BMJ Best Practice

Tetanus

Straight to the point of care

Last updated: Feb 25, 2025

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Summary

Tetanus is an acute infection caused by the bacterium *Clostridium tetani*. Tetanus spores are highly prevalent in soil and manure and may be introduced into the body via broken skin (e.g., a puncture wound, burn, or scratch).

Prevention of tetanus includes appropriate management of tetanus-prone wounds and complete active immunization, with passive immunization administered when required.

Diagnosis is based on clinical findings that include trismus, muscle rigidity, spasms, respiratory embarrassment, dysphagia, or autonomic dysfunction.

Management of clinical tetanus includes supportive care, wound debridement, antimicrobials, passive and active immunization, control of muscle spasms, and management of autonomic dysfunction.

Definition

Tetanus is a life-threatening neurologic syndrome characterized by tonic muscle spasms and hyperreflexia, caused by the exotoxin of *Clostridium tetani*, a gram-positive spore-forming obligate anaerobe.

Epidemiology

Following the introduction of universal vaccination with tetanus toxoid-containing vaccines, incidence of tetanus declined significantly in the US in the 1940s and the UK in the 1960s.[3] [4]

In the US, there are an average of 30 cases of tetanus reported each year.[5] Surveillance during 2001 to 2008 found the highest incidence was among people aged over 65 years (0.23 cases/million), people of Hispanic ethnicity (most of these were people who injected drugs), and older adults with diabetes mellitus. The majority of cases occurred in people whose immunization history was incomplete or unknown and who sustained an acute injury.[6] There were a total of 22 tetanus cases reported in the US in 2022, with an incidence of 0.1 cases/million total population.[7]

In the UK between 2001 and 2014, 96 cases of tetanus were reported (ranging from 3 to 21 cases per year) with an annual average incidence of 0.13/million.[8] The highest incidence of tetanus was observed among adults over the age of 64 years. Among cases with information on immunization status, few had been appropriately immunized for their age.[8] Between July 2003 and September 2004, 25 cases of tetanus were reported in people who inject drugs in the UK.[9] Injection of drugs intramuscularly or subcutaneously ("popping") was associated with tetanus infection in this cluster, and contamination of heroin distributed from Liverpool was thought to account for the outbreak. Since this cluster in 2003/2004, a further 13 sporadic cases of tetanus were reported in people who inject drugs to the end of 2020.[10] In England, there were four reported cases of tetanus in 2022; all had a history of domestic or work-related injury.[11]

Tetanus remains a considerable threat in developing countries, with up to 1 million cases estimated to occur worldwide every year.[12] Estimates from the global burden of disease study suggest there were in excess of 56,000 deaths due to tetanus in 2015.[13] Significant progress has been made in reducing the incidence of maternal and neonatal tetanus over the last two decades. World Health Organization (WHO) figures estimate that 24,000 newborns died from neonatal tetanus in 2021, an 88% reduction from the situation in 2000.[14] The Maternal and Neonatal Tetanus Elimination (MNTE) initiative (a partnership between the WHO, United Nations International Children's Emergency Fund (UNICEF), and the United Nations Population Fund [UNFPA]) has adopted the "high risk approach." In high-risk areas, tetanus immunization is provided through supplemental immunization activities targeting all women of childbearing age (including pregnant women) with 3 doses of tetanus toxoid-containing vaccine.[2] [14] [15] [16] [WHO: protecting all against tetanus] (https://www.who.int/publications/i/item/protecting-all-against-tetanus) The ultimate goal of the MNTE initiative is the worldwide elimination of maternal and neonatal tetanus, but this has yet to be achieved in 11 countries, and tetanus resulting from unhygienic delivery practices remains a problem in many resource-poor settings.[14] [16] [17] The COVID-19 pandemic had a significant impact on global childhood immunization programs, leading to millions of children missing vaccine doses. The WHO and UNICEF estimate in a 2023 Centers for Disease Control and Prevention (CDC) report that during 2021 and 2022, Diphtheria-Tetanus-Pertussis-Containing Vaccines1 (DTPcv1) and DTPcv3 uptake improved in all WHO regions except in Africa, where coverage stagnated at 80% and 72%, respectively, and remained below the 2019 coverage (83% and 77%, respectively).[18]

Etiology

Clostridium tetani is a slender gram-positive rod with a terminal spore. It is an obligate anaerobe, which is a commensal of the human and animal gastrointestinal tract and is widely distributed in the environment, especially in manured soil. Spores are extremely resistant to heat and light; autoclaving at 248°F (120°C), 1.5 bar (21.7 psi) for 15 minutes ensures sterility.[19] Clinical disease follows inoculation of spores into

wounds and most cases occur after an acute injury, including trivial unnoticed injuries and injecting drug use. The incubation period is typically between 3 and 21 days, although it can range from 1 day (cephalic tetanus) to several months, depending on the nature of the wound and its distance from the central nervous system.

Pathophysiology

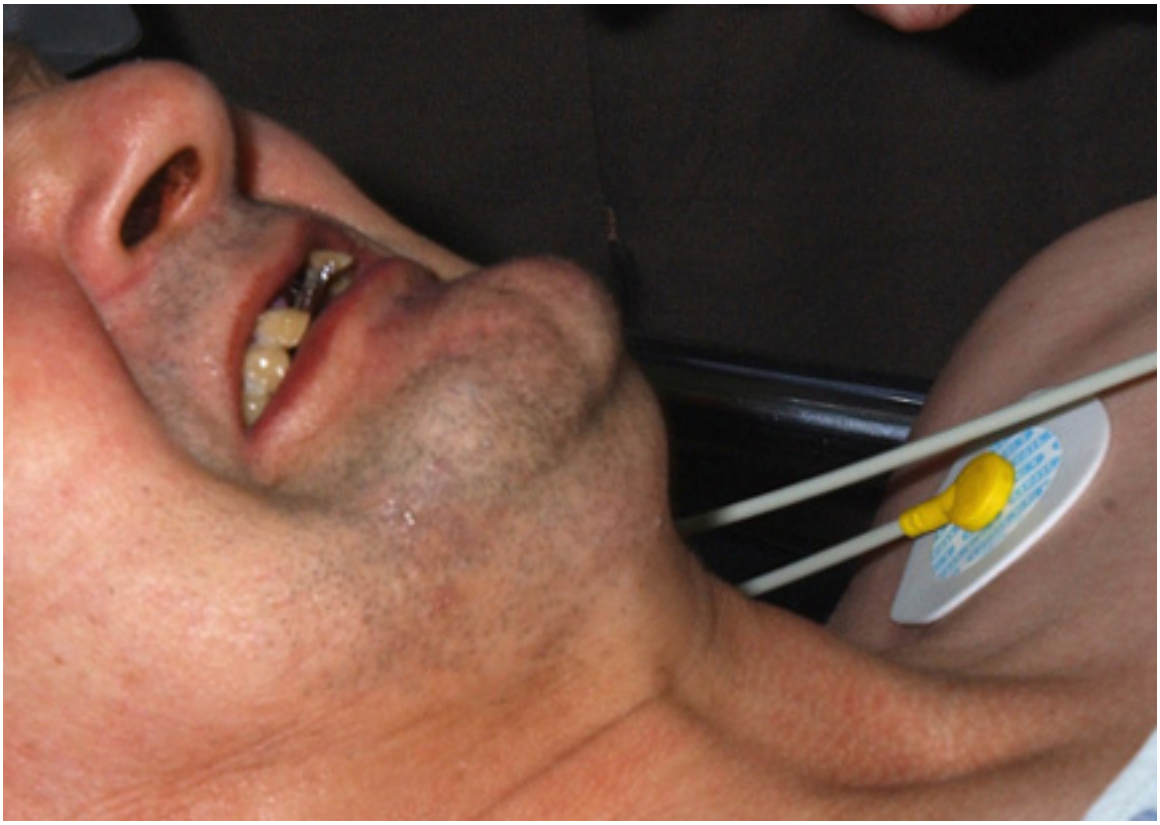
When spores of *Clostridium tetani* are inoculated into a wound, they can germinate under anaerobic conditions into rod-shaped bacteria, which produce tetanospasmin. This single-polypeptide toxin undergoes post-translational cleavage into heavy and light chain fragments.[19] The heavy chain attaches to gangliosides on peripheral nerves. Subsequently the toxin enters the presynaptic terminal and travels from the peripheral nerve terminals to the central nervous system by retrograde axonal transport and trans-synaptic spread. Free toxin can also enter the bloodstream and lymphatics, disseminating widely to motor neurons at disparate sites. The light chain is a zinc metalloprotease that cleaves synaptobrevin on the membrane of synaptic vesicles.[20] Synaptobrevin is required for the fusion of synaptic vesicles with the presynaptic membrane. Cleavage of synaptobrevin prevents the synaptic vesicles from releasing the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) into the synaptic cleft. Alpha-motor neurons therefore undergo uninhibited excitatory discharge resulting in muscle spasms. Disinhibition of autonomic neurons causes autonomic instability. Uncontrolled catecholamine release creates a hypersympathetic state with sweating, tachycardia, and hypertension.

Tetanospasmin-induced effects on the spinal cord, brainstem, and peripheral and autonomic nerves are long-lasting; growth of new axonal nerve terminals is necessary for recovery, which may take 4 to 6 weeks.

Case history

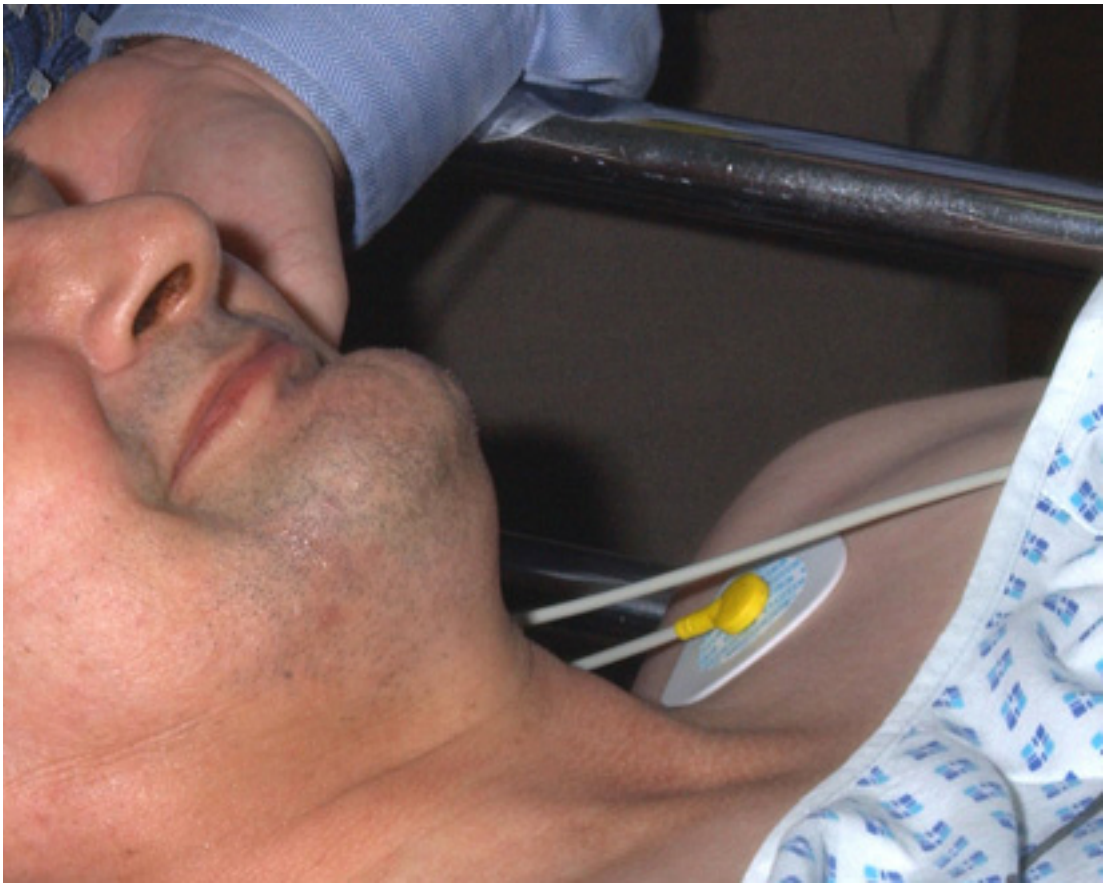
Case history #1

A 63-year-old man sustained a cut on his hand while gardening. His immunization history is significant for not having received a complete tetanus immunization schedule. He presents with signs of generalized tetanus with trismus ("lock jaw"), which results in a grimace described as "risus sardonicus" (sardonic smile). Intermittent tonic contraction of his skeletal muscles causes intensely painful spasms, which last for minutes, during which he retains consciousness. The spasms are triggered by external (noise, light, drafts, physical contact) or internal stimuli, and as a result he is at the risk of sustaining fractures or developing rhabdomyolysis. The tetanic spasms also produce opisthotonus, board-like abdominal wall rigidity, dysphagia, and apneic periods due to contraction of the thoracic muscles and/or glottal or pharyngeal muscles. During a generalized spasm the patient arches his back, extends his legs, flexes his arms in abduction, and clenches his fists. Apnea results during some of the spasms. Autonomic overactivity initially manifests as irritability, restlessness, sweating, and tachycardia. Several days later this may present as hyperpyrexia, cardiac arrhythmias, labile hypertension, or hypotension.



Trismus

From the collections of Nicholas J. Beeching and Christopher M. Parry



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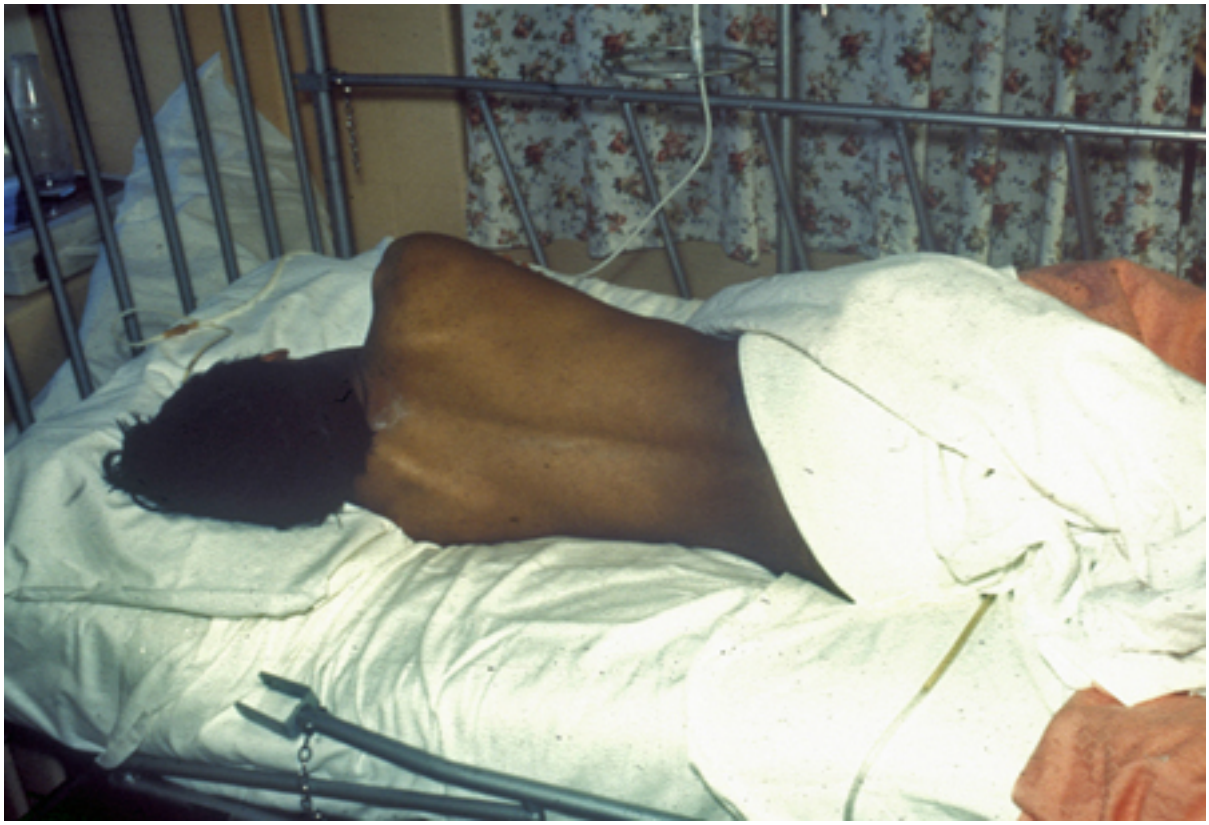

