



Considerations for Tetanus While Treating an Exposure to Rabies

Since rabies and tetanus are not as common in the United States (US) as they used to be,^{1,2} people may not be fully aware of these diseases and their substantial consequences. These people may not know how to respond to potential exposure incidents, which may delay access to care and increase the risk of developing disease.

Q: Can you get tetanus from an animal bite?

A: Yes, people can be exposed to tetanus the same way as with rabies: through a bite or saliva of an infected animal.^{1,3}

It is important to know that the bacterium that causes tetanus in humans, *Clostridium tetani*, and its spores, which produce a potent neurotoxin, occur naturally and are widely distributed in our environment.¹ For example, spores from the tetanus bacterium can be found in soil, dust, saliva of many animals, and animal feces.^{1,3} Humans can be exposed to the spores of this pathogen through wounds or other breaches of the skin, or through mucous membranes.^{1,3,4} Under anaerobic conditions, which may occur with deep puncture wounds, these spores can germinate and produce the potent neurotoxin that causes disease in people.^{1,4}

So, stepping on a rusty nail that has been outdoors for a long time and has tetanus spores adhered to it can introduce those spores into a person's body through a skin wound. Or, a person may be exposed to tetanus by having an existing open skin wound or mucous membranes come into contact with soil containing tetanus spores, or through a puncture wound from thorns on a rose bush or, as with rabies, a bite or saliva from an infected animal.^{1,3}



Q: Aren't rabies and tetanus rare diseases nowadays?

A: Both diseases are relatively rare in large part because of successful vaccination programs.^{1,2} But rabies and tetanus are still extremely important health risks to the individual people who are exposed to these pathogens each year. Healthcare professionals need to remain vigilant for cases of rabies or tetanus exposure that present for medical attention.

Following the large-scale implementation of rabies vaccination programs targeted at dogs in the middle of the 20th century, transmission of canine-variant rabies virus within this species has been eliminated.⁵ However, more than 4400 rabies cases among wild animals, such as bats, raccoons, skunks, and foxes, were reported to the US Centers for Disease Control and Prevention (CDC) in 2016.⁶ Humans who may be exposed to these animals continue to be at risk of rabies, as made clear by the 40 confirmed human rabies cases reported in the US and Puerto Rico from 2003 through October 2017.⁶

Tetanus is not as common as it used to be, before universal vaccination programs began in the US in the mid-1940s. However, 462 tetanus cases were reported in the US from 2001 through 2016. In almost all cases, disease developed in people who were either unvaccinated or inadequately vaccinated, or had unknown or uncertain vaccination histories. The CDC reported that the case-fatality ratio (ie, the percentage of fatalities among people reported to have the disease) was 18% from 1998 to 2000 and 8% from 2001 to 2016.¹

Q: Since potential exposure to sources of either tetanus or rabies may not be considered medical emergencies, won't people be able to wait and see if they develop symptoms before going to a doctor?

A: No. While exposure to sources of tetanus and/or rabies may not be medical emergencies like a heart attack or trauma after a car accident, experts consider them “medical urgencies” and recommend that people seek medical attention as soon as possible after a potential exposure incident.^{7,8} This is especially true for people who are the most susceptible to disease, such as those who have never been vaccinated against these diseases and those who have not stayed up to date with tetanus booster doses following completion of an initial tetanus vaccination series in the past, which may include older adults and people without consistent access to medical care, such as immigrant populations.^{1,2,4,8} Additionally, the severity/depth and location of wounds associated with potential exposures to rabies and/or

tetanus, as well as the extent of wound contamination (for tetanus risk), are key factors in a clinician's evaluation of the exposure incident, risk of disease, and need for clinical intervention.^{1,7} More severe wounds located closer to the central nervous system are associated with higher risks of disease transmission, shorter incubation times, more severe disease, and worse clinical prognosis.^{1,4,7,9} Therefore, the sooner postexposure prophylaxis (PEP) is started, the better the chances will be to prevent disease.

