

Review Article

The threat of a new tetanus outbreak due to urban flooding disaster requires vigilance: a narrative review

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Vaccines for tetanus prevention have rapidly progressed, and the number of outbreaks, especially the incidence of tetanus in developed countries, has decreased dramatically. However, the mortality rate associated with severe tetanus remains high. Tetanus eradication is difficult owing to the widespread presence of the spores of tetanus bacteria in the environment, but tetanus can be prevented by acquired immunity from vaccines. Older people, intravenous drug users, and migrants are at a high risk of tetanus in developed countries owing to the lack of booster vaccination programs. Natural disasters, especially floods, often cause an increase in the prevalence of tetanus because of the associated injuries. Precautions should be taken to combat the threat of a new tetanus outbreak due to floods in urban areas owing to global warming. In particular, Japan is facing a high risk of urban flooding-induced tetanus, despite its status as a developed country. This review aims to highlight the data on the epidemiology, causes, treatment, and prevention of tetanus and problems associated with tetanus countermeasures during future floods.

Key words: Disaster medicine, flooding, infection control, tetanus, urban flood

INTRODUCTION

TETANUS IS A rare but fatal condition.¹ Increased attention should be paid to the risk of a tetanus outbreak in the community, particularly during natural disasters. Previous studies have reported the occurrence of tetanus outbreaks during natural disasters. However, most of the studies focused on earthquakes and tsunamis.^{2–4} The occurrence of flooding due to typhoons and torrential rains has increased worldwide.⁵ There are concerns about urban flooding causing disease outbreaks.⁶ Tetanus prevention is largely dependent on adequate vaccination, but it might also be influenced by climate change and not necessarily the level of development of a country. In the future, it will be necessary for not only developing countries but also developed countries that are susceptible to climate change to be on guard against urban flooding-induced tetanus. Herein, we wish to report the epidemiology, causes, treatment, and prevention of tetanus and anticipated problems regarding tetanus countermeasures in future floods. For this narrative review, the PubMed (National Center for Biotechnology

Information, National Institutes of Health; Bethesda, Maryland, USA) database was searched for articles published from 2010 to 2022, using the keywords “tetanus”, “disaster”, “flooding disaster”, “prevention and control”, and “urban flood.” In addition, the World Health Organization (WHO) website and government databases such as the Centers for Disease Control and Prevention (CDC) website were searched for articles in English. We selected articles published in the last 10 years but did not exclude commonly referenced and highly regarded older publications.

REVIEW

Epidemiology

VACCINES AGAINST TETANUS have rapidly progressed, and the number of outbreaks has decreased dramatically. However, many cases occur in countries where vaccination has not shown much progress (e.g., the 3350 non-neonatal tetanus cases reported in 2014 in Uganda or the 139 tetanus cases that occurred following the Yogyakarta earthquake in 2010). Assessing the true burden of tetanus occurrence globally is difficult because most cases are reported in developing countries, where surveillance systems for tetanus are insufficient and vaccine programs are still immature.¹ Approximately 80% of deaths due to tetanus

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have been reported to occur in south Asia and Africa.⁷ According to the WHO data published in 2019, 14,745,000 cases of tetanus were reported worldwide.⁸ Approximately 1,000,000 people contract the disease each year, and more than 200,000 people die from it.⁹ Tetanus is most likely to be fatal in persons aged ≥ 60 years and those who are unvaccinated.¹⁰ Severe tetanus has a high fatality rate.⁹

In developed countries, the occurrence of tetanus is rare, and most cases include those of older people aged ≥ 60 years.^{11,12} An increasing occurrence of tetanus has been reported among patients with diabetes.¹ Intravenous drug users are known to be at a high risk of contracting tetanus and may also contract it *via* contaminated heroin.¹³ The herd immunity, especially that afforded by vaccines against tetanus, tends to decline over time.¹⁴ Migrants who have not received the vaccine despite living in developed countries might become the new high-risk group in such countries.¹⁵ In developing countries, without intensive care and appropriate ventilatory support, deaths from severe tetanus exceed 50% of all severe tetanus. A mortality rate of 10% is considered an acceptable goal in developed countries.¹⁶ The mortality rate of severe tetanus in Japan has been reported to be 6.8%,¹⁷ which is an acceptable rate of mortality for a developed country; however, the number of incidences is higher than that in other developed countries (27 cases per year in the United Kingdom, five cases in France). According to Nakajima *et al.*¹⁷ who reported the incidence using a National Database in Japan, there were 499 tetanus cases between 2010 and 2016; the median age of the patient group was 74 years, probably due to low immunity in older individuals.

