

Tetanus: An Overview

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Although tetanus was first described by Hippocrates more than 25 centuries ago, it was not until the late 1800s that an antitoxin was developed, after the organism responsible for this disease was isolated by French and Japanese scientists. The US military used passive tetanus immunization for their personnel during World War I and active tetanus immunization during World War II, resulting in a marked decrease in the number of tetanus cases among military personnel.^{1,2} These immunization efforts mark the first times large groups of at-risk individuals were vaccinated for tetanus. Because of the effectiveness of these efforts, tetanus immunization continued after World War II in civilian populations of several countries, including the United States.

Today, the number of reported deaths from tetanus has decreased to approximately 50 per year in the United States. However, there are still approximately 1 million cases of tetanus annually worldwide.² According to estimates, more than half a million children in developing countries die of tetanus every year. The incidence of neonatal tetanus worldwide is approximately 6 per 1000 live births.³ Persons who contract the disease are predominantly male, even among neonates. The death rate for all cases continues to be approximately 50%, with neonatal mortality above 85%.⁴ In the United States the populations primarily at risk are the young (ie, persons < age 20 years), the elderly (persons > age 60 years), intravenous drug users, and immigrants.⁵⁻⁸

This article examines the pathogenesis, clinical manifestations, diagnosis, and management of tetanus. Prophylactic wound care is discussed, as are the history of and current recommendations for tetanus immunization.

PATHOGENESIS

Tetanus is caused by *Clostridium tetani*, a gram-positive anaerobic organism found predominantly in areas with



warm climates that are rich in organic soil. However, tetanus spores are ubiquitous, are highly resistant to destruction, and can survive on almost any surface for long periods of time. Any break in the skin potentially can allow spores to enter the body, where they can become vegetative and subsequently produce tetanospasmin, a very potent neurotoxin. Spores become vegetative only if the oxygen tension of the local tissue is low, as occurs in

necrotic tissue and poorly vascularized areas.

Once tetanospasmin is produced, it binds to vesicles of the peripheral nerves and is propagated axonally, via retrograde transmission, to the central nervous system. The toxin travels approximately 0.25 cm daily and then migrates across a synapse to presynaptic terminals, until it reaches the end plates of the inhibitory afferent neurons. Here, tetanospasmin irreversibly binds and blocks release of the inhibitory neurotransmitters glycine and γ -aminobutyric acid (GABA), thus preventing the usual inhibitory activity of the neurons from occurring. The result is rapid axonal firing with no inhibition, leading to unrelenting muscle spasms, also known as *tetany*. Any stimulus—sensory, visual, or even auditory—can lead to tetany. The incubation period for tetanus ranges from days to months; once bound to the end plate, tetanospasmin remains there until it is degraded (days to weeks after initial binding).

CLINICAL FEATURES

As different muscle groups go into spasm and more powerful ones overpower their counterparts, typical clinical features appear. Masseter muscle contractions cause trismus, also referred to as *lockjaw*, and spasms in

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Figure 1. Clinical photograph of a neonate with tetanus exhibiting the typical features of trismus and opisthotonos. Note the flexion of the arms, the clenched fists, and the dorsiflexion of the toes. Photograph used with permission of the author.



Figure 2. Clinical photograph of a young girl with tetanus exhibiting the typical features of trismus and risus sardonicus. The patient had sustained second- and third-degree burns of the chest. Photograph used with permission of the author.

muscles of the back cause opisthotonos. Flexion of the arms and legs, accompanied by clenched fists and dorsiflexion of the toes, also commonly occurs. Some typical clinical features are illustrated in **Figures 1** and **2**.

Patients can die of the complications of tetanus. Most patients develop respiratory complications, which include atelectasis, pneumonia, hypoxia, and respiratory failure. Other known complications include peptic ulcer disease, ileus, and bowel and bladder sphincter spasms leading to skin breakdown and (possibly) sepsis. There is also significant autonomic dysfunction, leading to fluctuating blood pressures and arrhythmias.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Tetanus is a clinical diagnosis. Tetanus spores are rarely identified at the portal of entry, and tetanus antibody levels are not routinely available. The diagnosis of tetanus must be made after other illnesses that can cause trismus and opisthotonos are excluded. Differential diagnosis includes peritonsillar abscess, mandibular injury or fracture, temporomandibular joint syndrome, dystonic reaction, conversion reaction, strychnine poisoning, and early rabies or poliomyelitis. Because of the highly variable incubation period, only half of the patients with tetanus can recall the specific history of a wound.

MANAGEMENT OF TETANUS

Tetanus induces a highly catabolic state that requires vigorous fluid resuscitation. Patients also should be sedated and kept in a quiet environment, because even a slight stimulus (such as a sound or light) can result in tetanic activity. Affected patients typically remain alert and conscious throughout the acute phase of the illness. Because of the high rate of respiratory complications and failure, patients often require a tracheostomy. Specific treatment includes administration of tetanus immunoglobulin with metronidazole or penicillin.

Once a patient recovers, tetanus toxoid must be given, because the very small quantity of tetanospasmin required to produce the disease is insufficient to induce adequate antibody titers. In fact, patients who survive tetanus are more likely to develop tetanus again if they are not immunized with tetanus toxoid.

