally recommended, although they may play a minor role, and it is of vital importance to emphasize that unless adequate wound debridement is performed, antimicrobial therapy may fail. Metronidazole is the preferred treatment and should be given for a total of 7 days but penicillin is a safe alternative. Multiple other agents can be used such as doxycycline, macrolides, clindamycin, vancomycin, and chloramphenicol; however, the data on these agents is based upon in vitro susceptibility. Since tetanus toxin is irreversibly bound to tissues, much emphasis is placed on neutralizing the toxin before it enters the nervous system. Human anti tetanus immunoglobulin (HTIg) is the treatment of choice. The CDC recommends a single dose of 500 units intramuscularly with part of the dose infiltrated around the wound. Many studies have explored the efficacy of intrathecal immunoglobulin, but the evidence for its benefit is not concrete. All patients with tetanus should receive active immunization with a full series given immediately upon diagnosis. The tetanus toxoid should be given at a separate site from immunoglobulin administration.

Benzodiazepines remain the backbone of treatment regimens for tetanus, and the standard therapy for controlling muscle spasms. Diazepam is the most popular and has been used widely but other benzodiazepines are as effective. The use of magnesium sulfate has also been established since the 1980s due to its effect on reducing autonomic instability and controlling muscle spasms. Several studies concluded the beneficial effects of high dose magnesium sulfate infusion in tetanus, but it may be inadequate as sole therapy in patients with severe disease. Several other drugs which have been reported to be useful are labetalol, clonidine, morphine sulfate, intrathecal baclofen, dantrolene, and vitamin C. Despite all these interventions, the reported fatality rate ranges from 12–53%

VACCINE SCHEDULES

In the US, diphtheria-tetanus-acellular pertussis (DTaP) vaccine is routinely administered to children at 2, 4, and 6 months, followed by boosters at 15–18 months and 4–6 years. Single booster dose of a vaccine containing tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) is recommended for 11- to 12-year-olds and every ten years after that. In 2020, ACIP released new recommendations allowing either Tdap or Td to be used as the booster or for wound management while previously only Td was recommended.[5]

Individuals who have not been previously vaccinated against tetanus should complete a series of three tetanus and diphtheria toxoid vaccines, which includes at least 1 Tdap dose. The preferred schedule is 1 dose of Tdap, followed by 1 dose of either Td or Tdap at least 4 weeks afterward, and 1 dose of either Td or Tdap 6–12 months later.

In 2011, when ACIP first considered administration of Tdap during pregnancy, safety data on women and their infants were limited. However, additional evidence continues to be reassuring for mother and child, with no reported increase in adverse events including major malformations, stillbirth, preterm birth, or small for gestational age. Pregnant women should get Tdap during the early part of the 3rd trimester of every pregnancy.

ACIP has recommended administering tetanus toxoid containing vaccine and tetanus immune globulin (TIG) when indicated as part of standard wound management to prevent tetanus. For patients who have received fewer than three doses or an unknown number of doses of a tetanus toxoid-containing vaccine, tetanus immunization should be administered. For patients with clean minor wounds who have completed 3-dose primary tetanus vaccination series, another dose should be given if the last dose was given 10 or more years ago. For patients with dirty wounds (such

as, but not limited to, wounds contaminated with dirt, feces, soil, or saliva; puncture wounds; avulsions; wounds resulting from missiles, crushing, burns, or frostbite) who have completed 3-dose primary tetanus vaccination series, another dose should be given if the last dose was given five or more years ago. If there is any doubt about whether or not an adult completed the primary series, three doses of Td or Tdap (with Tdap given for at least one of the doses) should be administered; the first dose and second dose should be separated by four weeks and the third dose should be given 6 to 12 months later. The pertussis component may dwindle after 3-4 years as data show the vaccine fully protects 4 in 10 individuals 4 years after receiving Tdap. For travelers or during pertussis outbreak settings it is safe to administer Tdap as early as 2 years after the prior dose.