Pathogen and pathogenesis, diagnosis, and treatment

Pathogen and pathogenesis

Tetanus is caused by *Clostridium tetani*. *C. tetani* is an anaerobic Gram-positive and spore-forming bacteria. The spores of tetanus bacteria are widespread in the environment; they are found mainly in soil, and the intestines and feces of some farm animals such as horses, cattle, and chickens. Spores are also present in the saliva of infected patients and in contaminated heroin. The spores are extremely resistant to heat and disinfectants. They can survive autoclaving at 249.8°F (121°C) for 10–15 min. The spores are also relatively resistant to phenol and other chemical agents. In the presence of anaerobic conditions, the spores germinate. Tetanus is caused by two exotoxins: tetanospasmin and tetanolysin. Both are secreted under anaerobic conditions found in necrotic or infected tissue. Tetanospasmin is a neurotoxin that causes muscle spasms in

patients with tetanus.¹⁰ Tetanolysin is thought to be capable of damaging otherwise viable tissue surrounding the infected area and optimizing the conditions for bacterial multiplication.¹⁸ Tetanospasmin inhibits the release of γ -aminobutyric acid and glycine in the central nervous system.¹⁶ Once tetanospasmin is activated, the heavy chain of tetanospasmin travels in a retrograde fashion into the central nervous system.^{19–21} Tetanospasmin cleaves to synaptobrevin (a vesicle-associated membrane protein) after reaching the spinal cord and brainstem. It inhibits glycine release and γ -aminobutyric acid, both of which are skeletal muscle inhibitors. Clinical muscle spasm is caused by this mechanism.^{21–25}

The spores usually enter the body through broken skin caused by injuries. Wounds contaminated with dirt, feces, or saliva; puncture wounds (caused by an object such as a nail or needle); burns; crash injuries; and injuries causing tissue necrosis are common sources of tetanus infection. *C. tetani* can also infect a person through breaks in the skin caused by surgical procedures, insect bites, dental infections, intravenous drug use, and intramuscular injections. In most cases, the period of symptom onset (incubation period) is approximately 8 days (range 1–21 days). The shorter the incubation period, the more severe the disease and the higher the mortality. The distance of the wound from the central nervous system is also associated with the duration of the incubation period.¹⁰

Tetanus is clinically classified as generalized, neonatal, local, and cephalic (Table 1).¹⁰ Generalized tetanus is the most common form (>80% of reported cases). The first sign is spasm of the muscles of the jaw, or “lockjaw,” followed by stiffness of the neck, difficulty in swallowing, rigidity of abdominal muscles, and reflex spasms. Reflex spasms can occur with minimal external stimuli and increase in frequency with disease progression. Autonomic disturbances are seen in severe cases with other extra-muscular symptoms including fever, sweating, hypertension, and tachycardia. On the other hand, hypotension, bradycardia, and asystole may arise from increased vagal tone and activity.^{26,27} “Autonomic storm” occurs with marked cardiovascular instability. Severe hypertension and tachycardia may occur alternately with profound hypotension, bradycardia, or recurrent cardiac arrest.^{28,29}

Diagnosis

Tetanus must be diagnosed clinically, but there are very few confirmatory tests available at present. Wound cultures frequently yield negative results for *C. tetani*. *C. tetani* is recovered from the wound in only 30% of cases and can be isolated from patients who do not have tetanus.³⁰ Tetanus is

Table 1. Clinical classifications of tetanus

Classification	Description
Generalized	The most common type (more than 80%). Trismus or lockjaw, followed by stiffness of the neck, difficulty in swallowing, rigidity of abdominal muscles, and dysautonomia such as high temperature, sweating, abnormal blood pressure, and episodic rapid heart rate. Spasm continues for 3–4 weeks. It takes months to recover completely.
Neonatal	Neonatal tetanus is a form of generalized tetanus that occurs in newborn infants without protective immunity because of lack of mother's immunity. It usually occurs through infection of the unhealed umbilical stump
Localized	Contraction of muscles are limited to the sight of injury.
Cephalic	Involvement of the cranial nerves, especially in the facial area. Occasionally occurring with otitis media or following head injury.