Opisthotonus

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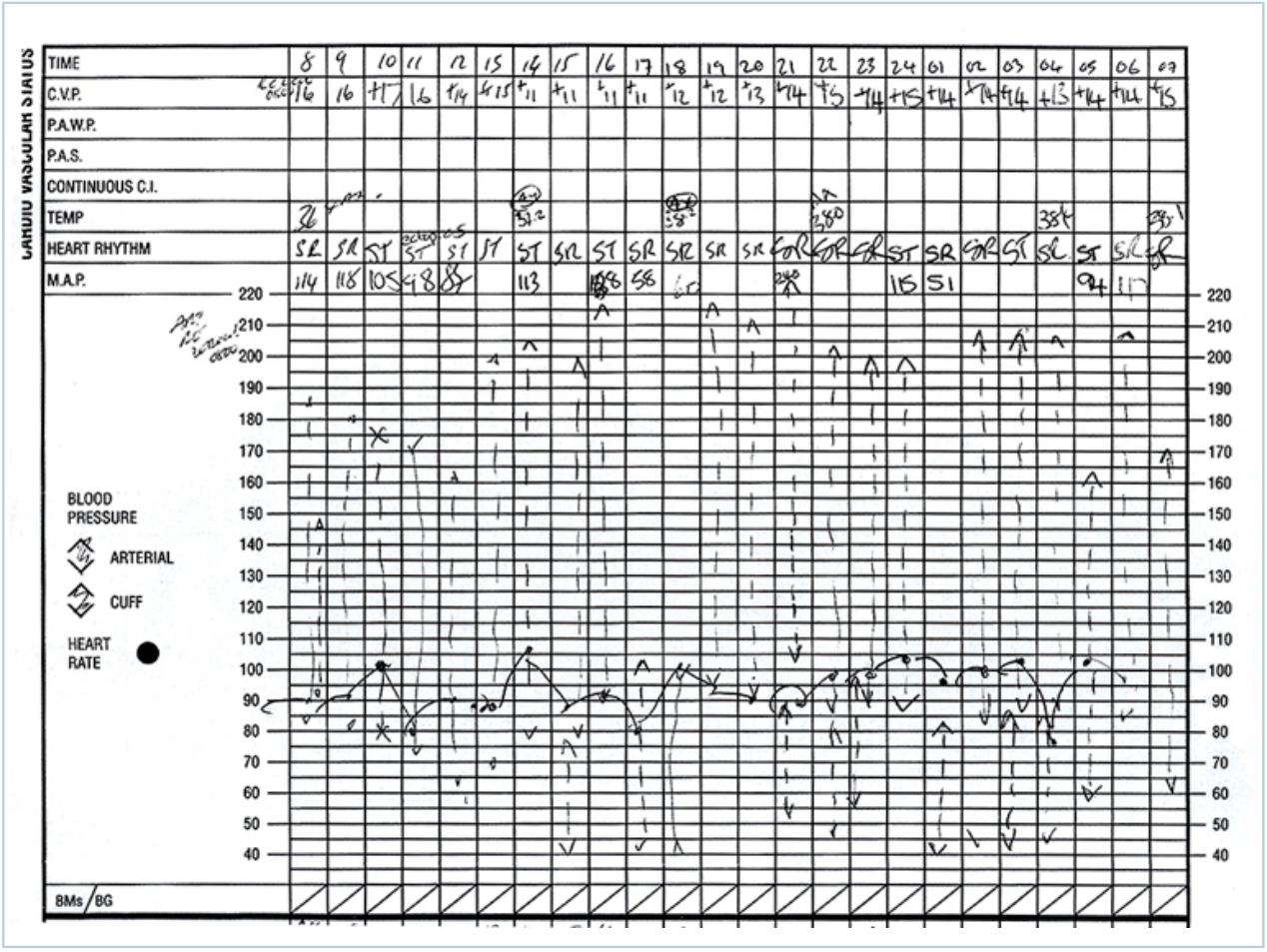


Observation chart illustrating autonomic dysfunction with extreme fluctuation in blood pressure

From the collections of Nicholas J. Beeching and Christopher M. Parry

Other presentations

Localized tetanus presents with muscle spasms limited to one extremity or body region near the site of injury. It may become generalized if the diagnosis is not recognized. Alternatively it may persist for weeks or months with subsequent complete resolution.[1] Cephalic tetanus follows head injury or middle ear infection with a short incubation period of 1 to 2 days. Cranial nerve palsies occur that may progress to generalized tetanus. The facial nerve is most frequently affected.[1] Patients may present with dysphagia, trismus, and/or focal cranial neuropathies. Neonatal tetanus usually presents 3 to 14 days postpartum, mostly on days 6 to 8.[2] Trismus and lip muscle rigidity interfere with normal sucking and feeding and the child is irritable. Early features include excessive crying and poor feeding. As the disease progresses, muscle rigidity extends throughout the body and spasms commence. Opisthotonus, seizures, and autonomic disturbance occur. The onset period, or time from first symptom to first spasm, ranges from a few hours to 5 days, usually 1 to 3 days.[2] Onset and progression are more rapid than in non-neonatal tetanus, possibly as a result of shorter axonal length.

Approach

The diagnosis is usually a clinical one and may be delayed in regions where tetanus is rarely seen: for example, in the developed world.[40]

History

Immunization status should be clarified. A tetanus-prone wound may be evident; otherwise, patients should be asked about recent injuries, medical interventions including intramuscular injections and obstetric procedures, ear infections, and needle exposure through illicit drug use, acupuncture, or ear piercing.

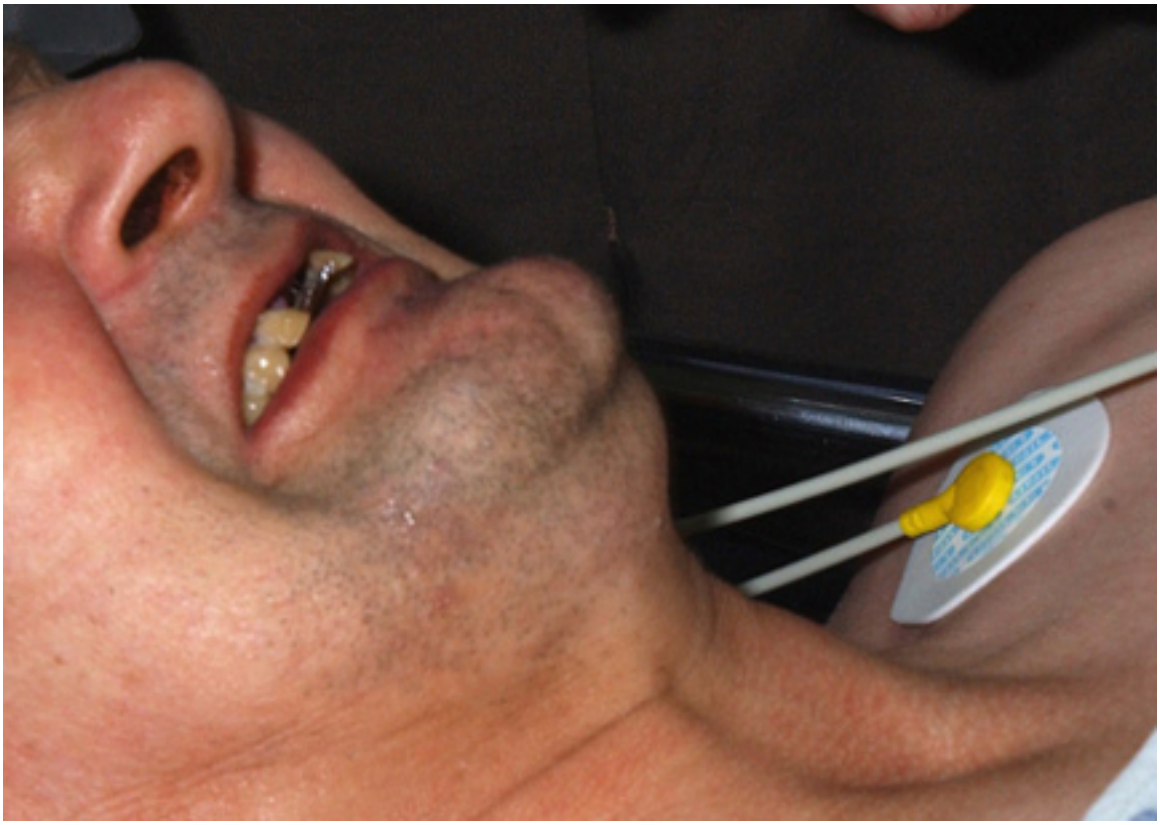
Wounds or burns that are considered to be tetanus prone include the following:[3] [4]

- Requiring surgical management but delay in intervention is more than 6 hours
- Puncture-type injury or a significant degree of devitalized tissue (especially in contact with soil or manure)
- Certain animal bites and scratches
- Foreign body-containing wounds
- Open fractures
- Concomitant systemic sepsis.

Examination

The diagnosis should be strongly suspected if there is trismus (which results in a grimace described as "risus sardonicus," or sardonic smile) and 1 or more of the following: muscle rigidity, spasms, respiratory distress, dysphagia, or autonomic dysfunction (hyperpyrexia, labile blood pressure, cardiac arrhythmias). Intermittent tonic contraction of their skeletal muscles causes intensely painful spasms, which may last for minutes, during which consciousness is retained. The spasms are often triggered by external (noise, light, drafts, physical contact) or internal stimuli and may cause fractures or rhabdomyolysis. Tetanic spasms can produce opisthotonus, board-like abdominal wall rigidity, dysphagia, and apneic periods due to contraction of the thoracic muscles and/or glottal or pharyngeal muscles. During a generalized spasm patients classically arch their back, extend their legs, flex their arms in abduction, and clench their fists. Apnea may be a feature of such a spasm. Autonomic overactivity initially manifests as irritability, restlessness, sweating, and tachycardia. Several days later, hyperpyrexia, cardiac arrhythmias, labile hypertension, or hypotension can occur.

Wounds should be inspected; a patient with no wounds should be examined for other evidence of a portal of entry for spores.



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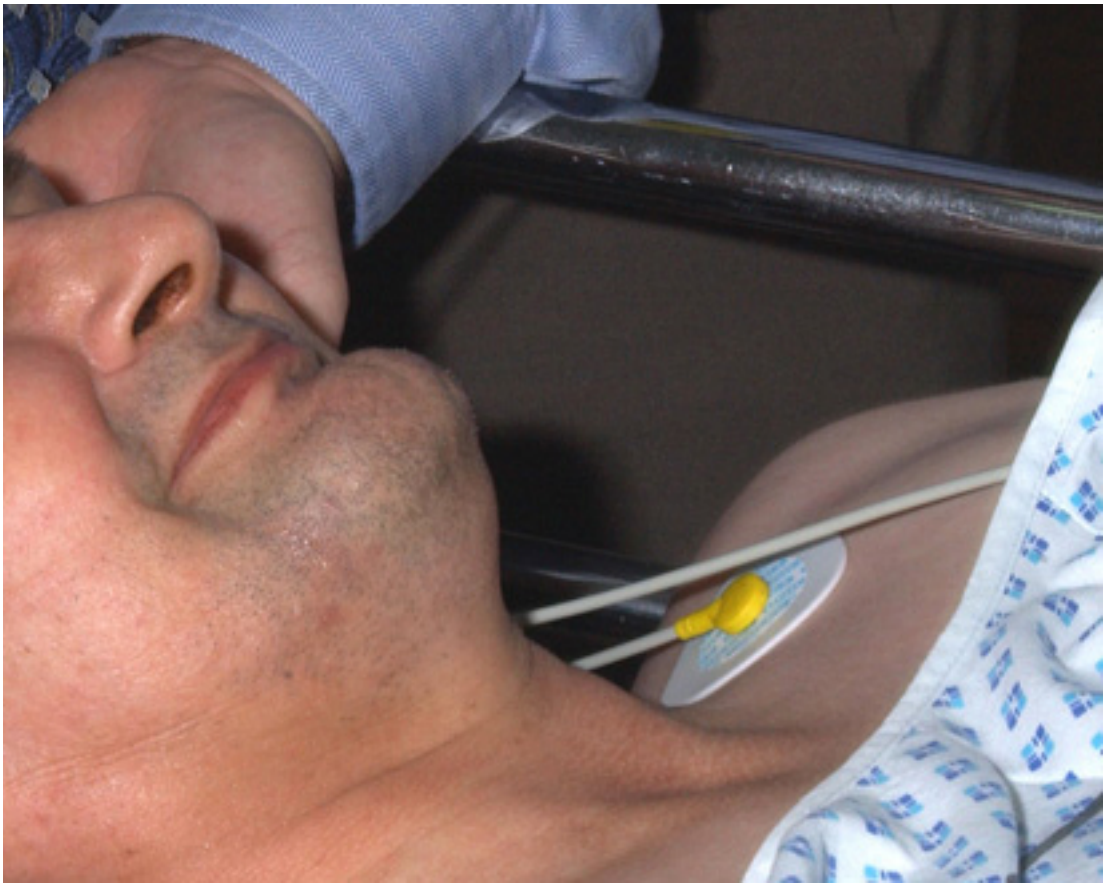

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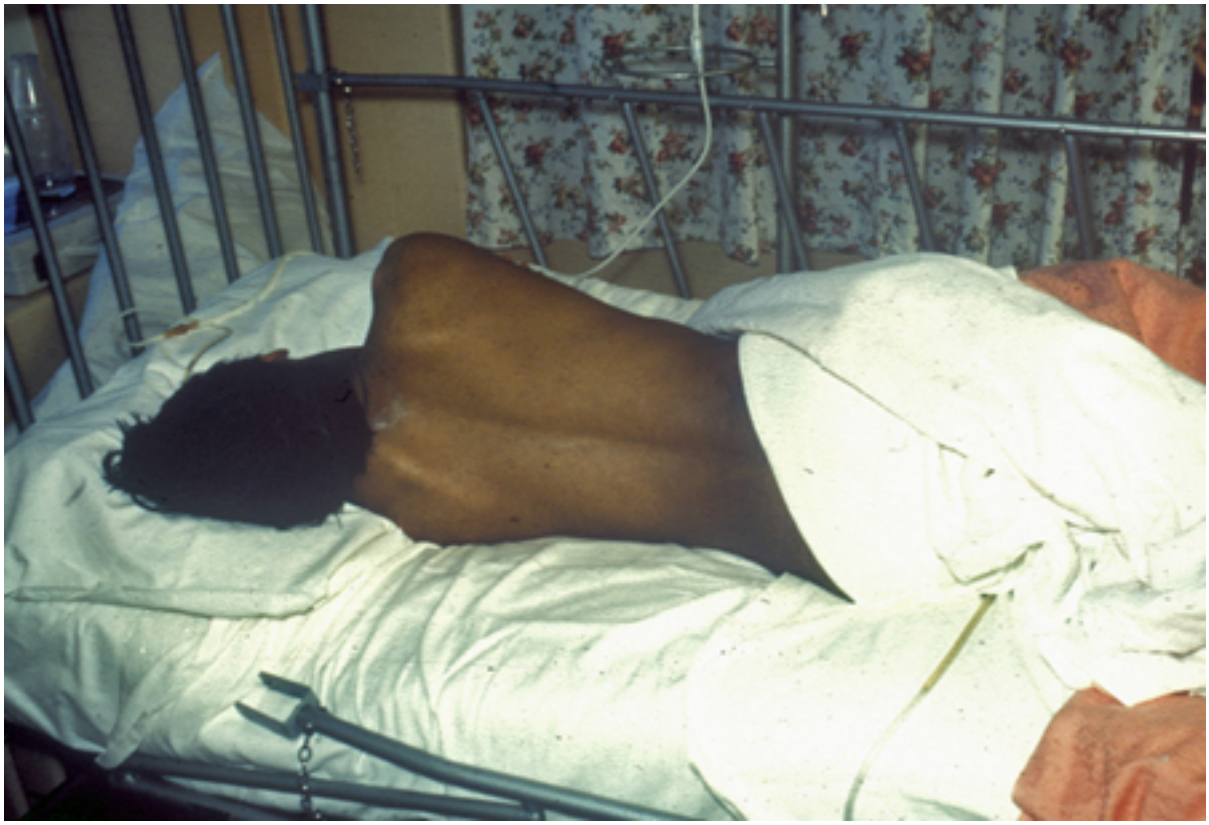