For both rabies and tetanus, PEP begins with thorough wound cleansing with soap and water and, if available, a virucidal agent such as povidine-iodine solution for rabies.^{2,4} Subsequent management will depend on the clinician's evaluation of several factors, including the exposure type and severity, the patient's immune status and vaccination history, and the disease status of the animal involved in a potential rabies exposure, if available.^{1,2,7,10}

Q: Won't it be too late to get shots after being exposed to rabies or tetanus?

A: No, PEP has been developed for exactly this purpose—to prevent the development of symptomatic disease after a person has been exposed to rabies and/or tetanus. The need for rabies and/or tetanus PEP will depend on the type of wound and the patient's prior vaccination status.^{1,2,7} The first step in prevention of either infection following potential exposure is appropriate wound management.^{2,4}

Wound care for suspected rabies exposure includes cleansing with soap and water. If available, a virucidal agent, such as povidine-iodine solution, can also be used to irrigate the wound. Subsequent management, with administration of rabies vaccine with or without human rabies immune globulin (HRIG), depends on the patient's rabies vaccination history. Patients who have not been previously vaccinated against rabies should receive rabies PEP that includes four 1-mL doses of a rabies vaccine, with the first dose given as soon as possible after the exposure incident (the date of the first dose is defined as day 0 of the rabies PEP regimen). The vaccine doses should be administered intramuscularly into the deltoid area in adults and in the anterolateral aspect of the thigh in children. The remaining 3 subsequent vaccine doses should be administered on days 3, 7, and 14. These patients should also receive a dose of HRIG on day 0. The HRIG dose should be injected into and around all wound areas, with any remaining HRIG volume injected intramuscularly at a site away from the rabies vaccine administration

site to avoid interaction with the vaccine. Patients who have previously been vaccinated with the rabies vaccine should not receive HRIG but should receive additional doses of vaccine. Specifically, these patients should receive two 1-mL doses of vaccine, one on day 0 (day of first vaccine dose), and one on day 3.²

Wound care for suspected tetanus exposure is important to minimize to the extent possible the number of *C tetani* spores that may have entered the body through a skin wound. On initial evaluation, the clinician should assess the wound and then clean the area thoroughly, removing dirt, foreign matter, and necrotic tissue. The clinician must then determine whether the wound is “clean and minor” or “dirty.” Dirty wounds include deeper puncture or penetrating wounds, such as animal bites, and wounds contaminated with dirt, feces, soil, or saliva. Puncture or penetrating wounds that are contaminated pose a higher risk of tetanus than wounds that are cleaner and superficial.^{1,4}

The clinician should then evaluate the patient’s vaccination status for tetanus toxoid-containing vaccine. The key question is whether the patient may still have protective levels of antitetanus toxoid antibodies from prior administration of the full 3-dose series of tetanus vaccine plus any booster doses within the past 5 or 10 years.¹

With that information, the clinician can then follow the Advisory Committee on Immunization Practices (ACIP) recommendations for tetanus prophylaxis, which may include vaccine with or without tetanus immune globulin. The ACIP recommendations are the official, approved guidelines of the CDC.¹

Q: If rabies and tetanus shots are given at the same time, why do I need both? Wouldn't just one of them help protect me against both diseases?

A: No, these are separate diseases that require separate interventions against rabies (which is caused by infection with the rabies virus) and against tetanus (which is caused by a neurotoxin produced by the bacterium *C tetani*).^{1,2} The confusion may come about because PEP against rabies (rabies vaccine + rabies immune globulin) and against tetanus (tetanus vaccine + tetanus immune globulin) may need to be given at the same time to certain people.⁷ These people may be at increased risk of developing both rabies and tetanus following incidents that may expose them to both the rabies viruses and the tetanus bacterium (for example, animal bites that puncture the person’s skin and expose the person to the animal’s saliva).^{1,7}

Important Safety Information

HyperTET[®] S/D (tetanus immune globulin [human]) is indicated for prophylaxis against tetanus following injury in patients whose immunization is incomplete or uncertain.

HyperTET S/D should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations.

In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, HyperTET S/D should be given only if the expected benefits outweigh the risks.