Produced table refer to "Pink Book", CDC.

Source: "Pink Book", Centers for Disease Control and Prevention (US).¹⁰

a vaccine-preventable disease; acquired immunoglobulin G antibodies after vaccination afford immunity against tetanus. Measuring antibody concentrations using ELISA (cut-off antibody concentrations for protection: 0.1–0.2 IU/mL)¹ or rapid immunoassay [using the Tetanus Quick Stick (TQS); Nephrotek Laboratory, Rungis, France] may be useful in emergency departments.^{31,32} Tetanus in the presence of protective concentrations of antibody is rare, and therefore a diagnosis of tetanus should be considered unlikely in individuals with serum antibody titers of more than 0.1 IU/mL, as tested by ELISA.¹ However, conventional tetanus antibody assays by ELISA are laboratory based and challenging to implement in clinical settings, such as the emergency room. Thus, the usefulness of the rapid immune assay in clinical settings, such as the emergency room, has been recommended.^{31,32}

The Ablett classification system score (Table 2) is the most widely used system for defining tetanus severity.³³ The Ablett classification has been used in intensive care units (ICUs) outside the United States to identify the severity of tetanus and prevent airway and respiratory complications, which are the most common causes of death. The classification can be used as a guide to identify patients with upper

Table 2. Ablett classification of severity of tetanus

Grade	Severity	Symptoms
I	Mild	Mild trismus; general spasticity; no respiratory distress; no spasms; no dysphasia
II	Moderate	Moderate trismus; rigidity, short spasms, mild dysphasia, moderate respiratory distress, respiratory rate greater than 30 breaths/min.
III	Severe	Severe trismus, generalized rigidity, reflex prolonged spasms; severe dysphasia, apneic spells; increased respiratory greater than 40 breaths/min, heart rate greater than 120 beats/min.
IV	Very severe	Grade III autonomic disturbances. The cardiovascular system; severe hypertension and tachycardia alteration

airway obstruction of Grade II or higher severity, who may benefit from early tracheostomy, or difficult respiratory management.³⁴

Management

There are four basic patient management strategies: aggressive wound care including surgical debridement and antibiotic treatment for the wound, reducing muscle spasms and controlling autonomic instability, neutralizing the circulating toxin with human tetanus immunoglobulin, and general support to prevent complications. Airway and breathing complications are the most concerning complications of tetanus due to laryngospasm.²¹ Aspiration pneumonia is also a common complication of tetanus in the late phase, as evidenced in 50%–70% of autopsied cases.¹⁰ Tracheostomy is preferable to endotracheal intubation, and it reduces the risk of tracheal stenosis after prolonged mechanical ventilation.¹ Heavy sedative and paralytic condition using by much sedative drugs or neuromuscular blockade by muscle relaxants supported by ventilation are used for patients with severe tetanus in routine practice, and many kinds of drugs have been used so far for tetanus management; however, establishing evidence-based management by conducting clinical trials is difficult for ethical reasons. Tetanus is less incident but more severe than other diseases and occurs in different medical settings. Rodrigo *et al.*³⁵ reviewed the drugs used for treating tetanus in terms of action mechanism and recommendations. The key management strategy for tetanus is shown in Table 3.