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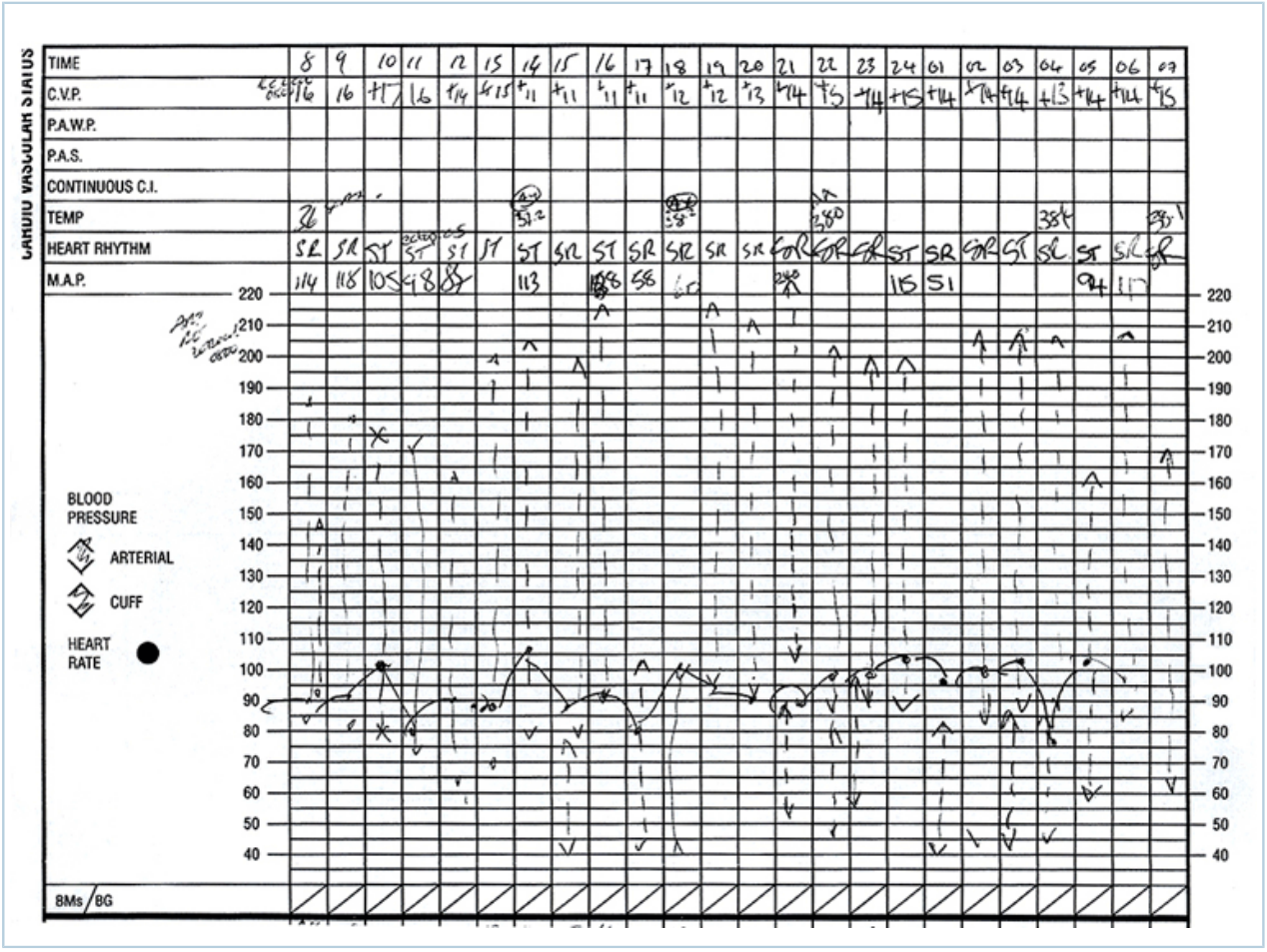

Observation chart illustrating autonomic dysfunction with extreme fluctuation in blood pressure

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Laboratory tests

The diagnosis is clinical, but laboratory tests are available to support or confirm the diagnosis. Treatment should never be delayed to wait for laboratory results.

Tetanus toxin can be detected in serum, confirming a clinical diagnosis. Samples should be collected before tetanus immune globulin (TIG) treatment. Absence of toxin in the serum does not exclude the clinical diagnosis.[39]

Clostridium tetani may be detected in the infection site by direct polymerase chain reaction and using strict anaerobic culture methods on wound tissue or swabs. A negative result does not exclude tetanus.[39] A positive wound culture does not indicate whether the organism produces a toxin. The bacteria may be present without causing tetanus in patients with protective immunity.[19]

Demonstration of low levels of tetanus toxin antibodies in serum can support but not confirm a clinical diagnosis. Samples should be taken before TIG treatment, but treatment of clinical tetanus should not be delayed waiting for laboratory result.[39] Conversely, severe and fatal tetanus has been reported in patients with protective antibody levels.[41]

Drug samples or paraphernalia can be tested for the presence of spores after discussion with the relevant health authority.

If clinical diagnosis is uncertain additional investigations may be performed to exclude alternative diagnoses (e.g., hypocalcemia, meningitis). In tetanus infection cerebrospinal fluid findings are usually normal, although cerebrospinal fluid protein - immunoglobulin G - may be slightly elevated.[25] [42] Electroencephalogram is normal while electromyogram may be normal or show nonspecific changes.[1]

History and exam

Key diagnostic factors

antecedent tetanus-prone injury (common)

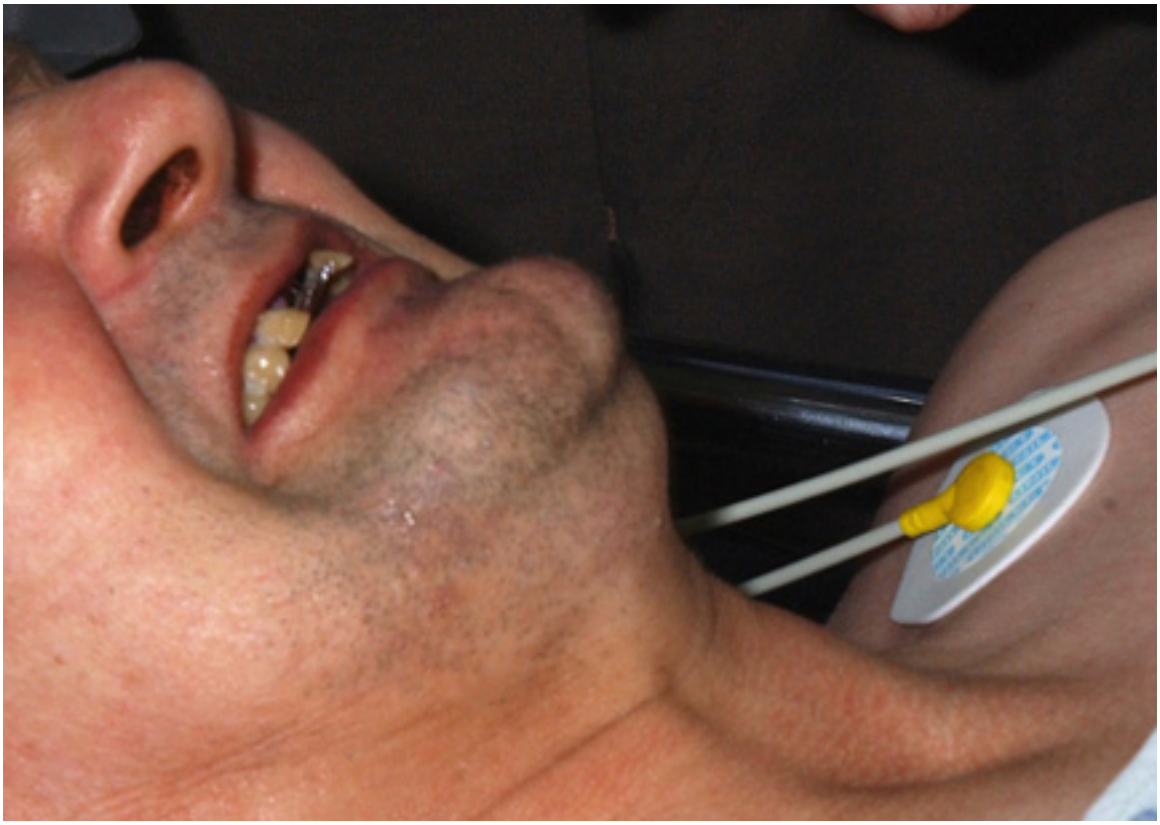
- Tetanus-prone wounds include: wounds/burns requiring surgical intervention that is delayed for over 6 hours; wounds/burns with extensive devitalized tissue; puncture-type injuries; certain animal bites and scratches; wounds containing foreign bodies or in contact with soil or manure; open fractures; wounds or burns in patients with systemic sepsis.[3] [4]

tetanus immunization status (common)

- Of patients diagnosed with tetanus in England and Wales between 1984 and 2000, 63% of those whose immunization status was known had never been immunized.[43] Incomplete vaccination is more likely in older people and immigrant populations.

trismus (lock jaw) (common)

- The presenting symptom in over 75% of cases. Present in 96% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19] Trismus arises due to spasm of the masseter muscle and results in a grimace described as "risus sardonicus" (sardonic smile).



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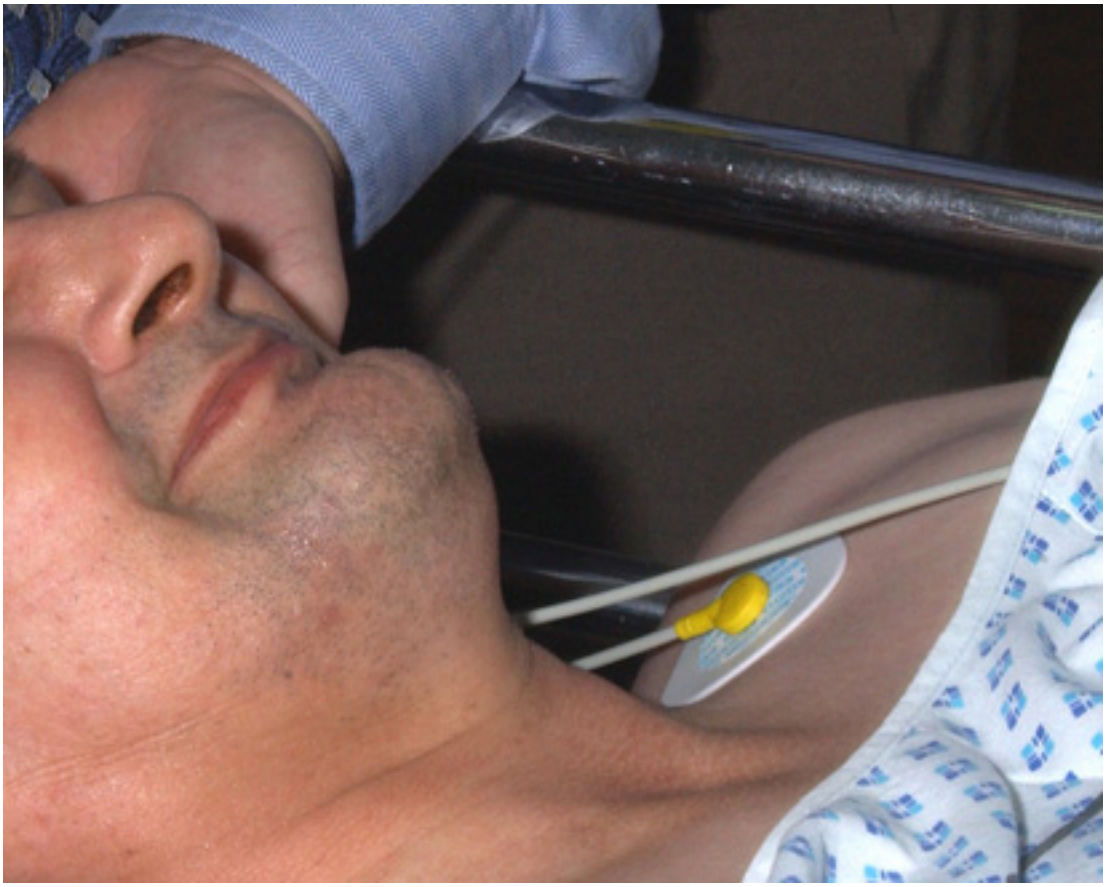

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back pain (common)

- Present in 94% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]

muscle stiffness/increased tone (common)

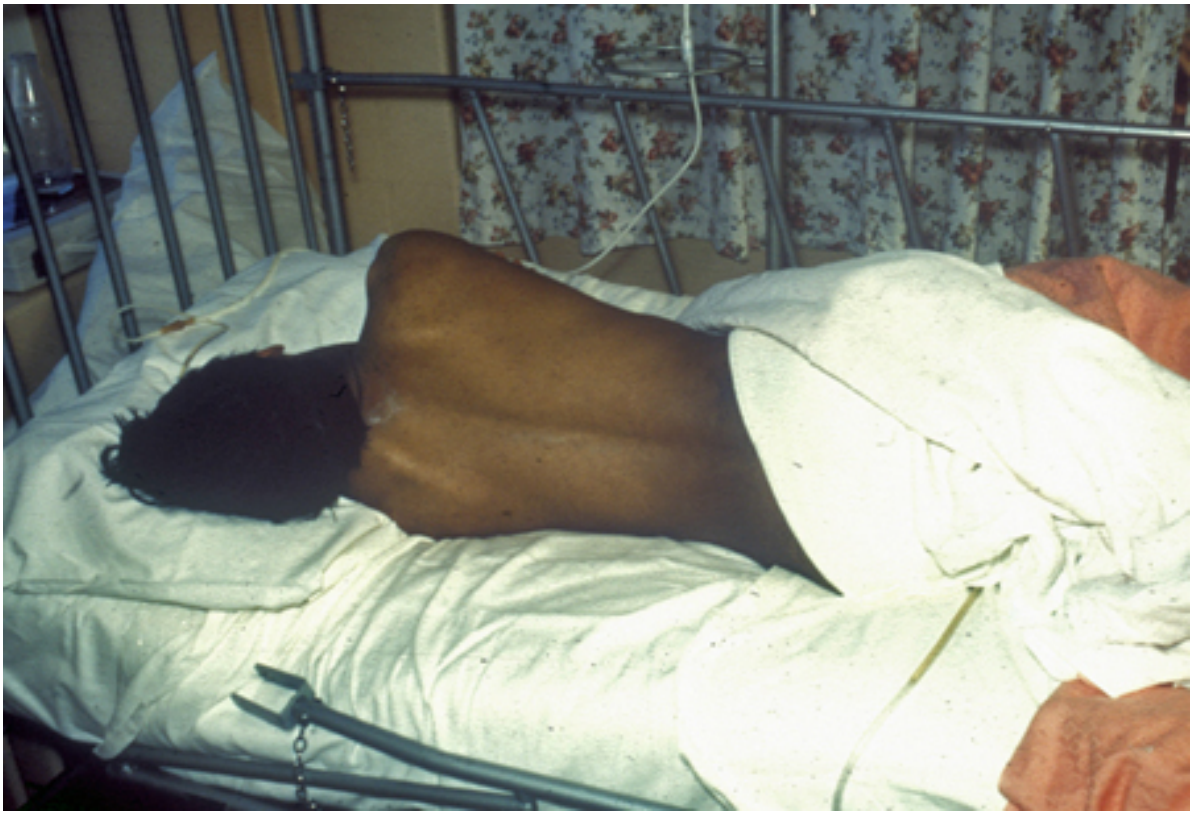
- Present in 94% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]

dysphagia (common)

- Present in 83% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]

spasms (common)

- Spasms are very painful and can affect any of the voluntary muscles. As the illness progresses, more muscle groups are affected. Contraction of the paraspinal muscles can result in severe opisthotonus and in infants the soles of the feet may touch the head.[1] Spasms can cause fractures of the vertebrae or other bones and hemorrhage into muscles. Spasms were present in 41% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]



Opisthotonus

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Other diagnostic factors

people who inject drugs (common)