HUMAN TETANUS IMMUNE GLOBULIN

In addition to tetanus immunization, human tetanus immune globulin (250 units intramuscularly) is indicated in unvaccinated or incompletely vaccinated individuals who have sustained a wound that is more severe than a clean and minor wound (eg, wounds contaminated with dirt, feces, soil, or saliva; puncture wounds; avulsions; wounds resulting from missiles, crushing, burns, or frostbite).

People with human immunodeficiency virus (HIV) infection regardless of their CD4 count or with severe immunodeficiency who have contaminated wounds should also receive human tetanus immune globulin, regardless of their immunization status.

Appropriate tetanus prophylaxis should be administered as soon as possible following a wound but should be given even to patients who present late for medical attention. This is because the variable incubation period which ranges from 3 to 21 days (median: 7 days), with extremes of 1 day to several months.

Tetanus toxoid is one of the most extensively used vaccines globally. Mild local reactions (i.e., redness, pain and tenderness, and mild swelling) are common while more systemic reactions, such as fever, malaise, lymphadenopathy are less common but might still occur. Although there is a slight increase in injection site events with decreasing interval since a previous immunization, Tdap can be safely administered at intervals of > or = 18 months since a previous TD/Td vaccine.[6] Severe reactions, including neurologic complications (e.g., peripheral neuropathy, particularly brachial plexus neuropathy, Guillain-Barré syndrome, and acute encephalopathy) and hypersensitivity reactions (anaphylaxis, and angioedema) are rare. Arthus reactions – severe local and sometimes generalized vasculitic reactions - are now only rarely reported with newer tetanus vaccine preparations. ACIP recommends that persons who have experienced an Arthus reaction following a dose of tetanus toxoid or diphtheria toxoid–containing vaccine should not receive a tetanus toxoid–containing vaccine more frequently than every 10 years, even for tetanus prophylaxis as part of wound management.

CONCLUSION

Tetanus is a lethal infection, but vaccine preventable. Tdap offers protection against diphtheria and pertussis not only to children but also adults. All healthcare workers must emphasize and raise awareness of the importance of immunization. Protection against tetanus by vaccination is vital because there is no natural immunity against tetanus and no effective treatments exist. Inter-professional collaboration of physicians, nurses other clinical practitioners and pharmacists together with public health officials can place particular emphasis on education regarding the importance of up-to-date vaccination and reduce the morbidity and mortality of tetanus worldwide.

References

1. Gasse F. 1995. Neonatal tetanus: review of progress. International Journal of Gynecology and Obstetrics 50(suppl 2):S67–S72.
2. Liang JL, Tiwari T, Moro P, et al. Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2018;67(No. RR-2):1–44.
3. Kyu HH, Mumford JE, Stanaway JD, et al. Mortality from tetanus between 1990 and 2015: findings from the global burden of disease study 2015. BMC Public Health 17, 179 (2017).
4. McQuillan GM, Kruszon-Moran D, Deforest A, Chu SY, Wharton M. Serologic immunity to diphtheria and tetanus in the United States. Ann Intern Med. 2002;136(9):660-666.
5. Havers FP, Moro PL, Hunter P, Hariri S, Bernstein H. Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccines: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2019. MMWR Morb Mortal Wkly Rep 2020;69:77–83.
6. Halperin SA, Sweet L, Baxendale D, et al. How soon after a prior tetanus-diphtheria vaccination can one give adult formulation tetanus-diphtheria-acellular pertussis vaccine? Pediatr Infect Dis J. 2006;25(3):195-200.

Authors

Alexandre Khoury, MD, Internal medicine and emergency medicine, PGY6, Icahn School of Medicine at Mount Sinai.

John D. Cahill, MD, Assistant Professor of Medicine and Emergency Medicine, Icahn School of Medicine at Mount Sinai; Adjunct Professor of Emergency Medicine, Alpert Medical School of Brown University, Providence, RI.

Correspondence

John D. Cahill, MD
Assistant Professor of Medicine and Emergency Medicine,
Icahn School of Medicine at Mount Sinai
2109 Broadway, New York, NY 10023
212-523-8672
johndcahill@gmail.com