Slight soreness at the site of injection and slight temperature elevation may be noted at times. Sensitization to repeated injections of human immunoglobulin is extremely rare. In the course of routine injections of large numbers of persons with immunoglobulin, there have been a few isolated occurrences of angioneurotic edema, nephrotic syndrome, and anaphylactic shock after injection. Administration of live virus vaccines (eg, MMR) should be deferred for approximately 3 months after tetanus immune globulin (human) administration.

HyperTET S/D is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses and theoretically, the Creutzfeldt-Jakob (CJD) agent that can cause disease. There is also the possibility that unknown infectious agents may be present in such products.

Please see accompanying full Prescribing Information for HyperTET S/D.

**You are encouraged to report negative side effects
of prescription drugs to the FDA. Visit www.fda.gov/medwatch,
or call 1-800-FDA-1088.**

Indication and Usage

HYPERRAB[®] (rabies immune globulin [human]) is indicated for postexposure prophylaxis, along with rabies vaccine, for all persons suspected of exposure to rabies.

Limitations of Use

Persons who have been previously immunized with rabies vaccine and have a confirmed adequate rabies antibody titer should receive only vaccine.

For unvaccinated persons, the combination of HYPERRAB and vaccine is recommended for both bite and nonbite exposures regardless of the time interval between exposure and initiation of postexposure prophylaxis.

Beyond 7 days (after the first vaccine dose), HYPERRAB is not indicated since an antibody response to vaccine is presumed to have occurred.

Important Safety Information

For infiltration and intramuscular use only.

Severe hypersensitivity reactions may occur with HYPERRAB. Patients with a history of prior systemic allergic reactions to human immunoglobulin preparations are at a greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available for treatment of acute allergic symptoms, should they occur.

HYPERRAB is made from human blood and may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

The most common adverse reactions in >5% of subjects during clinical trials were injection-site pain, headache, injection-site nodule, abdominal pain, diarrhea, flatulence, nasal congestion, and oropharyngeal pain.

Do not administer repeated doses of HYPERRAB once vaccine treatment has been initiated as this could prevent the full expression of active immunity expected from the rabies vaccine.

Other antibodies in the HYPERRAB preparation may interfere with the response to live vaccines such as measles, mumps, polio, or rubella. Defer immunization with live vaccines for 4 months after HYPERRAB administration.

Please see accompanying full Prescribing Information for HYPERRAB.

**You are encouraged to report negative side effects
of prescription drugs to the FDA. Visit www.fda.gov/medwatch,
or call 1-800-FDA-1088.**

REFERENCES

1. Liang JL, Tiwari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2018;67(2):1-44.
2. Rupprecht CE, Briggs D, Brown CM, et al; Centers for Disease Control and Prevention (CDC). Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2010;59(RR-2):1-9.
3. Iannelli V. 5 myths about tetanus and tetanus shots. <https://vaxopedia.org/2017/04/12/5-myths-about-tetanus-and-tetanus-shots/>. Accessed June 26, 2018.
4. Centers for Disease Control and Prevention. Tetanus: for clinicians. <https://www.cdc.gov/tetanus/clinicians.html>. Updated May 31, 2018. Accessed June 26, 2018.
5. Centers for Disease Control and Prevention. US declared canine-rabies free. 2007. <http://www.cdc.gov/media/pressrel/2007/r070907.htm>. Updated May 20, 2014. Accessed June 19, 2018.
6. Ma X, Monroe BP, Cleaton JM, et al. Rabies surveillance in the United States during 2016. *J Am Vet Med Assoc*. 2018;252(8):945-957.
7. Manning SE, Rupprecht CE, Fishbein D, et al; Advisory Committee on Immunization Practices Centers for Disease Control and Prevention (CDC). Human rabies prevention—United States, 2008: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2008;57(RR-3):1-28.
8. Immunization Action Coalition. Ask the experts: diphtheria, tetanus, pertussis. http://www.immunize.org/askexperts/experts_per.asp. Updated June 18, 2018. Accessed June 26, 2018.
9. Tetanus. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book®: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:793-798.
10. World Health Organization. *WHO Expert Consultation on Rabies: Third Report*. WHO Technical Report Series 1012. Geneva, Switzerland: World Health Organization; 2018.

This article may be downloaded, printed, and distributed freely without copyright restriction. For more information, go to www.rabieswatch.com