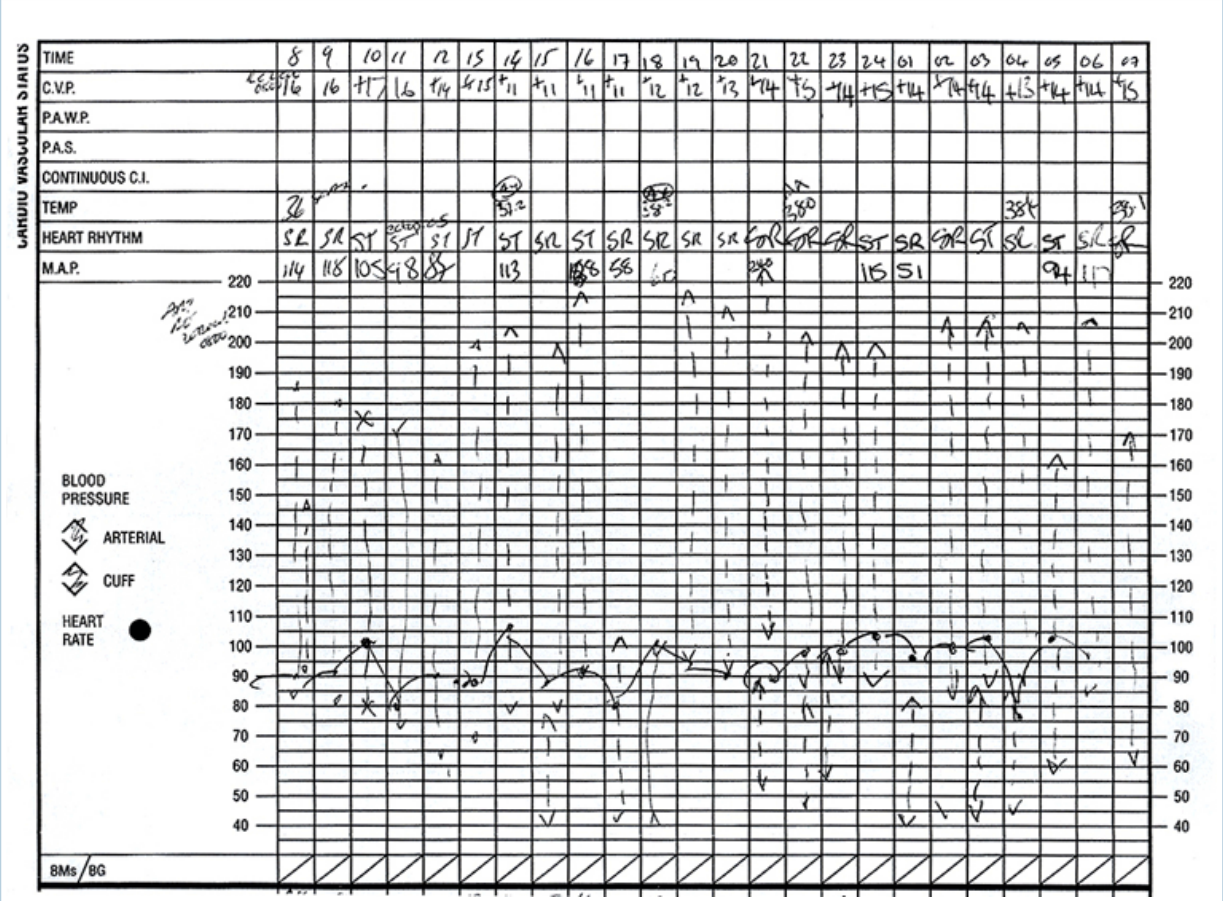
- An "outbreak" of 25 cases of tetanus occurred in people who inject drugs in the UK between July 2003 and September 2004.[9] Skin popping and intramuscular injection were associated with increased risk.

respiratory distress (common)

- Apnea is common due to laryngeal or pharyngeal spasms and/or vice-like contraction of the thoracic muscles. Increased intra-abdominal pressure during spasms further contributes to respiratory distress, and dysphagia increases the risk of aspiration. Respiratory difficulties were present in 10% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]

labile blood pressure, pulse rate, and temperature (common)

- Autonomic dysfunction is manifest early as irritability, restlessness, sweating, and tachycardia. In the second week of illness in those with severe tetanus profuse sweating, cardiac arrhythmias, labile hypertension or hypotension, and fever are commonly present. Fluctuations may be extreme and life-threatening. Sudden cardiac arrest can occur.[19]



Observation chart illustrating autonomic dysfunction with extreme fluctuation in blood pressure

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sweating (uncommon)

- Present in 10% of patients on admission to the Tetanus Unit at the Centre for Tropical Diseases, Ho Chi Minh City, Vietnam, in a study of 500 consecutive non-neonatal patients with tetanus.[19]

Risk factors

Strong

incomplete tetanus immunization

- Older people are less likely to have received complete immunization, and there is a hypothesis that protective antibody levels decline over time.[21] People from developing countries or from areas where public health infrastructure has collapsed due to war or natural disaster are also less likely to be immunized.
- The COVID-19 pandemic had a significant impact on global childhood immunization programs, leading to millions of children missing vaccine doses. The World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) estimate in a 2023 Centers for Disease Control and Prevention (CDC) report that during 2021 and 2022, Diphtheria-Tetanus-Pertussis-Containing Vaccines1 (DTPcv1) and DTPcv3 uptake improved in all WHO regions except in Africa, where coverage stagnated at 80% and 72%, respectively, and remained below the 2019 coverage (83% and 77%, respectively).[18]

injury

- Penetrating injuries on the lower limbs and open fractures are particularly prone to tetanus.

aseptic obstetric practices

- Uterine clostridial infection may follow septic abortions or occur postpartum. Maternal tetanus is defined as tetanus during pregnancy or within 6 weeks of the end of pregnancy (due to birth, miscarriage, or abortion) and has been associated with increased mortality compared with other types of adult tetanus.[2] Tetanus following abortion carries a particularly high risk of mortality, perhaps because women delay seeking medical attention.[22]
- Umbilical stump infection may occur in the offspring of inadequately immunized mothers, resulting in neonatal tetanus. Birth practices involving umbilical anointment with mud, animal feces, or ghee contribute to the risk of tetanus in some cases. Prevention of maternal and neonatal tetanus is achieved using a combination of immunization of pregnant women, and improvement in birth hygiene and perinatal care.[16]

people who inject drugs

- Injecting drug use may be strongly implicated in case clusters. Tetanus is particularly associated with intramuscular or subcutaneous use.[9] Drug practices that are less tetanus-prone can be encouraged, such as avoiding intramuscular and subcutaneous injection and using as little citric acid as possible, which devitalizes tissue.[23]

asterile intramuscular injection

- Intramuscular injection of quinine in particular is associated with a high mortality.[24] The acidic pH causes tissue ischemia and creates an ideal milieu for clostridial multiplication.

Weak

abdominal surgery

- Necrotic infections involving bowel flora may complicate abdominal surgery. Rare cases may be caused by asterile surgical catgut or contaminated theater ventilation systems.

acupuncture, ear piercing, pedicures, toothpicks

- Implicated in tetanus in unusual cases.[12] [19] In a minority of patients no antecedent portal of entry can be identified.

necrotic tumors

- Necrotic tumors are weakly associated with tetanus.[12]

middle ear infection

- "Otogenic tetanus" has been attributed to poor hygiene and negligence in treating middle ear infections.[25]

Tests

1st test to order

Test	Result
clinical diagnosis • Diagnosis of tetanus is primarily based on clinical features and further testing is usually not necessary.	**features of tetanus**

Other tests to consider

Test	Result
serum toxin • Tetanus toxin can be detected in serum, confirming a clinical diagnosis. Samples should be collected before tetanus immune globulin treatment, but treatment of clinical tetanus should not be delayed waiting for laboratory results. Absence of toxin in the serum does not exclude the clinical diagnosis.[39]	**positive**
Clostridium tetani detection from wound tissue or swab • *Clostridium tetani* may be detected in the infection site by direct polymerase chain reaction and strict anaerobic culture methods.[39] A negative result does not exclude tetanus.[39] A positive wound culture does not indicate whether the organism produces a toxin. The bacteria may be present without causing tetanus in patients with protective immunity.[19]	**presence of *Clostridium tetani***
serum antitoxin antibodies • Demonstration of low levels of tetanus toxin antibodies in serum can support but not confirm a clinical diagnosis. Samples should be taken before tetanus immune globulin treatment, but treatment of clinical tetanus should not be delayed waiting for laboratory results.[39] Conversely, severe and fatal tetanus has been reported in patients with protective antibody levels.[41]	**low**
spores on drug samples or paraphernalia • Drug samples or paraphernalia can be tested for the presence of spores after discussion with the relevant local health authority.	**presence of spores**
lumbar puncture • If clinical diagnosis is uncertain additional investigations may be performed to exclude alternative diagnoses. In tetanus, cerebrospinal fluid (CSF) findings are usually normal, although CSF protein - immunoglobulin G - may be slightly elevated.[25] [42]	**CSF protein may be slightly elevated**
electroencephalogram • If clinical diagnosis is uncertain additional investigations may be performed to exclude alternative diagnoses. In tetanus, electroencephalogram is normal.	**normal**
electromyogram • If clinical diagnosis is uncertain additional investigations may be performed to exclude alternative diagnoses. In tetanus, electromyogram may be normal or show nonspecific changes.[1]	**normal or may show nonspecific changes**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Drug-induced dystonias, for example, phenothiazines	• Features may include torticollis, retrocollis, trismus, glossopharyngeal dystonia, opisthotonus, and often deviation of the eyes. Tetanus is not associated with ocular deviation. • A compatible drug history would support a diagnosis of drug-induced dystonia.	• Anticholinergic agents such as procyclidine or benztropine usually ameliorate drug-induced dystonias but have no effect on tetanus.
Strychnine poisoning	• Strychnine is a white, odorless, poisonous powder that can be taken by mouth, inhaled (e.g., mixed with cocaine/heroin), or injected intravenously in solution. It is a competitive antagonist of the inhibitory neurotransmitter glycine at receptors in the spinal cord, brainstem, and higher centers. • Symptoms of poisoning usually appear within 15 to 60 minutes of ingestion and include heightened awareness, agitation, restlessness, painful muscular spasms and rigidity, trismus, opisthotonus, and hypersensitivity to stimuli.[44] Respiratory muscle spasm can cause respiratory arrest. • Ingestion of large amounts can lead to painful generalized convulsions, during which the patient retains consciousness. • Patient may give a history of snorting street drugs or deliberate/accidental ingestion of strychnine, which may be present in pesticide preparations, particularly rat poison.	• Blood, urine, and tissue assays for strychnine should be requested in suspected poisoning or when apparent tetanus presents in a fully immunized patient or in the absence of an antecedent tetanus-prone injury.
Neuroleptic malignant syndrome	• An idiosyncratic reaction to antipsychotic medication, featuring rapid onset of	• Clinical diagnosis.

Condition	Differentiating signs / symptoms	Differentiating tests
	hyperthermia, muscular rigidity, extrapyramidal signs, autonomic dysfunction, mutism, confusion, and even coma. Tremor and urinary incontinence may be present. • The condition is attributed to dopamine receptor blockade. The patient's drug history should indicate a possible cause. All classes of antipsychotic agents (dopamine D2 receptor antagonists) have been implicated, as well as non-antipsychotic agents, which block central dopamine pathways such as metoclopramide. • It is more likely to develop after initiation of antipsychotic therapy or an increase in dose, but can occur at any time during treatment, even years after starting therapy. Withdrawal of anti-Parkinson medication can also precipitate the syndrome. • Altered mental status is less common in tetanus.	
Stiff person syndrome	• Severe progressive muscle rigidity of the trunk and limbs with superimposed spasms, which may be triggered by voluntary movements, external stimuli, or emotional stress. • Trismus and facial spasms are absent. • The patient may experience unprotected falls like a tin soldier. • Symptom onset is typically between the ages of 30 and 50 years. Most cases begin insidiously and progress over years, although some can develop over weeks. • Patients often have other autoimmune conditions.	• Glutamic acid decarboxylase autoantibodies in 60% of patients. Electromyogram reveals a characteristic abnormality. There is a rapid response to diazepam.
Hypocalcemia	• Perioral and peripheral numbness/tingling and	• Hypocalcemia is confirmed by laboratory measurement

Condition	Differentiating signs / symptoms	Differentiating tests
	muscle cramps, which may progress to carpopedal spasm. • There may be a history of irritability, confusion, reduced intellectual capacity, or depression. Seizures can occur as well as movement disorders, for example, choreoathetosis, dystonic spasms, parkinsonism, and hemiballismus. • Wheezing may arise due to bronchospasm. Cardiac abnormalities include arrhythmias and congestive heart failure. • Clinical signs of chronic hypocalcemia may be present, for example, brittle nails, coarse hair/alopecia, dry skin. • The patient's history, drug history, and physical examination may suggest an underlying cause for hypocalcemia. Bisphosphates, anticonvulsants, foscarnet, and cisplatin can lead to hypocalcemia. • It may be possible to elicit Chvostek and Trousseau signs, which are suggestive of hypocalcemia.	of ionized calcium. ECG may show prolonged QT interval. Further investigations may establish the underlying cause: phosphate, alkaline phosphatase, magnesium, PTH, 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D, renal and liver function, amylase, etc.
Dental/parapharyngeal/ parotid/tonsillar infection or diphtheria	• These infections can cause trismus without spasms or generalization. • Localized swelling, tenderness, or exudate may be apparent.	• Radiologic imaging may confirm deep abscesses.
Meningitis	• Meningitis and meningoencephalitis can produce trismus, rigidity, seizures, and opisthotonus, but risus sardonicus is absent.[25]	• The cerebrospinal fluid findings differentiate between these conditions and tetanus. The protein may be slightly elevated in tetanus, but the cell count is normal.[25]
Generalized seizures in children	• The differentiation between seizures and tetanus may be particularly difficult in neonates. However, in epilepsy consciousness is	• Abnormal electroencephalogram in epilepsy.

Condition	Differentiating signs / symptoms	Differentiating tests
	impaired, and the muscles are often hypotonic and flaccid in the postictal state.[25]	