PROPHYLACTIC WOUND CARE AND IMMUNIZATION

The best treatment for tetanus is appropriate tetanus immunoprophylaxis of wounds into which tetanus spores can enter. When wounds do occur, practitioners must make an appropriate evaluation of them to determine if they are tetanus prone (**Table 1**). Tetanus-prone wounds (ie, necrotic and ischemic wounds with a lower oxygen tension) are more likely to harbor tetanus spores and permit them to become vegetative. Consequently, all such wounds must be cleansed

Table 1. Wound Evaluation

Clinical Features	Non-Tetanus-Prone Wounds	Tetanus-Prone Wounds
Age of wound	< 8 hours	> 8 hours
Depth	Superficial, linear	Deep, irregular
Mechanism of injury	Cuts from sharp edges	Burn, crush, puncture
Signs of infection (eg, cellulitis)	No	Yes
Dirty wound (contaminated)	No	Yes
Purulent, necrotic tissue	No	Yes

appropriately, débrided (if necessary), watched closely, and rechecked frequently. Antibiotics should be used as indicated.

A history of tetanus immunization must be obtained during the initial visit for care of a wound. If indicated, patients should be given appropriate active and passive immunization (**Table 2**); tetanus immunoglobulin is used for passive immunization. A clean minor wound is not considered to be tetanus prone. For patients whose tetanus immunization status is not up-to-date or is unknown, a complete primary series of immunizations must be given (**Table 3**). It is extremely rare for a patient who has completed a primary tetanus series to develop tetanus.⁹ In a small study of emergency department patients, the 11 patients who contracted tetanus reported not having any recent tetanus immunization.¹⁰

Adult patients should receive diphtheria-tetanus toxoids as opposed to only tetanus toxoid. Unlike tetanus, diphtheria is a respiratory illness and can be spread very rapidly through a susceptible population. Despite published guidelines of the Advisory Committee on Immunization Practices (ACIP), many physicians still use only tetanus toxoid for tetanus immunoprophylaxis, leading to declining diphtheria antibody levels in the overall population.^{9,11} In elderly patients, decreased diphtheria antibody titers were commonly associated with nonprotective levels of tetanus antibodies, suggesting noncompliance with ACIP guidelines.¹¹ Currently, nearly 50% of elderly patients have nonprotective titers of tetanus antibodies.^{5,6,7} For this reason, the ACIP now recommends that all patients be evaluated for tetanus and diphtheria immunization at age 50 years (instead of age 65 years, as previously recommended) and that they be reevaluated every 10 years thereafter.¹²

Recently, the Centers for Disease Control and Prevention reported a group of approximately 60 intravenous drug users from California who had contracted tetanus over the last several years.⁸ This high number might be explained by the multiple abscesses in this group of patients, as well as the patients' potential of

Table 2. Tetanus Prophylaxis in Routine Wound Management

Prior Doses of Adsorbed Tetanus Toxoid	Clean, Minor Wound		All Other Wounds	
	Td*	TIG	Td	TIG
Uncertain, or < 2	Yes	No	Yes	Yes
3 or more	No [†]	No	No [‡]	No

Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin.

*For children younger than 7 years, diphtheria-tetanus-pertussis vaccine or diphtheria-tetanus toxoids should be administered.

[†]Yes, if last immunization was more than 10 years ago.

[‡]Yes, if last immunization was more than 5 years ago.

Adapted from Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Morb Mortal Wkly Rep 1991;40(No. RR-10):1–28.

Table 3. Recommended Immunization Schedule for Persons Older Than 7 Years

Immunization	Interval	Antigen
Primary dose (#1)	1st visit	Td
#2	4–8 weeks after #1	Td
#3	6 mo–1 y after #2	Td

Td = tetanus-diphtheria toxoids.

Adapted from Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Morb Mortal Wkly Rep 1991;40(No. RR-10):1–28.

being immunocompromised, both of which considerations place them at higher risk. Moreover, many immigrants in this group may have never had the opportunity for a primary tetanus immunization series, which also places them at increased risk for contracting tetanus.

Physicians must be diligent in immunizing at-risk groups and ensuring that all patients receive a primary tetanus immunization series. The antibody response to a single tetanus immunization among elderly patients without protective titers has been shown to have a response rate close to 90%.¹³ The question now is how long these protective levels will last and how other diseases will affect antibody response rates. Certain persons (eg, immunocompromised patients) might have difficulty mounting an antibody response; for these patients, both acute and passive immunization might be indicated in the acute setting. Wound management guidelines also might need to be altered for at-risk groups.

ADVERSE REACTIONS TO TETANUS IMMUNIZATION

Adverse effects of tetanus immunization include local irritation, erythema, pain, and induration. Patients also have reported fever, an Arthus-type sensitivity reaction, and even anaphylaxis.⁹ The practitioner must take care not to administer pediatric diphtheria-tetanus toxoid vaccine to adults, because it has approximately 3 to 13 times the concentration of the diphtheria antigen and can cause adult patients to become very ill. If there is great concern regarding the diphtheria portion of the vaccine, standard tetanus toxoid can be used. Both tetanus toxoid and tetanus-diphtheria toxoids can be used safely during pregnancy.¹⁴

Historically, the tetanus immune globulin used for passive immunization was obtained from horse serum, resulting in numerous adverse reactions. Many patients who state that they have had a reaction to vaccination against tetanus are referring to the passive immunization they received with horse serum. The current preparation of pooled human globulin causes far fewer adverse effects. Tetanus immunoglobulin has had no reported adverse effects in pregnant patients¹⁵ but is classified as a category C drug in pregnancy. Consequently, it is recommended for pregnant women only if clearly indicated.

CONCLUSION

Ever since World War II, the number of tetanus cases has decreased significantly in the United States. After immunization of military personnel during that war, the practice of immunizing school-aged children began in the 1950s and continues today.

Tetanus is a preventable disease. The mortality continues to be approximately 50% worldwide. The World

Health Organization continues to promote immunization of pregnant women and women of childbearing age in developing countries, and this effort has resulted in a dramatic decrease in the number of cases of neonatal tetanus. Even in the developed world, immunization recommendations must be followed closely to prevent tetanus in at-risk populations. **HP**

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