Table 3. Management of tetanus

Treatment	Purpose	Overview and recommendation
Aggressive wound care (surgical debridement, antibiotic treatment for the wound)	Prevention for toxin production	There are no trials to suggest the benefits of using antibiotics for tetanus treatment. Either penicillin or metronidazole may be used as the antibiotic choice in tetanus (expert opinion).
Agents Benzodiazepines Neuromuscular blockade Magnesium Intrathecal baclofen Dantrolene, ketamine, propofol, botulinum toxin	Reducing muscle spasms, controlling of autonomic instability and to avoid exhaustion	Benzodiazepines is readily available and used as standard of care (Favors use: expert opinion). Magnesium should be considered depending on clinician judgment. Meta-analysis shows no mortality benefit (Evidence A), inadequate evidence in terms of positive impact on intensive care unit or hospital stay. Intrathecal baclofen may be harmful in lack of monitoring setting (Evidence C).
Agents Clonidine, morphine, bupivacaine with sufentanil, labetalol Pacemaker (if bradycardic)		Dantrolene, ketamine, propofol, botulinum toxin may be reasonable on a case by case. Clonidine, morphine, bupivacaine with sufentanil, labetalol may be reasonable on a case by case (Evidence C).
Immunoglobulins (TIG, IVIG)/ tetanus toxoid (Td)	Neutralization of the circulating toxin immediately/Active immunization	
Intubation, ventilation, and nutrition support appropriately	General support to prevent complication	Consider tracheotomy early case by case

Produced this table refer to Rodrigo *et al.*³⁵
IVIG, intravenous immunoglobulin; TIG, tetanus immune globulin.

Prevention

As there is no herd immunity against tetanus, and immunity is not conferred even after being afflicted by the illness, vaccination is essential. The risk of tetanus should be assessed according to wound condition and immune status. All wounds should be cleaned, and the suspicion of tetanus should not be ruled out in patients with wounds contaminated by dirt. Depending on the history of a patient receiving prior doses of tetanus toxoid-containing vaccines (TT), age-appropriate tetanus toxoid-containing vaccination is needed. Tetanus immunoglobulin should be administered to high-risk patients as soon as possible because it cannot neutralize toxins that are already bound to the nerves (Table 4).³⁶

Preparation for tetanus mitigation during flood disasters

Flooding risk

Recently, flooding has been the most common type of disaster reported globally, responsible for almost half of all victims of natural disasters.⁶ The risk of floods is considered to

be increasing worldwide due to torrential rains brought about by climate change, which is a result of global warming caused by the release of greenhouse gases. The risk is also accelerated by socioeconomic factors,⁵ such as population growth, increased development along coasts and riverbanks, land subsidence due to increased number of settlements along coastal areas, and over-extraction of groundwater. According to a report by the World Resources Institute, the number of people affected by floods is expected to double by 2030,³⁷ and people living in urban areas are also at risk of experiencing flood disasters in the future. One reason is that three-quarters of large cities are located on waterfronts, and large populations cluster along water sources. Furthermore, the urban population is expected to reach 5 billion in 2030.⁶

Vaccination

Natural disasters themselves do not cause epidemics of infectious diseases. Tetanus is caused by physical trauma during disasters, and not the natural disaster itself.¹⁰ Vaccination programs for eradicating tetanus have greatly reduced

Table 4. Guide to tetanus prophylaxis in routine wound management

History of TT [†]	Clean or minor wound TT [†] (DT, DTaP, Tdap, or Td)	Clean wound TIG [‡]	All other wounds [§] TT [†] (DT, DTaP, Tdap, or Td)	All other wounds TIG [‡]
Unknown or <3	Yes	No	Yes	Yes
≥3	No [¶]	No	No ^{††}	No

Reproduced table from “Pink Book”, CDC.

Source: “Pink Book”, Centers for Disease Control and Prevention (US).¹⁰

[†]DT, diphtheria and tetanus toxoid–containing vaccine; DTaP, tetanus toxoid combined with diphtheria and acellular pertussis vaccine; Td, tetanus and diphtheria toxoid–containing vaccine (Td contains reduced amounts of diphtheria toxoid compared with DT); Tdap, Tdap contains the same pertussis components, but a reduced quantity of some pertussis antigens and diphtheria toxoid; TT, tetanus toxoid–containing vaccine; D.

[‡]TIG, tetanus immune globulin. People with HIV infection or severe immunodeficiency who have contaminated wounds (including minor wounds) should receive TIG, regardless of the history of tetanus immunizations.

[§]All other wounds are, but not limited to, wounds contaminated by dirt, feces, soil, or saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

[¶]Yes, if ≥10 years since the last tetanus toxoid–containing vaccine dose.