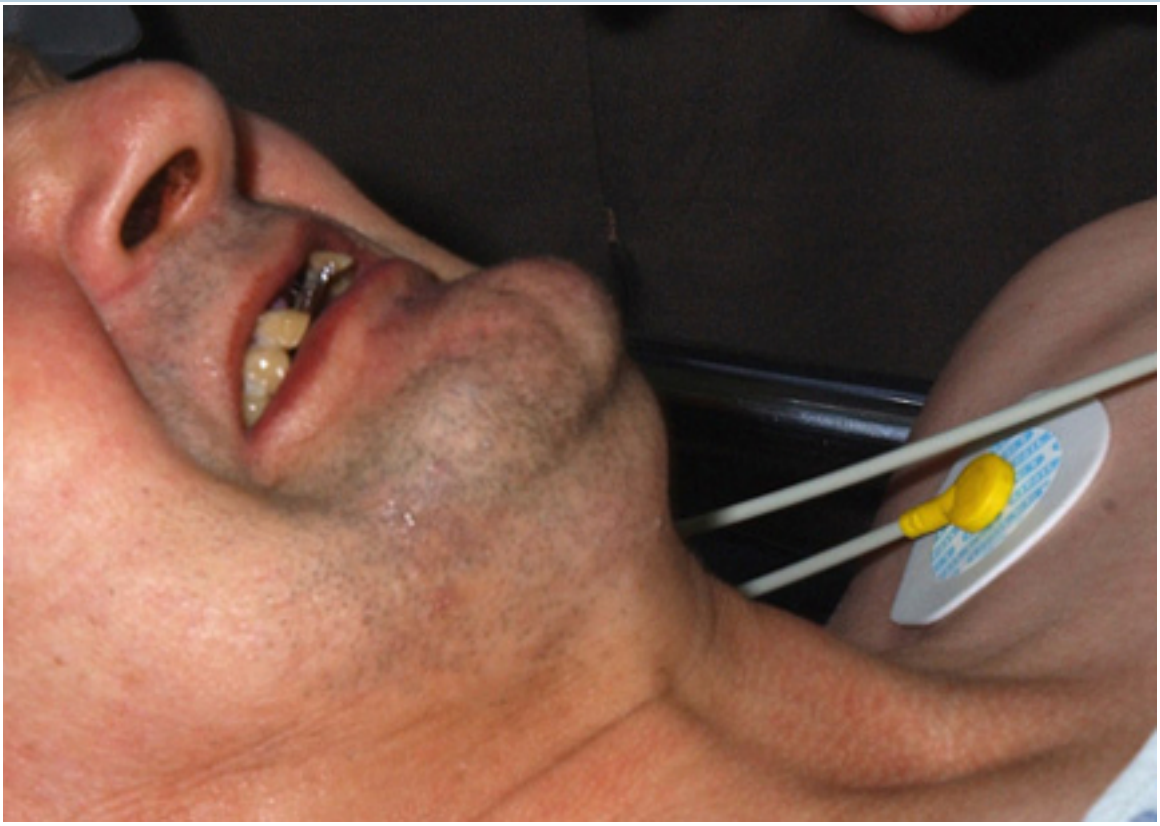
Criteria

Generalized

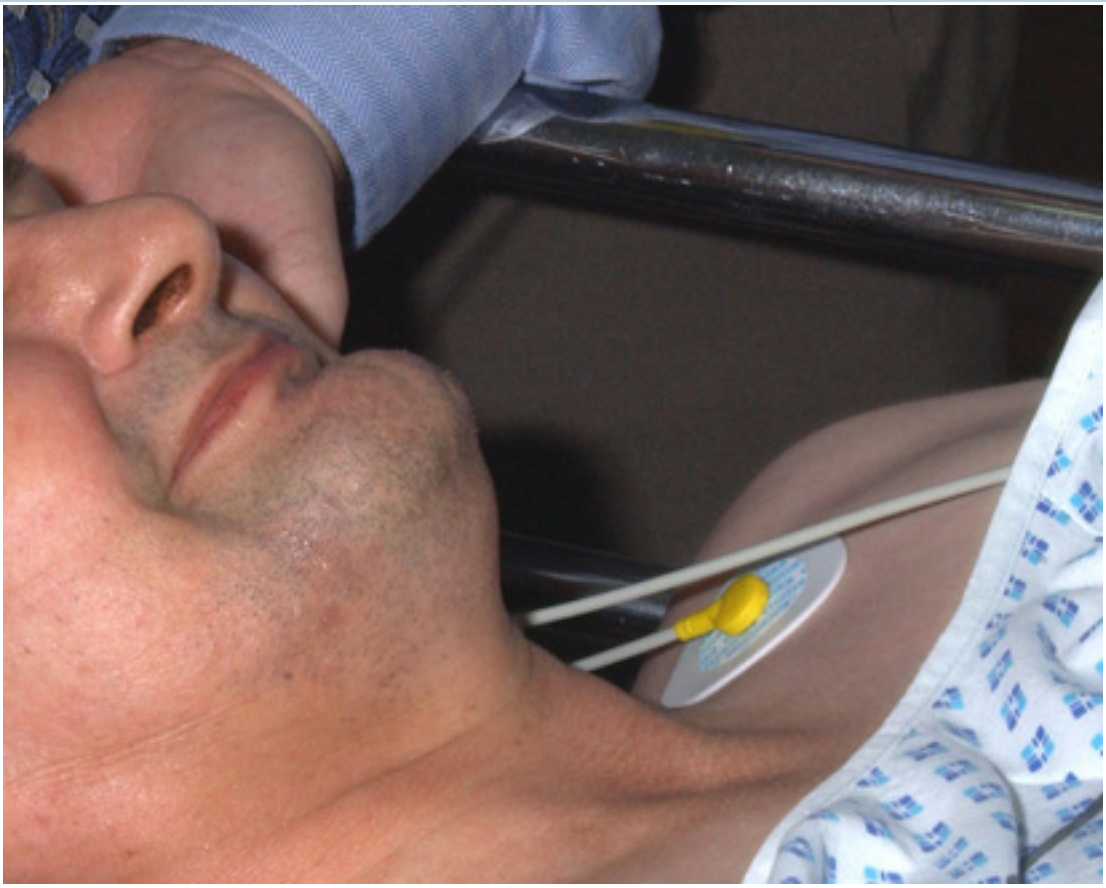
The most common clinical form, frequently presenting with trismus ("lock jaw") due to spasm of the masseter muscle. Repeated painful spasms occur affecting any part of the body. Restlessness, irritability, dysphagia, opisthotonus, and seizures can be seen, as well as respiratory failure due to vice-like contraction of the intercostal muscles or involvement of the glottis or diaphragm.[45] [46] Severe autonomic dysfunction may arise after several days.

Generalized tetanus can be further classified according to severity. The grading system described by Ablett is the most widely used:[47]

- Grade 1 (mild): mild/moderate trismus and general spasticity, little or no dysphagia, no respiratory embarrassment, no spasms.
- Grade 2 (moderate): moderate trismus and generalized spasticity, plus mild dysphagia and fleeting spasms. Moderate respiratory embarrassment may occur.
- Grade 3a (severe): severe trismus and generalized spasticity. Severe dysphagia and respiratory difficulties. Severe and prolonged spasms (both spontaneous and on stimulation).
- Grade 3b (very severe): as for grade 3a plus marked autonomic dysfunction.



Trismus
From the collections of Nicholas J. Beeching and Christopher M. Parry



Trismus
From the collections of Nicholas J. Beeching and Christopher M. Parry

Localized

A rare, milder form with a good prognosis. Muscle spasms are limited to one extremity or body region.

Cephalic

The rarest form; it follows head injury or middle ear infection. Cranial nerve palsies occur that may progress to generalized tetanus. The prognosis is very poor.

Neonatal

A form of generalized tetanus occurring in the first 28 days of life, widespread in the developing world; it is associated with umbilical stump infection in neonates born to mothers who have not been immunized. The mortality rate is high, with infants dying of complications such as central nervous system hemorrhage, pneumonia, pulmonary hemorrhage, and laryngeal spasms.[48]

Maternal

Maternal tetanus is defined as tetanus during pregnancy or within 6 weeks of the end of pregnancy (due to birth, miscarriage, or abortion), and has been associated with increased mortality compared with other types of adult tetanus.[2] Tetanus following abortion carries a particularly high risk of mortality, perhaps because women delay seeking medical attention.[22]

Approach

Prevention of tetanus is always preferable to management of the clinical tetanus syndrome. See Primary prevention .

The management of clean and tetanus-prone wounds should take into account the patient's immunization status. Immunosuppressed patients may not be adequately protected and additional boosting and/or tetanus immune globulin (TIG) may be required; in the US, immunosuppressed patients should be managed as if they were incompletely immunized.[3] [4] [38]

The principles of management for the clinical tetanus syndrome include supportive care, wound debridement, antimicrobials, passive and active immunization, control of muscle spasms, and management of autonomic dysfunction.[1] [45] [46]

Management of clean and minor wounds and tetanus-prone wounds

Tetanus toxoid-containing vaccine and/or TIG may be used depending on the patient's immunization history and risk assessment of the wound.

Wounds or burns that are considered to be tetanus prone include the following:[3] [4]

- Requiring surgical management but delay in intervention is more than 6 hours
- Puncture-type injury or a significant degree of devitalized tissue (especially in contact with soil or manure)
- Certain animal bites and scratches
- Foreign body-containing wounds
- Open fractures
- Concomitant systemic sepsis.

Tetanus toxoid is only available in combination with other antigens such as diphtheria and pertussis. The following vaccines are recommended for active vaccination in patients with tetanus-prone wounds: diphtheria/tetanus/acellular pertussis vaccine (DTaP); tetanus/diphtheria vaccine (Td for children ≥7 years of age and adults; or DT for children up to 7 years of age); and tetanus/low-dose diphtheria/acellular pertussis vaccine (Tdap). DTaP is recommended for children aged <7 years. DT is used when the pertussis vaccine component is contraindicated. Tdap can be given if the person is 11 years of age or older and has not yet received Tdap.[3] [29] [38]

In the US, patients with clean, minor wounds who have only had up to 2 doses of a tetanus toxoid-containing vaccine or an uncertain vaccination history should be given tetanus toxoid-containing vaccine, while patients who have received ≥3 doses do not require tetanus toxoid-containing vaccine unless they have not received a dose in the last 10 years. Clean or minor wounds do not require human TIG.[3] [38]

For all other wounds, patients who have only had up to 2 doses of tetanus toxoid-containing vaccine or an uncertain vaccination history should be given tetanus toxoid-containing vaccine and intramuscular TIG; patients who have received ≥3 doses do not require tetanus toxoid-containing vaccine unless they have not received a dose in the last 5 years. These patients do not require TIG.[3] [38]

If a tetanus booster is indicated for wound management during pregnancy, Tdap should be administered instead of Td if the woman has not received Tdap previously.[35]

Vaccination history	Clean and minor wounds		All other wounds	
	DTaP, Tdap, or Td*	TIG	DTaP, Tdap, or Td*	TIG**
Unknown or <3 doses	Yes	No	Yes	Yes
≥3 doses	No (Yes if >10 years since the last tetanus toxoid-containing vaccine dose)	No	No (Yes, if ≥5 years since the last tetanus toxoid-containing vaccine dose)	No

*US recommendations for tetanus wound management. DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin. *DTaP is recommended for children aged <7 years. Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series. **Immunosuppressed patients should be managed as if they were incompletely immunized (i.e., those with contaminated wounds should also receive TIG, regardless of their history of tetanus immunization)*

Liang JL 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;67:1-44.

When indicated, intramuscular TIG is the treatment of choice for prevention of tetanus and should be used if it is available.[1] [4] [38] Tetanus antitoxin (equine) is cheaper to produce and is more widely available in the developing world (it may not be available or may be difficult to access in some countries), but has a higher incidence of anaphylaxis (20% of cases) and a much shorter half-life (2 days).[19] Tetanus antitoxin (human) may also be available in some countries. If TIG cannot be sourced, guidelines in the UK recommend that the subcutaneous or intramuscular formulation of human normal immune globulin may be given intramuscularly as an alternative.[4] [39] This strategy could also be considered in similar circumstances outside the UK.

Management of clinical tetanus: supportive care

- Patients should be stabilized and their airway secured to ensure adequate ventilation (which can be compromised by the muscle spasms) and to prevent aspiration of gastric contents into the lungs. Patients should be transferred to an intensive care unit. External stimulation, which can precipitate muscle spasms, should be minimized.

Airway management

- There is a high risk of aspiration of gastric contents into the lungs resulting from reduced ability to cough due to muscle rigidity and sedation, pharyngeal spasms, dysphagia, gastric stasis, and increased intra-abdominal pressure during spasms. In severe tetanus, spasms may increase rapidly in frequency and duration; establishing a secure airway early is paramount before laryngeal obstruction and/or aspiration occurs.
- Prolonged mechanical ventilation is often required, sometimes for weeks, and early percutaneous tracheostomy is appropriate.[49] Patients with tetanus have increased salivation and bronchial

secretions; mouth care, regular tracheal suction, and chest physical therapy are crucial to prevent secondary pulmonary infection and atelectasis. Boluses of sedation and neuromuscular blocking agents are required for these procedures to avoid stimulation.

Nutritional support

- Energy demands in tetanus can be extremely high due to repeated spasms and sympathetic overdrive. Nutritional support should be initiated early, ideally by enteral feeding to maintain gastrointestinal integrity.[19]
- Percutaneous endoscopic gastrostomy is preferred to avoid the stimulation and reflux associated with nasogastric tubes.

Stress ulceration

- A proton-pump inhibitor may be prescribed to reduce stress ulceration.

Venous thromboembolism prophylaxis

- Compression stockings, subcutaneous heparin, and calf pumps are indicated.

Physical therapy

- Limb physical therapy should be started as soon as spasms have abated.

Decubitus ulcer prevention

- Management should include prevention of decubitus ulcers, as patients can be bed bound for weeks.

Management of clinical tetanus: wound debridement

Wound debridement removes spores and necrotic tissue, eradicating the anaerobic conditions that facilitate clostridial growth. Antibiotic penetration into devitalized tissue is likely to be poor, emphasizing the importance of adequate wound debridement.[50]

Management of clinical tetanus: antibiotic therapy

Antibiotics halt bacterial replication and thereby reduce the production of new toxins. Metronidazole has superseded penicillin G as the antimicrobial of choice for the treatment of tetanus. Penicillin G has traditionally been used for this purpose.[19] However, penicillin G is structurally similar to gamma-aminobutyric acid (GABA) and competitively antagonizes this neurotransmitter, an action that could potentiate the effects of tetanus toxin in inhibiting release of GABA into the synaptic cleft and enhancing central nervous system excitability.[19]

Evidence suggests that, compared with penicillin G, metronidazole was associated with reduced mortality.[51] Other evidence indicates no difference in mortality, but that metronidazole is associated with a lower requirement for muscle relaxants and sedatives.[52] This difference may be attributable to the GABA antagonist effect of penicillin G. Alternative antibiotics include clindamycin, tetracycline, and vancomycin.[1]

Management of clinical tetanus: use of human TIG

Intramuscular TIG should be administered to patients with clinical tetanus.[1] [38] It should be administered as soon as possible after the injury.[1] Passive immunization neutralizes unbound toxin, reducing the duration and severity of tetanus.

Intramuscular TIG (half-life 24.5 to 31.5 days) is the treatment of choice.[1] [38] If intramuscular TIG is unavailable, intravenous human normal immune globulin may be used.[38] Tetanus antitoxin (equine) is more widely available in the developing world (it may not be available or may be difficult to access in some countries), but has a higher incidence of anaphylaxis (20% of cases) and a much shorter half-life (2 days).[19] Tetanus antitoxin (human) may also be available in some countries.

Management of clinical tetanus: active immunization with tetanus vaccine

Patients with clinical tetanus should receive immunization with tetanus toxoid-containing vaccine to stimulate long-term humoral and cellular immunity. In addition, it is thought that tetanus toxoid saturates ganglioside receptors, blocking the binding of wild-type toxin.[19] Toxoid should be injected at a different site from immune globulin so that it is not "neutralized" by the passive immunization.

Management of clinical tetanus: control of muscle spasms

Muscle spasms are extremely painful and potentially life-threatening if they cause airway compromise or respiratory failure. Benzodiazepines have been the mainstay of controlling muscle spasms, and in addition have anticonvulsant, sedative, and anxiolytic effects. They block an endogenous inhibitor at the GABAA receptor. Diazepam is often used.[1] High doses may necessitate ventilatory assistance and have been associated with lactic acidosis due to the excipient propylene glycol.[53] Diazepam metabolites are active with long half-lives (desmethyldiazepam has a half-life of greater than 100 hours), and for this reason midazolam infusions may be preferred in adults.[54] [55] In children, diazepam may cause significant respiratory depression; therefore, midazolam or lorazepam may be preferred.

There is some evidence that diazepam is more effective in treating tetanus than alternative sedatives such as phenothiazines and barbiturates.[56] However, the studies concerned were limited by their small size, lack of data on drug safety, and other methodologic drawbacks. Large multicenter randomized controlled trials are needed to establish whether diazepam is superior to phenobarbital and chlorpromazine.

Some patients require paralysis with nondepolarizing neuromuscular blocking agents in addition to sedation. Traditionally pancuronium was used, although this was known to potentially aggravate autonomic instability.[57] Vecuronium and rocuronium are associated with less autonomic disturbance, and are preferred.

Baclofen stimulates postsynaptic GABAB receptors and has been found to improve muscle spasms when given by intrathecal bolus or infusion, but only in a few small studies.[58] [59] [60] [61] In a retrospective outcome study from a single centre in Portugal during 1998 to 2003, intrathecal baclofen was given as an initial bolus, followed by a continuous infusion.[62] This controlled spasms and rigidity in 21 of 22 patients with grade 3 tetanus. Most patients required therapy for at least 3 weeks (range 8 to 30 days). One patient developed meningitis secondary to infection of the intrathecal catheter. Intrathecal baclofen has a narrow therapeutic range and considerable inter-individual pharmacodynamic variability.[58] Treatment with intrathecal baclofen should only be considered under specialist guidance and administration.

Management of clinical tetanus: autonomic dysfunction

Autonomic dysfunction is extremely difficult to control. It arises in patients with severe disease, usually in the second week of illness.

Magnesium sulfate is a presynaptic neuromuscular blocker, blocks catecholamine release from nerves and the adrenal medulla, and reduces receptor responsiveness to catecholamines. It is also an anticonvulsant and a calcium antagonist in the myocardium.[19] Electromyogram studies have suggested that magnesium tends to spare the respiratory muscles, although at high doses ventilation may be depressed, mandating ventilatory support.[54] [63] Magnesium sulfate has previously been reported to be both an effective adjunct in controlling autonomic disturbance in heavily sedated patients with severe tetanus and successful in relieving spasms in nonventilated patients.[64] [65] [66] One randomized controlled trial found that magnesium sulfate significantly reduced the requirement for other drugs (e.g., midazolam) used for the control of muscle spasms and showed that patients are less likely to need verapamil for cardiovascular instability, when compared with placebo.[67] There was no difference in the need for mechanical ventilation.[67] An earlier, small prospective observational study suggested that magnesium sulfate reduces not only the use of neuromuscular blocking agents to control severe spasms but also the requirement for mechanical ventilation when compared with historical controls.[68] Conflicting results may reflect differences in study design and magnesium administration.[67] A loading dose of 5 g of magnesium sulfate given intravenously over 20 minutes has been advocated, followed by magnesium infusion, the rate of which is titrated to the control of spasms and rigidity.[54] The aim is not to completely abolish muscle rigidity, but to reduce it to a level that is acceptable to the patient and allows swallowing of saliva, mouth care, and limb physical therapy. Doses as high as 4 to 5 g/hour may be necessary, with monitoring for respiratory depression. One meta-analysis of 3 controlled trials found no reduction in mortality for patients treated with magnesium sulfate compared with placebo or diazepam therapy. Conclusions about the effects of magnesium on duration of intensive care stay, duration of hospital stay, and requirement for ventilatory support could not be drawn due to large methodological differences between the studies included.[69]

Sedation helps to reduce autonomic instability, and both benzodiazepines and morphine sulfate are useful in this regard. Morphine sulfate reduces sympathetic tone in the heart and the vascular system, improving cardiovascular stability without compromising cardiac performance.[1] [70]

Beta-blockade may be required in further management of the autonomic instability. Choice and dosing of a beta-blocker should be decided in consultation with a specialist. Pure beta-blockade, with propranolol, has been associated with sudden death.[71]

Atropine, clonidine, and epidural/spinal bupivacaine have been reported to improve autonomic disturbance in either individual patients or very small series. Larger trials are needed to adequately assess outcome measures for these treatments.[72] [73] [74] [75] [76] [77]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial (summary)		
clean and minor wound		
	1st	wound debridement
	adjunct	tetanus vaccine
tetanus-prone wound		
	1st	wound debridement
	plus	tetanus vaccine ± tetanus immune globulin (TIG) or tetanus antitoxin or human normal immune globulin

Acute (summary)		
with clinical tetanus		
	1st	supportive care
	plus	benzodiazepine
	plus	wound debridement
	plus	antibiotics
	plus	tetanus immune globulin (TIG) or tetanus antitoxin or human normal immune globulin + intramuscular tetanus vaccine
▪ with severe muscle spasms	plus	nondepolarizing neuromuscular blocking agents or intrathecal baclofen
▪ with autonomic dysfunction	plus	magnesium sulfate + sedation + beta-blockade

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Initial

clean and minor wound

1st **wound debridement**

» Prevention of tetanus is always preferable to management of the clinical syndrome.

» All wounds should be thoroughly cleaned and debrided.[3] [4] [38]

» Wound debridement removes spores and necrotic tissue, eradicating the anaerobic conditions that facilitate clostridial growth. Antibiotic penetration into devitalized tissue is likely to be poor, emphasizing the importance of adequate wound debridement.[50]

adjunct **tetanus vaccine**

Treatment recommended for SOME patients in selected patient group

» The management of clean and minor wounds should take into account the patient's immunization status. Immunosuppressed patients may not be adequately protected and additional boosting and/or immune globulin may be required; in the US, immunosuppressed patients should be managed as if they were incompletely immunized.[3] [4] [38]

» Clean and minor wounds do not require human tetanus immune globulin (TIG).[3] [4] [38]

» US recommendations for vaccination in patients with clean and minor wounds are as follows:[3] [38]

» Patients who have only had up to 2 doses of tetanus toxoid-containing vaccine or an uncertain vaccination history should be given tetanus toxoid-containing vaccine; patients who have received ≥3 doses do not require tetanus toxoid-containing vaccine unless they have not received a dose in the last 10 years.

» Tetanus toxoid is only available in combination with other antigens such as diphtheria and pertussis. The following vaccines are recommended for active vaccination in patients with tetanus-prone wounds: diphtheria/tetanus/acellular pertussis vaccine (DTaP); tetanus/diphtheria vaccine (Td for children ≥7 years

Initial

of age and adults; or DT for children up to 7 years of age); and tetanus/low-dose diphtheria/acellular pertussis vaccine (Tdap). DTaP is recommended for children aged <7 years. DT is used when the pertussis vaccine component is contraindicated. Tdap can be given if the person is 11 years of age or older and has not yet received Tdap.[3] [29] [38]

» If a tetanus booster is indicated for wound management during pregnancy, Tdap should be administered instead of Td if the woman has not received Tdap previously.[35]

tetanus-prone wound

1st **wound debridement**

» Prevention of tetanus is always preferable to management of the clinical syndrome.

» Wounds or burns that are considered to be tetanus prone and high risk include the following: requiring surgical management but delay in intervention over 6 hours; puncture-type injury or a significant degree of devitalized tissue (especially in contact with soil or manure); certain animal bites and scratches; foreign body-containing wounds; open fractures; concomitant systemic sepsis.[3] [4] [38]

» All wounds should be thoroughly cleaned and debrided.[3] [4] [38]

» Wound debridement removes spores and necrotic tissue, eradicating the anaerobic conditions that facilitate clostridial growth. Antibiotic penetration into devitalized tissue is likely to be poor, emphasizing the importance of adequate wound debridement.[50]

plus **tetanus vaccine ± tetanus immune globulin (TIG) or tetanus antitoxin or human normal immune globulin**

Treatment recommended for ALL patients in selected patient group

Primary options

» tetanus immune globulin (human): children and adults: see local specialist protocol for dosing guidelines

Secondary options

» immune globulin (human): children and adults: see local specialist protocol for dosing guidelines

MANAGEMENT

Initial

» The management of tetanus-prone wounds should take into account the patient's immunization status. Immunosuppressed patients may not be adequately protected and additional boosting and/or immune globulin may be required; in the US, immunosuppressed patients should be managed as if they were incompletely immunized.[3] [4] [38]

» US recommendations for vaccination in patients with tetanus-prone wounds are as follows:[3] [38]

» Patients who have only had up to 2 doses of tetanus toxoid-containing vaccine or an uncertain vaccination history should be given tetanus toxoid-containing vaccine and intramuscular TIG; patients who have received ≥3 doses do not require tetanus toxoid-containing vaccine unless they have not received a dose in the last 5 years. These patients do not require TIG.[3] [38]

» Tetanus toxoid is only available in combination with other antigens such as diphtheria and pertussis. The following vaccines are recommended for active vaccination in patients with tetanus-prone wounds: diphtheria/tetanus/acellular pertussis vaccine (DTaP); tetanus/diphtheria vaccine (Td for children ≥7 years of age and adults; or DT for children up to 7 years of age); and tetanus/low-dose diphtheria/acellular pertussis vaccine (Tdap). DTaP is recommended for children aged <7 years. DT is used when the pertussis vaccine component is contraindicated. Tdap can be given if the person is 11 years of age or older and has not yet received Tdap.[3] [29] [38]

» If a tetanus booster is indicated for wound management during pregnancy, Tdap should be administered instead of Td if the woman has not received Tdap previously.[35]

» Passive immunization with TIG:

» TIG neutralizes toxin, reducing the duration and severity of tetanus. Toxin binds irreversibly to tissues; therefore, only circulating and unbound toxin can be neutralized.

» Toxoid should be injected at a different site from TIG so that it is not "neutralized" by the passive immunization.[3]

» When indicated, intramuscular TIG is the treatment of choice and should be used if it is available.[1] [38] Tetanus antitoxin (equine) is more widely available in the developing world

Initial

(it may not be available or may be difficult to access in some countries), but has a higher incidence of anaphylaxis (20% of cases) and a much shorter half-life (2 days).[19] Tetanus antitoxin (human) may also be available in some countries. If intramuscular TIG cannot be sourced, in the UK, guidelines recommend that the subcutaneous or intramuscular formulation of human normal immune globulin may be given as an alternative.[39]

Acute

with clinical tetanus

1st **supportive care**

Primary options

» esomeprazole: children: consult specialist for guidance on dose; adults: 20-40 mg intravenously once daily

» Patients should be stabilized and an airway secured to ensure adequate ventilation (which can be compromised by the muscle spasms) and prevention of aspiration. Patients should be transferred to an intensive care unit. External stimulation, which can precipitate muscle spasms, should be minimized.

» Airway management: there is a high risk of aspiration; therefore, establishing a secure airway early is paramount before laryngeal obstruction and/or aspiration occurs.

» Prolonged mechanical ventilation is often required, sometimes for weeks, and early percutaneous tracheostomy is appropriate.[49] Patients with tetanus have increased salivation and bronchial secretions; mouth care, regular tracheal suction, and chest physical therapy are crucial to prevent secondary pulmonary infection and atelectasis. Boluses of sedation and neuromuscular blocking agents are required for these procedures to avoid stimulation.

» Management should include prevention of decubitus ulcers. Limb physical therapy can be started as soon as spasms have abated.

» Compression stockings, subcutaneous heparin, and calf pumps are indicated as prophylaxis for venous thromboembolism.

» A proton-pump inhibitor may be prescribed to reduce stress ulceration.

plus **benzodiazepine**

Treatment recommended for ALL patients in selected patient group

Primary options

» diazepam: children and adults: consult specialist for guidance on dose

OR

» lorazepam: children and adults: consult specialist for guidance on dose

Acute

OR

» midazolam: children and adults: consult specialist for guidance on dose

» Muscle spasms are both painful and potentially life-threatening if they cause airway compromise or respiratory failure.

» Benzodiazepines have been the mainstay of controlling muscle spasms, and in addition have anticonvulsant, sedative, and anxiolytic effects. Diazepam is often used.[1] Diazepam metabolites are active with long half-lives (desmethyldiazepam has a half-life of >100 hours), and for this reason midazolam infusions may be preferred.[54] [55] In children, diazepam may cause significant respiratory depression; therefore, midazolam or lorazepam may be preferred.

plus **wound debridement**

Treatment recommended for ALL patients in selected patient group

» All wounds should be thoroughly cleaned and debrided.[4] [38]

» Wound debridement removes spores and necrotic tissue, eradicating the anaerobic conditions that facilitate clostridial growth. Antibiotic penetration into devitalized tissue is likely to be poor, emphasizing the importance of adequate wound debridement.[50]

plus **antibiotics**

Treatment recommended for ALL patients in selected patient group

Primary options

» metronidazole: children: consult specialist for guidance on dose; adults: 500 mg intravenously every 6 hours for 7-10 days

Secondary options

» penicillin G potassium: children: consult specialist for guidance on dose; adults: 100,000 to 200,000 units/kg/day intravenously/intramuscularly given in divided doses every 4-6 hours for 7-10 days

Tertiary options

» clindamycin: children and adults: consult specialist for guidance on dose

Acute

OR

» tetracycline: children and adults: consult specialist for guidance on dose

OR

» vancomycin: children and adults: consult specialist for guidance on dose

» Antibiotics halt bacterial replication and thereby reduce the production of new toxins. Metronidazole has superseded penicillin G as the antimicrobial of choice for the treatment of tetanus.

» Evidence suggests that, compared with penicillin G, metronidazole was associated with reduced mortality.[51] Other evidence indicates no difference in mortality, but that metronidazole is associated with a lower requirement for muscle relaxants and sedatives.[52]

» Although penicillin G has traditionally been used,[19] it is structurally similar to gamma-aminobutyric acid (GABA) and competitively antagonizes this neurotransmitter, an action that could potentiate the effects of tetanus toxin in inhibiting release of GABA into the synaptic cleft and enhancing central nervous system excitability.[19]

» Alternative antibiotics include clindamycin, tetracycline, and vancomycin;[1] however, an infectious disease specialist should be consulted for doses and regimens for this indication.

plus **tetanus immune globulin (TIG) or tetanus antitoxin or human normal immune globulin + intramuscular tetanus vaccine**

Treatment recommended for ALL patients in selected patient group

Primary options

» tetanus immune globulin (human): children and adults: see local specialist protocol for dosing guidelines

Secondary options

» immune globulin (human): children and adults: see local specialist protocol for dosing guidelines

» Passive immunization with TIG:

Acute

» Intramuscular TIG should be administered to patients with clinical tetanus.[1] [38] It should be administered as soon as possible after the injury.[1] Passive immunization neutralizes toxin, reducing the duration and severity of tetanus.

» Intramuscular TIG (half-life 24.5 to 31.5 days) is the treatment of choice.[1] [38] If intramuscular TIG is unavailable, intravenous human normal immune globulin may be used.[38] Tetanus antitoxin (equine) is more widely available in the developing world (it may not be available or may be difficult to access in some countries), but has a higher incidence of anaphylaxis (20% of cases) and a much shorter half-life (2 days).[19] Tetanus antitoxin (human) may also be available in some countries.

» Active immunization with tetanus vaccine:

» All patients with clinical tetanus should receive immunization with tetanus toxoid-containing vaccine to stimulate long-term humoral and cellular immunity. In addition, it is thought that tetanus toxoid saturates ganglioside receptors, blocking the binding of wild-type toxin.[19]

with severe muscle spasms **plus** **nondepolarizing neuromuscular blocking agents or intrathecal baclofen**

Treatment recommended for ALL patients in selected patient group

Primary options

» vecuronium: children and adults: see local specialist protocol for dosing guidelines

OR

» rocuronium: children and adults: see local specialist protocol for dosing guidelines

Secondary options

» pancuronium: children and adults: see local specialist protocol for dosing guidelines

OR

» baclofen intrathecal: children and adults: see local specialist protocol for dosing guidelines

» Some patients require paralysis with nondepolarizing neuromuscular blocking agents in addition to sedation. Traditionally pancuronium was used, although this was known to potentially aggravate autonomic instability.[57] Vecuronium

Acute

and rocuronium are associated with less autonomic disturbance, and are preferred.

» Baclofen stimulates postsynaptic GABAB receptors and has been found to improve muscle spasms when given by intrathecal bolus or infusion, but only in a few small studies.[58] [59] [60] [61] In a retrospective outcome study from a single centre in Portugal during 1998 to 2003, intrathecal baclofen was given as an initial bolus, followed by a continuous infusion.[62] This controlled spasms and rigidity in 21 of 22 patients with grade 3 tetanus. Most patients required therapy for at least 3 weeks (range 8 to 30 days). One patient developed meningitis secondary to infection of the intrathecal catheter. Intrathecal baclofen has a narrow therapeutic range and considerable inter-individual pharmacodynamic variability.[58]

» Treatment with intrathecal baclofen should only be considered under specialist guidance and administration.

with autonomic dysfunction — **plus** — **magnesium sulfate + sedation + beta-blockade**

Treatment recommended for ALL patients in selected patient group

Primary options

» magnesium sulfate: children: consult specialist for guidance on dose; adults: 5 g intravenously as a loading dose, followed by 2-5 g/hour infusion, consult specialist for further guidance on dose
-and-
» morphine sulfate: children and adults: see local specialist protocol for dosing guidelines

Secondary options

» magnesium sulfate: children: consult specialist for guidance on dose; adults: 5 g intravenously as a loading dose, followed by 2-5 g/hour infusion, consult specialist for further guidance on dose
-and-
» morphine sulfate: children and adults: see local specialist protocol for dosing guidelines

--AND--

» labetalol: children and adults: see local specialist protocol for dosing guidelines
-or-
» esmolol: children and adults: see local specialist protocol for dosing guidelines

Acute

» Autonomic dysfunction is extremely difficult to control. It arises in patients with severe disease, usually in the second week of illness.