^{††}Yes, if ≥5 years since the last tetanus toxoid–containing vaccine dose.

the incidence of the illness.³⁸ However, outbreaks may still occur if there is an increase in the frequency of floods, lack of medical resources, delay in treatment interventions, and low vaccination rates.

Although there are limited reports on the topic, an increase in tetanus outbreaks after earthquakes has been reported previously. At the time of the Great East Japan Earthquake, 10 cases of tetanus were reported³⁹; at the time of the 2004 Indonesian tsunami, 106 cases were reported in 1 month; and in Haiti in 2010,³⁴ tetanus had spread at a high rate. In particular, there have been many reports of infections in areas where tetanus vaccination coverage is low.³⁴ It is believed that the tetanus bacillus that lives in the soil is brought out by flood water, thus increasing people’s susceptibility to the infection. Immunity acquisition is a problem in countries with low vaccination rates. Prevention is important for tetanus because of its high fatality rate. On a global scale, tetanus vaccination rates are decreasing due to the coronavirus disease 2019 (COVID-19) pandemic.⁴⁰

Urban floods

The construction of asphalt pavements due to unplanned urbanization and pumping of groundwater worsen the water retention capacity of groundwater, resulting in a land environment that is always wet, with water seeping out. This, in turn, exposes the area to the risk of flooding. Increased storm frequency can also push the limits of cities and result in inland flooding. There are also concerns related to unplanned urbanization.^{6,41}

Green infrastructure

Infrastructure development, such as levees, is not the only type of disaster mitigation plan that deserves consideration. Green infrastructure such as mangroves, reefs, and sand dunes also function as natural buffers against coastal storms, and protecting such natural infrastructure will also help prevent flooding and reduce greenhouse gas emissions.⁴² One method of mitigating urban disasters caused by global warming is the sponge city concept.⁶ Vegetation should be increased in cities for disaster mitigation, and because this would require unpaved areas of land, individuals could be residing in closer proximity to soil in cities than before. Urban flooding results in increased rates of infectious diseases⁴³ and proliferation of water-borne pathogens.^{44–46} The differences in the proliferation and degree of activation of each water-borne pathogen in a flood event in a paved environment have been demonstrated in papers.⁴⁷ Further, several studies have reported on the emergence of *Clostridium* spores in soils in Nigeria and Zambia after flooding.^{48,49} Huang *et al.*⁵⁰ used PCR and conducted a surveillance study on changes in *Clostridium* spp. in the soil in Taiwan after flooding. However, the effect of various urban developments on spore content and activation in soil in the context of disaster mitigation during flood events remains unclear.⁴⁴

Risk of tetanus in Japan

Tetanus has a low incidence in developed countries, and it has become a topic of little interest to clinicians.¹² As a result, early diagnosis of the illness has become difficult.

Furthermore, regarding vaccination issues, Japan had no booster vaccination program before 1967; therefore, lack of appropriate immunity acquisition is a major risk factor in Japan.⁵¹

Japan is located at the eastern end of monsoon-prone Asia, which is one of the zones with the heaviest rainfall, with the country experiencing an average annual rainfall of 1,718 mm, approximately two times the world average (880 mm). Furthermore, precipitation in Japan fluctuates widely from season to season, with it being concentrated in the rainy season and typhoon season. For example, the average monthly rainfall in Tokyo is 208.5 mm in September, which is the wettest month, and 39.6 mm in December, which is the driest month, and the difference between them is a factor of five.⁵²

According to the Global Climate Risk Index 2021 published by Germanwatch in Germany, Japan ranks fourth, among 180 countries, in terms of the risk of climate change.⁵³ The Climate Risk Index is an index that analyzes the damage caused by natural disasters that actually occurred in a given fiscal year and captures the scale of future risks; the world's largest disaster database that is provided by Germany is used to assess the damage caused by extreme weather events such as droughts and floods in terms of both the number of deaths and economic impact. The majority of the damage on a global scale was due to the Cyclone Idai, which mainly hit Mozambique, Zimbabwe, and Malawi, and the damage caused by Hurricane Dorian, which hit the Bahamas. Developing countries generally tend to be more vulnerable to environmental changes, but Japan was the only developed country to make it to the top 10. Thinking back, Japan has faced torrential rains recently, such as the 2018 Japan floods, 2019 Typhoon Faxai, and 2020 Kyushu floods. For Japan, the magnitude of the economic loss is the main factor behind the judgment of high risk, and Japan's flood damage is a representative example of the severe impact of climate change on developed countries despite the small number of related deaths. Owing to the low incidence of tetanus and decreased tetanus vigilance in nondisaster periods, high rate of climate change, and lack of a booster vaccination program for those born before 1967, Japan may have the "perfect conditions" for a flooding-induced tetanus outbreak despite its status as a developed country.