» Magnesium sulfate has previously been reported to be both an effective adjunct in controlling autonomic disturbance in heavily sedated patients with severe tetanus and successful in relieving spasms in nonventilated patients.[64] [65][66] One randomized controlled trial found that magnesium sulfate significantly reduced the requirement for other drugs (e.g., midazolam) for the control of muscle spasms and showed that patients are less likely to need verapamil for cardiovascular instability, when compared with placebo.[67] There was no difference in the need for mechanical ventilation.[67] An earlier, small prospective observational study suggested that magnesium sulfate reduced not only the use of neuromuscular blocking agents to control severe spasms but also the requirement for mechanical ventilation when compared with historical controls.[68] Conflicting results may reflect differences in study design and magnesium administration.[67] The aim is not to completely abolish muscle rigidity, but to reduce it to a level that is acceptable to the patient and allows swallowing of saliva, mouth care, and limb physical therapy. One meta-analysis of 3 controlled trials found no reduction in mortality for patients treated with magnesium sulfate compared with placebo or diazepam therapy. Conclusions about the effects of magnesium on duration of intensive care stay, duration of hospital stay, and requirement for ventilatory support could not be drawn, due to large methodological differences between the studies included.[69]

» Sedation helps to reduce autonomic instability, and both benzodiazepines and morphine sulfate are useful in this regard. If patients are already on a benzodiazepine, treatment should be rationalized. Morphine sulfate reduces sympathetic tone in the heart and the vascular system, improving cardiovascular stability without compromising cardiac performance.[1] [70]

» Beta-blockade may be required in further management of the autonomic instability. Use, choice, and dosing of a beta-blocker should be decided in consultation with a specialist. Pure beta-blockade, with propranolol, has been associated with sudden death.[71] Labetalol has been used to provide combined alpha- and

Acute

beta-blockade in a small number of patients.[78] Esmolol is an extremely short-acting beta-blocker and has been reported to be effective in controlling autonomic instability in case reports.[79] [80]

Emerging

OnabotulinumtoxinA

Botulinum toxin acts on lower motor neuron terminals, inhibiting acetylcholine release and muscle activity. It may have a role in reducing muscle rigidity and spasms in tetanus; it has been used in a very small number of patients to treat, for example, trismus, by injection into the masseter and temporalis muscles. Its use in tetanus has not yet been evaluated in a clinical trial.[81]

Intrathecal tetanus antitoxin

A randomized controlled trial in Vietnam on intrathecal tetanus antitoxin in the treatment of adults with tetanus concluded that intrathecal antitoxin administration was safe but did not provide overall benefit in addition to intramuscular administration of antitoxin. The study also found no advantage of intramuscular human antitoxin over intramuscular equine antitoxin.[82]

Primary prevention

Active immunization with tetanus vaccine protects against tetanus.[26] In most cases, 5 intramuscular doses at appropriate intervals give lifelong immunity. The vaccine is a purified toxin extracted from a strain of *Clostridium tetani* , which is treated with formaldehyde to produce tetanus toxoid.[4]

US schedule for tetanus immunization[27] [28] [29]

- Primary immunization in infants and children at ages 0 to 6 years: 5-dose series of DTaP (D=diphtheria, T=tetanus, aP=acellular pertussis) given at 2, 4, 6, and 15 to 18 months of age, and 4 to 6 years of age.
    - Dose 4 may be administered as early as ages 12 months if ≥5 months since dose 3
    - If 4th dose inadvertently administered ages 12 to 14 months it may be counted if ≥4 months since dose 3
    - Dose 5 is not necessary if dose 4 was administered at age ≥4 years, and ≥6 months after dose 3.
- First booster in adolescents ages 11 to 12 years: 1 dose of Tdap (T=tetanus, d=low-dose diphtheria, ap=acellular pertussis).
- Second booster, all patients: 1 dose of Td (T=tetanus, d=low-dose diphtheria) or Tdap should be given every 10 years.
- Patients who did not previously receive Tdap at or after age 11 years should receive one dose of Tdap, then Td or Tdap every 10 years. Adults who have not previously received the primary vaccination series should be given one dose of Tdap, followed by one dose of Td or Tdap at least 4 weeks later, and then another dose of Td or Tdap 6 to 12 months after the second dose. Td or Tdap booster doses are then given every 10 years.
- A hexavalent vaccine is also approved by the US Food and Drug Administration to prevent diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* b, and hepatitis B. The DTaP-IPV-Hib-HepB vaccine is licensed for use in children ages 6 weeks to 4 years and is indicated for the primary vaccination series in infants at ages 2, 4, and 6 months.[30]
- Pregnant women should be vaccinated with Tdap during each pregnancy, ideally between 27 and 36 weeks' gestation.
- Tdap may be administered regardless of the time interval since the most recent tetanus-containing or diphtheria-toxoid-containing vaccine.

Other schedules for tetanus immunization

- International immunization recommendations and schedules may vary, and local guidelines should be consulted.
- The second booster dose is given every 10 years in most countries. Exceptions include France and Sweden, which recommend boosters every 20 years for immune competent adults, and the Czech Republic, which recommends boosters every 10 to 15 years.[31]
- Experts have suggested limiting boosters in adults to ages 30 and 60, and then every 10 years after age 65. This suggestion aims to address concerns of over-immunization for tetanus, as antibody concentrations remain high after the primary immunization series in childhood.[32]

Travelers

- Travelers at greatest risk for exposure and infection include humanitarian aid workers, pregnant travelers, and travelers not current with tetanus toxoid-containing vaccine. It is particularly important that those traveling to remote areas check they are up to date with tetanus vaccination before departure as tetanus immune globulin (TIG) and proper wound management may not be available, should a tetanus-prone injury occur.[33]

People who inject drugs

- People who inject drugs should be fully immunized. Drug practices that are less tetanus prone can be encouraged, such as avoiding intramuscular and subcutaneous injection and using as little citric acid as possible, which devitalizes tissue.[23]

Pregnant women

- Immunization of pregnant women, or women of childbearing age, with at least 2 doses of tetanus toxoid is estimated to decrease mortality from neonatal tetanus by 94%.[34] The American College of Obstetricians and Gynecologists has made the following recommendations regarding immunization during pregnancy.[35]
    - The tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap [T=tetanus, d=low-dose diphtheria, ap=acellular pertussis]) vaccine should be administered during each pregnancy, as early in the 27 to 36 weeks' gestation window as possible.
        - In extenuating circumstances, it may be appropriate for a pregnant woman to receive the Tdap vaccine outside of this window, for example in cases of wound management or a pertussis outbreak.
    - If the Tdap vaccine is not administered during pregnancy, it should be given immediately postpartum if the woman has never received a prior dose of Tdap as an adolescent, adult, or during a previous pregnancy.
    - If the Tdap vaccine is administered early in the woman's pregnancy (i.e., before 27 to 36 weeks of gestation), the woman does not need to be vaccinated again during 27 to 36 weeks of gestation.

Neonatal tetanus

- In resource-poor settings, the World Health Organization advocates six clean methods to improve birth hygiene: clean birth surface, clean hands, clean perineum, cord cutting, cord tying, and cord care.[16] [36]
- Available evidence supports the implementation of immunization practices for women of childbearing age or pregnant women in communities with high levels of risk of neonatal tetanus.[37]

Management of tetanus-prone wounds

- All wounds should be thoroughly debrided.[4] [38] [39]
- Management of tetanus-prone wounds to prevent clinical tetanus depends on risk assessment of the wound and the immunization history of the patient.
- In the US, patients with clean, minor wounds who have only had up to 2 doses of a tetanus toxoid-containing vaccine or an uncertain vaccination history should be given tetanus toxoid-containing vaccine, while patients who have received ≥3 doses do not require tetanus toxoid-containing vaccine

unless they have not received a dose in the last 10 years. Clean, minor wounds do not require TIG.[3] [38] For all other wounds, patients who have only had up to 2 doses of tetanus toxoid-containing vaccine or have an uncertain vaccination history should be given tetanus toxoid-containing vaccine and TIG; patients who have received ≥3 doses do not require TIG and do not require tetanus toxoid-containing vaccine unless they have not received a dose in the last 5 years.[3] [38]

Vaccination history	Clean and minor wounds		All other wounds	
	DTaP, Tdap, or Td*	TIG	DTaP, Tdap, or Td*	TIG**
Unknown or <3 doses	Yes	No	Yes	Yes
≥3 doses	No (Yes if >10 years since the last tetanus toxoid-containing vaccine dose)	No	No (Yes, if ≥5 years since the last tetanus toxoid-containing vaccine dose)	No

*US recommendations for tetanus wound management. DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin. *DTaP is recommended for children aged <7 years. Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series. **Immunosuppressed patients should be managed as if they were incompletely immunized (i.e., those with contaminated wounds should also receive TIG, regardless of their history of tetanus immunization)*

Liang JL 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;67:1-44.

- Immunosuppressed patients may not be adequately protected and additional boosting and/or TIG may be required; in the US, immunosuppressed patients should be managed as if they were incompletely immunized.[3] [4] [38]
- If a tetanus booster is indicated for wound management during pregnancy, Tdap should be administered instead of Td if the woman has not received Tdap previously.[35]

Secondary prevention

Natural disease does not confer immunity; therefore, full tetanus immunization must be undertaken.

Patient discussions

Patients should be advised to ensure they follow the prescribed immunization recommendations and schedule including booster doses. See Primary prevention .

People traveling, especially to remote areas, should be advised check they are up to date with tetanus vaccination before departure.[33]

FOLLOW UP

Complications

Complications	Timeframe	Likelihood
fractures	**short term**	**high**
Muscle spasms can cause fractures of the vertebrae and other bones, as well as rhabdomyolysis (acute renal failure) and myositis ossificans circumscripta.[1]		
rhabdomyolysis (leading to acute renal failure)	**short term**	**high**
Muscle spasms can cause rhabdomyolysis, which in turn can result in acute renal failure.[1]		
myositis ossificans circumscripta	**short term**	**high**
Muscle spasms can cause intramuscular heterotopic calcification (myositis ossificans circumscripta).[1]		
aspiration	**short term**	**high**
There is a high risk of aspiration resulting from poor cough due to muscle rigidity and sedation, pharyngeal spasms, dysphagia, gastric stasis, and increased intra-abdominal pressure during spasms. In severe tetanus, spasms may increase rapidly in frequency and duration; establishing a secure airway early is paramount before laryngeal obstruction and/or aspiration occurs.		
nosocomial infection	**short term**	**medium**
Critical illness and assisted ventilation can lead to nosocomial infection. Hospital-acquired pneumonia (HAP) is a known complication of severe tetanus. A randomized controlled trial of 229 adults and children with severe tetanus in Vietnam found no difference in the incidence of HAP between those nursed in the semi-recumbent and supine positions, although this finding may not be generalizable to patients managed in an intensive care unit of a developed country.[90]		
decubitus ulcers	**short term**	**medium**
Prolonged immobilization can lead to decubitus ulcers.		
tracheal stenosis	**short term**	**medium**
Assisted ventilation can lead to tracheal stenosis.		
gastrointestinal hemorrhage	**short term**	**medium**
Critical illness can lead to gastrointestinal hemorrhage.		
deep vein thrombosis	**short term**	**medium**
Critical illness and prolonged immobilization can lead to venous thromboembolism.		
neurologic sequelae	**long term**	**low**
Most adult survivors experience no neurologic sequelae, although convalescence may be prolonged with residual muscle rigidity for several months.[1] In one retrospective study of 102 patients with tetanus		

Complications	Timeframe	Likelihood
managed at a tertiary center in Tanzania, 8.6% of survivors were discharged with permanent disability (persistent vegetative state due to hypoxic brain damage, limb amputations, and abnormal gait).[91] Some small studies have suggested that neurologic sequelae following neonatal tetanus may be more common. The frequency of such complications may vary according to the medical facilities available.[2] Some evidence has demonstrated appreciable handicaps (cerebral palsy, mental deficit, behavioral disturbances) in survivors of neonatal tetanus, which have been attributed to anoxic brain damage resulting from prolonged spasms and apnea.[92] The frequent finding of enuresis, intellectual disability, and impairment of growth among Turkish children who had survived neonatal tetanus was described in a study.[93] In survivors of neonatal tetanus in Kenya, an increased frequency of microcephaly, mild neurologic abnormalities, developmental impairment (particularly fine motor difficulties), and behavioral problems was found, compared with other children in the community matched for age, sex, and locality.[94]		
pulmonary embolism	**variable**	**low**
Critical illness and prolonged immobilization can lead to venous thromboembolism.		

Prognosis

The case fatality rate is 12% to 53%.[83] In settings with facilities for mechanical ventilation, the most common causes of death are autonomic dysfunction and hospital-acquired pneumonia. Where facilities do not allow for mechanical ventilation, the most common cause of death is asphyxia, resulting from laryngeal spasm, respiratory muscle spasm, or extreme fatigue.[12]

Prompt diagnosis and prediction of severity are vital in order to determine timely management, including transfer to an intensive care unit and early airway protection. This preempts the life-threatening complications of severe disease.

Predictors of severe disease and therefore worse outcome are as follows:

- Incubation period (time from injury to first symptom) is inversely related to disease severity. An incubation period of less than 7 days is said to predict grade 3b disease.[47]
- Onset period (time from first symptom to first spasm) is also inversely related to disease severity.
- Site of infection: umbilical, uterine, head, and neck predict more severe disease.
- Intramuscular quinine injections are reported to carry a mortality of 96%.[24] Heroin is often "cut" or diluted with quinine, and this may contribute to the high mortality described in drug addicts with tetanus.[54]
- Comorbidity.
- Extremes of age.[2]
- Autonomic dysfunction.
- Lack of immunity. Previous immunization, even if incomplete, is associated with milder disease.[2]

Various groups have devised scoring systems to determine prognosis in tetanus. The Phillips score provides a severity index based on the incubation period, site of infection, state of immunity, and complicating factors.[84] The Dakar score assesses incubation period, onset period, site of injury, and presence of spasms, fever, and tachycardia on admission.[85] In a study of 500 consecutive patients (non-neonates) admitted to the Tetanus Unit at the Hospital for Tropical Diseases (HTD) in Ho Chi Minh City, Vietnam, between May 1997 and February 1999, a Dakar score of 3 or greater was associated with a 59% mortality compared with 14% mortality for patients with a Dakar score less than 3. Those with a Phillips score of 17 or greater had a mortality of 34% compared with 11% in the group with a Phillips score less than 17.

FOLLOW UP

A tetanus severity score has been devised using prospectively acquired data from consecutive patients admitted to the HTD with multivariate logistic regression.[83] The authors compared their new score with the Phillips and Dakar scores, which were published in the 1960s/1970s without validation data. Their tetanus severity score had a sensitivity of 77% and a specificity of 82% for a fatal outcome when tested with resubstituted data and showed significantly better discrimination between survivors and nonsurvivors than the Dakar or Phillips scores.

In neonatal tetanus - age less than 10 days - an incubation period of 6 days or less, the presence of risus sardonicus, opisthotonus, fever, and weight less than 2.5 kg, indicate a poor prognosis and high risk of death.[86] [87] [88]

Age (years)	Score
≤70	0
71-80	5
>80	10
Time from first symptom to admission (days)	**Score**
≤2	0
3-5	-5
>5	-6
Difficulty breathing on admission	**Score**
No	0
Yes	4
Co-existing medical conditions	**Score**
Fit and well	0
Minor illness / injury	3
Moderately severe illness	5
Severe illness not immediately life-threatening	5
Immediately life-threatening illness	9
Entry site	**Score**
Internal (includes postoperative, postpartum and open fractures) or injection (intramuscular, intravenous or subcutaneous)	7
Other	0
Highest systolic BP recorded during first day in hospital (mmHg)	**Score**
≤130	0
131-140	2
>140	4
Highest systolic heart rate recorded during first day in hospital (bpm)	**Score**
≤100	0
101-110	1
111-120	2
>120	4
Lowest heart rate recorded during first day in hospital (bpm)	**Score**
≤110	0
>110	-2
Highest temperature recorded during first day in hospital (°C)	**Score**
≤38.5	0
38.6-39	4
39.1-40	6
>40	8

Tetanus severity score. The final score is calculated from the sum of the scores for each section. A total of ≥8 indicates predicted death; <8 indicates predicted survival
From Thwaites CL, Yen LM, Glover C, et al. Predicting the clinical outcome of tetanus: the tetanus severity score. Trop Med Int Health. 2006;11:279-287

One study of 107 cases of neonatal tetanus in Vietnam confirmed the association of young age and lower weight with a poor outcome, and that a delay in hospital admission and presence of leukocytosis are significant additional factors.[89]

Treatment guidelines

International

Child and adolescent immunization schedule by age: recommendations for ages 18 years or younger, United States, 2025 (https://www.cdc.gov/vaccines/site.html) [27]

Published by: Centers for Disease Control and Prevention **Last published:** 2024

Adult immunization schedule by age: recommendations for ages 19 years or older, United States, 2025 (https://www.cdc.gov/vaccines/site.html) [28]

Published by: Centers for Disease Control and Prevention **Last published:** 2024

CDC Yellow Book 2024: health information for international travel. Section 5: travel-associated infections and diseases - tetanus (https://wwwnc.cdc.gov/travel/page/yellowbook-home) [33]

Published by: Centers for Disease Control and Prevention **Last published:** 2023

Use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines: updated recommendations of the Advisory Committee on Immunization Practices — United States, 2019 (https://www.cdc.gov/acip-recs/hcp/vaccine-specific/dtap-tdap-td.html?CDC_AAref_Val=https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/dtap.html) [29]

Published by: Centers for Disease Control and Prevention **Last published:** 2020

Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) (https://www.cdc.gov/acip-recs/hcp/vaccine-specific/dtap-tdap-td.html?CDC_AAref_Val=https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/dtap.html) [3]

Published by: Centers for Disease Control and Prevention **Last published:** 2018

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Images

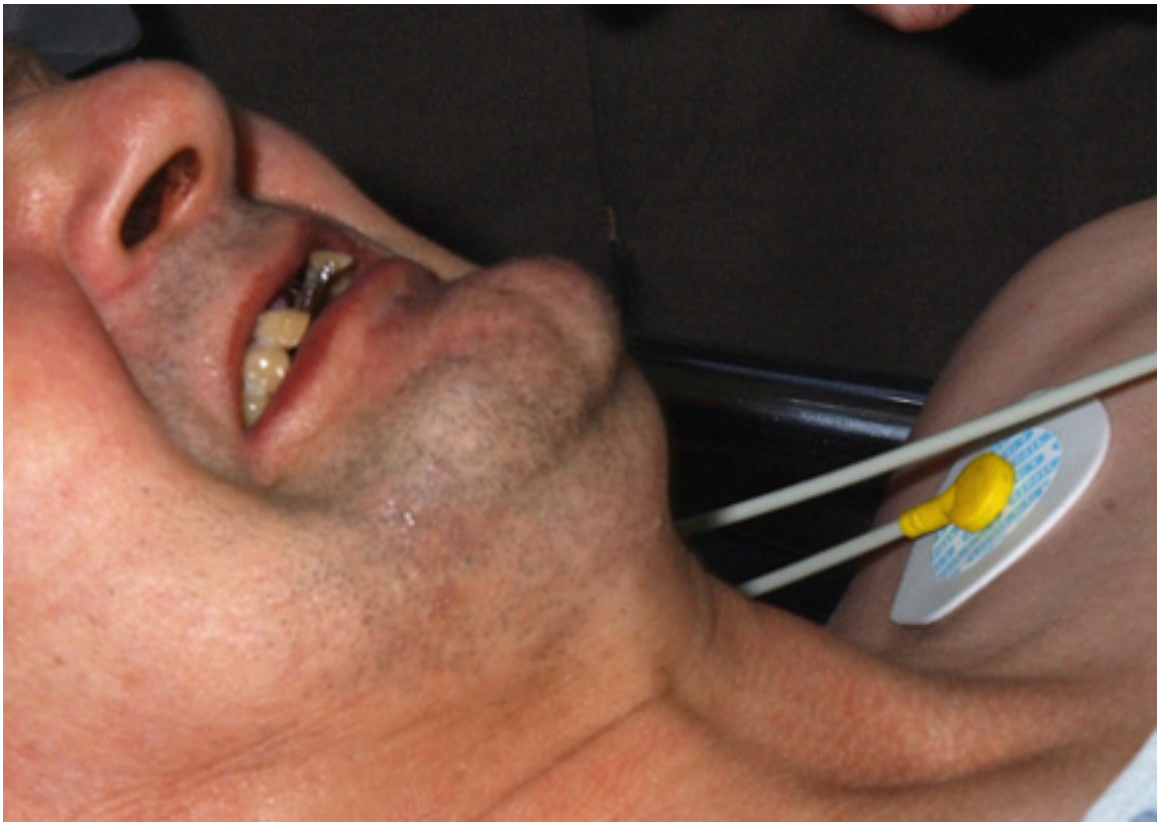

Figure 1: Trismus

From the collections of Nicholas J. Beeching and Christopher M. Parry

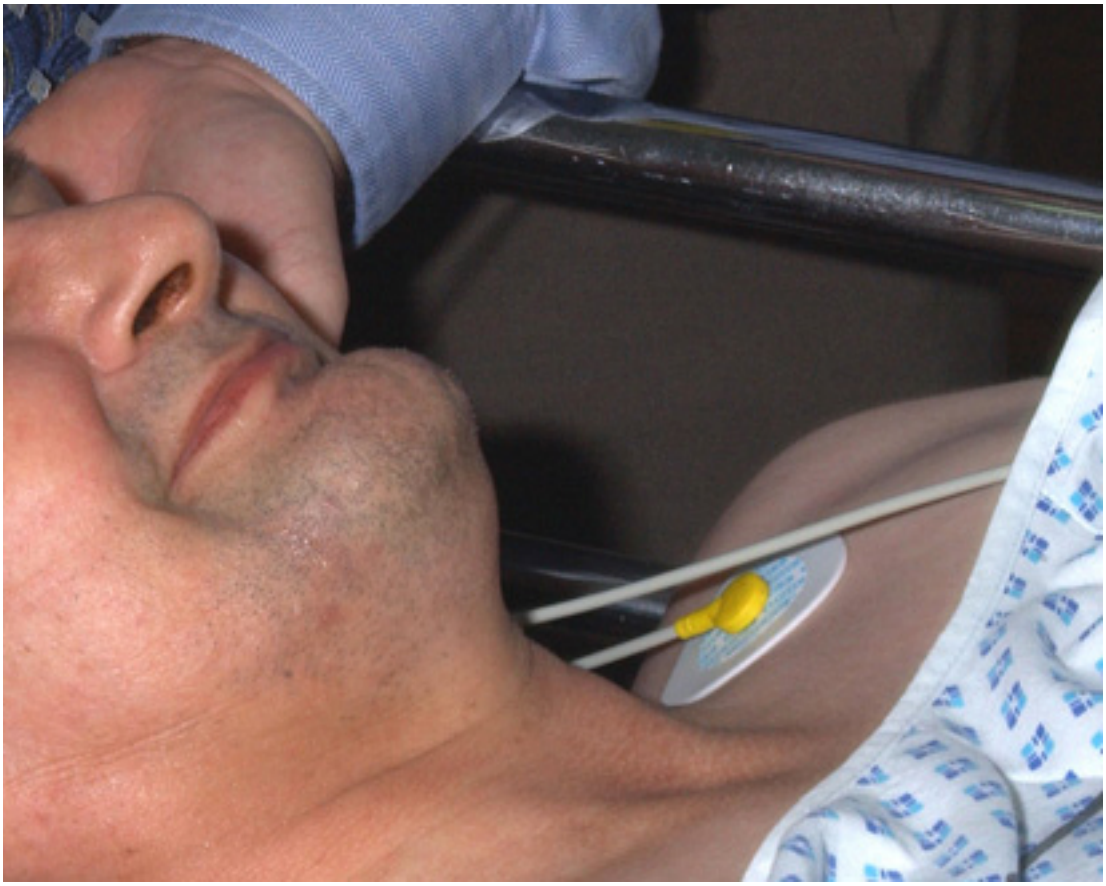

Figure 2: Trismus

From the collections of Nicholas J. Beeching and Christopher M. Parry

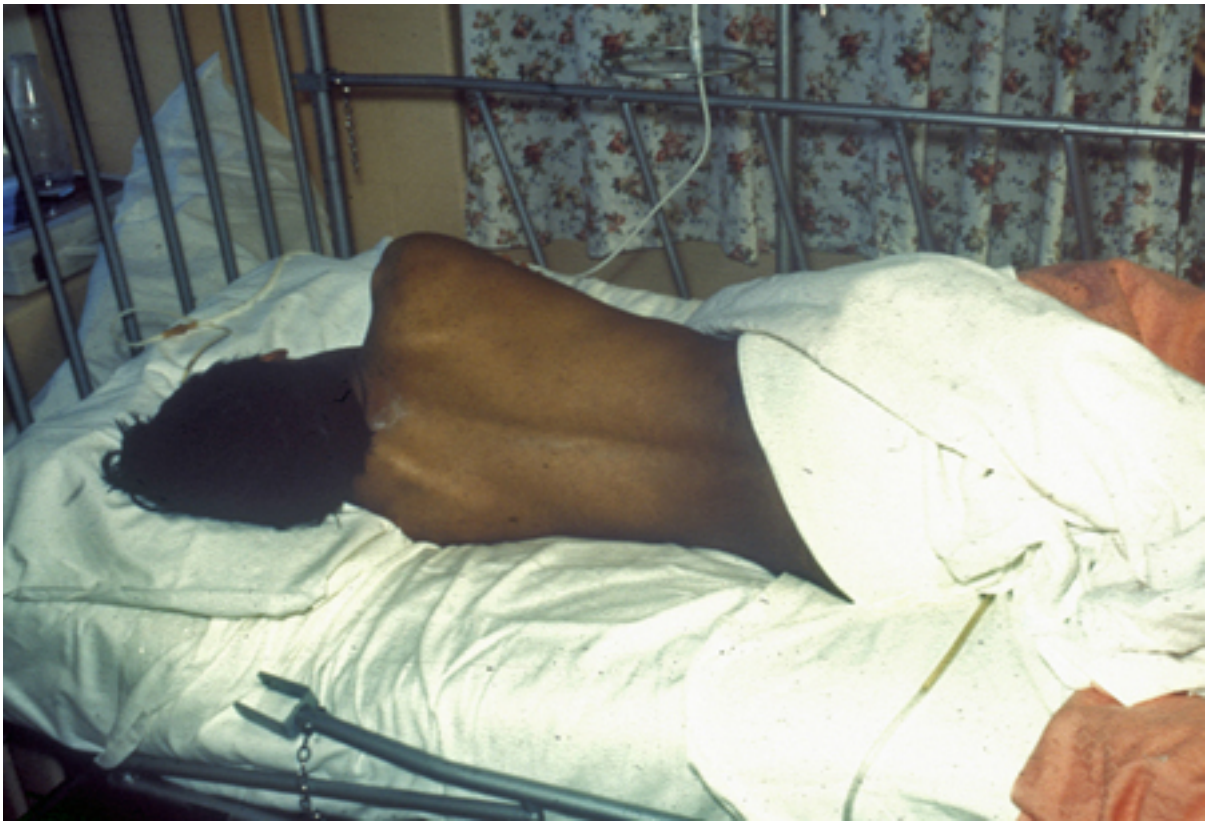

Figure 3: Opisthotonus

From the collections of Nicholas J. Beeching and Christopher M. Parry

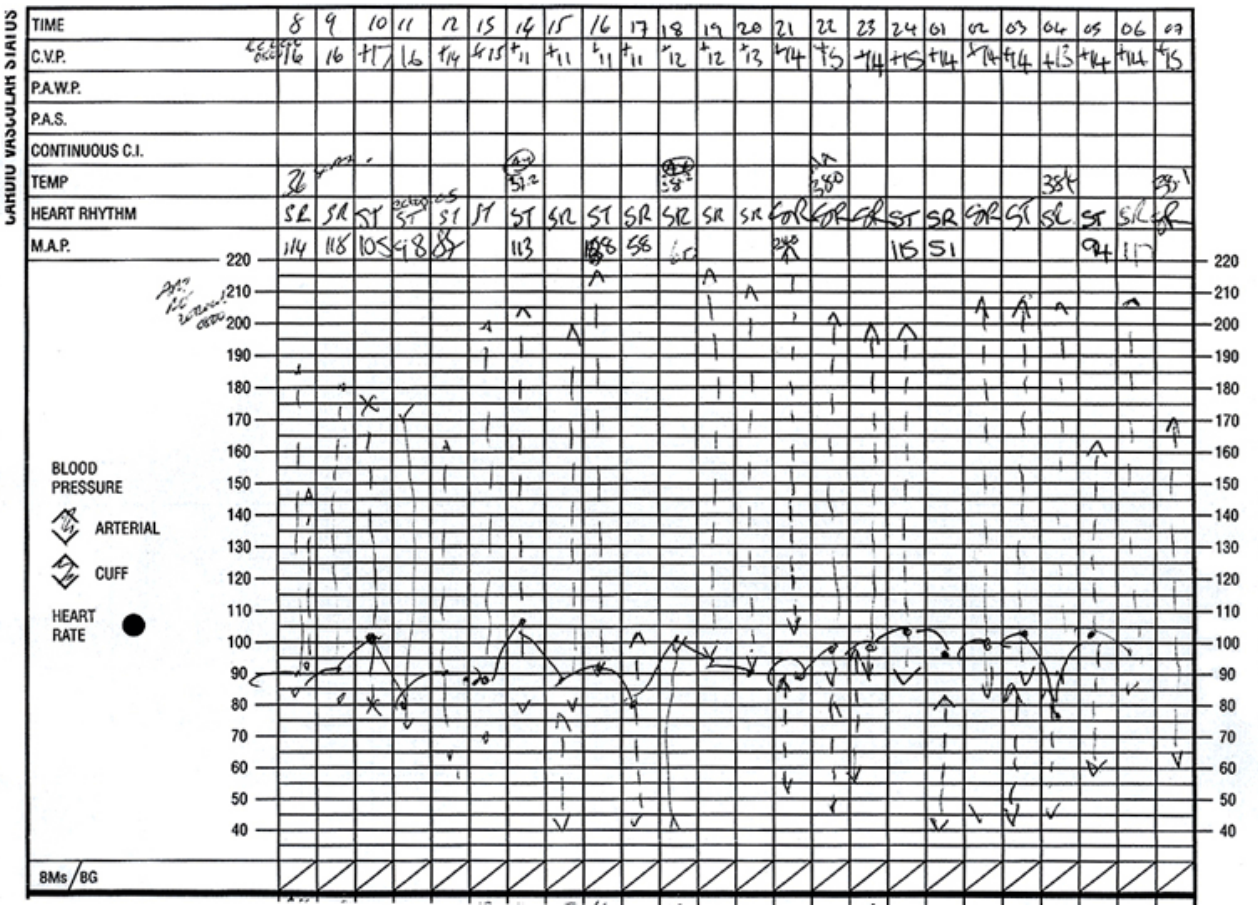

Figure 4: Observation chart illustrating autonomic dysfunction with extreme fluctuation in blood pressure

From the collections of Nicholas J. Beeching and Christopher M. Parry

Vaccination history	Clean and minor wounds		All other wounds	
	DTaP, Tdap, or Td*	TIG	DTaP, Tdap, or Td*	TIG**
Unknown or <3 doses	Yes	No	Yes	Yes
≥3 doses	No (Yes if >10 years since the last tetanus toxoid-containing vaccine dose)	No	No (Yes, if ≥5 years since the last tetanus toxoid-containing vaccine dose)	No

*Figure 5: US recommendations for tetanus wound management. DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin. *DTaP is recommended for children aged <7 years. Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series. **Immunosuppressed patients should be managed as if they were incompletely immunized (i.e., those with contaminated wounds should also receive TIG, regardless of their history of tetanus immunization)*

Liang JL 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;67:1-44.

Age (years)	Score
≤70	0
71-80	5
>80	10
Time from first symptom to admission (days)	**Score**
≤2	0
3-5	-5
>5	-6
Difficulty breathing on admission	**Score**
No	0
Yes	4
Co-existing medical conditions	**Score**
Fit and well	0
Minor illness / injury	3
Moderately severe illness	5
Severe illness not immediately life-threatening	5
Immediately life-threatening illness	9
Entry site	**Score**
Internal (includes postoperative, postpartum and open fractures) or injection (intramuscular, intravenous or subcutaneous)	7
Other	0
Highest systolic BP recorded during first day in hospital (mmHg)	**Score**
≤130	0
131-140	2
>140	4
Highest systolic heart rate recorded during first day in hospital (bpm)	**Score**
≤100	0
101-110	1
111-120	2
>120	4
Lowest heart rate recorded during first day in hospital (bpm)	**Score**
≤110	0
>110	-2
Highest temperature recorded during first day in hospital (°C)	**Score**
≤38.5	0
38.6-39	4
39.1-40	6
>40	8

Figure 6: Tetanus severity score. The final score is calculated from the sum of the scores for each section. A total of ≥8 indicates predicted death; <8 indicates predicted survival

From Thwaites CL, Yen LM, Glover C, et al. Predicting the clinical outcome of tetanus: the tetanus severity score. Trop Med Int Health. 2006;11:279-287

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Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a paediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

Where your version of BMJ Best Practice does not integrate with a local drug formulary, you should consult a local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing before prescribing.

Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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// Acknowledgements:

Dr Russell W. Steele would like to gratefully acknowledge Dr Christopher M. Parry, Dr Nicholas J. Beeching, Dr Lucy E. Cottle, and Professor Enitan D. Carrol, the previous contributors to this topic.

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