Prevention and treatment for tetanus in Japan in times of disaster

For avoiding tetanus outbreak in Japan, we would like to add comments to inform readers about specific measures regarding prevention and treatment.

Raise awareness of vaccination before the disaster (especially for the elderly)

We believe that it is necessary to educate the elderly about tetanus vaccination. The tetanus toxoid vaccine (TT) was introduced in 1952, and routine immunization against the diphtheria, pertussis, and tetanus combined vaccine under the Immunization Law began in 1968; however, the number of cases and deaths in Japan have decreased considerably since 1967. This indicates that the majority of individuals born before 1967 are at risk of not having received tetanus antitoxin. The incidence of tetanus and mortality is reportedly higher among the elderly in Japan.¹⁷ Antibody titers are low in the elderly, which could be due to inadequate vaccination before 1968.⁵¹ Thus, tetanus vaccination should be administered with the expectation of a booster effect.

Prevention of trauma

Tetanus is considered a trauma-related infection. It is important to encourage volunteer staff and citizens in the affected area to wear gloves when cleaning up after a flood or other water-related disaster to prevent traumatic injuries.

Rapid diagnosis

Early diagnosis and therapeutic intervention are essential; as cases are rarely encountered in developed countries, it is important to be able to recall and diagnose tetanus in the event of a disaster. As mentioned earlier, this is a trauma-related infection, but there are cases where the trauma is not identified or the wound site is not clear; thus, it is necessary to consider the risk of tetanus when treating patients.

Disaster preparedness for tetanus treatment

As medical resources would be scarce in some areas during a disaster, TT and tetanus immune globulin (TIG) stockpiling and supply may be required to have treatment in place (Table 4). Considering the effective use of resources during times of disaster, the risk identification shown in Table 4 may be challenging to apply, because vaccination history may be difficult to ascertain during a disaster, and the risk of tetanus with unspecified trauma might be present. Savioli *et al.*⁵⁴ reported that many individuals are not aware of their vaccination history; this is especially the case among the elderly who are reported to be less aware of their vaccination history. Thus, the elderly is a target group for whom TQS could be useful in identifying tetanus morbidity risk according to their study. They also mentioned the usefulness of

TQS considering vaccination risk and cost-effectiveness to avoid unnecessary TT and TIG.

Thus, publishing guidelines in times of disaster that allow consideration of administering TT and TIG doses to more suitable victims after identifying risk identification using rapid antibody kits (TQS) could be useful. In fact, some foreign countries have already incorporated rapid tetanus immune antibody testing kits into their prophylaxis protocols.⁵⁵

As the reason for low tetanus mortality in developed countries is the availability of ICU-based multidisciplinary care, early planning for medical evacuation to areas where ICUs are available may be necessary. Since medical transport after the patient has become severely ill is highly risky, we believe that an appropriate strategy is warranted to enable early medical transport that can provide ICU-based treatment for patients with tetanus at an early stage.

Further reduction in mortality may require improvements in surveillance content that could investigate the relationship between treatment administered to patients with severe tetanus and the outcome for establishing appropriate treatment for patients with severe tetanus.

CONCLUSION

ERADICATION OF TETANUS is considered impossible because of the abundance of tetanus spores in the environment. Even people who live in urban cities are exposed to abundant tetanus spores due to new threats such as urban flooding caused by global warming, a problem that we have not experienced so far. Precautions should be taken against the possibility of a new tetanus outbreak due to flooding in urban areas.

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DISCLOSURE

APPROVAL OF THE Research Protocol with Approval No. and Committee Name: This paper comprises brief literature presented as a narrative review. No formal research ethics approval was required.

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