

## Two Adverse Reaction Cases of Tetanus Antitoxin Desensitization Injection

Author's Details: <sup>(1)</sup>Ning Tang <sup>(2)</sup>Shuchang Li <sup>(3)</sup>Yingmin Wang

<sup>(1)</sup>Corresponding author, E-mail: [tang0139@flinders.edu.au](mailto:tang0139@flinders.edu.au) and/or [nt920000@yahoo.com](mailto:nt920000@yahoo.com), Department of Public Health, Flinders University, Australia <sup>(2)(3)</sup>Yejin Hospital, Xingtai, Hebei, China

### Abstract

*A forty-year-man with a cut injury in his left hand was prescribed intramuscular tetanus toxoid (TT) desensitization injection after intra dermal sensitivity test at Yejin Hospital, Xingtai. The patient felt itching on upper body, dizziness, nausea, vomit, abdominal pain, diarrhea after one hour. On examination, his blood pressure and pulse were respectively 16/11kPa (Kilopascal) and 90 beats/minute, and systemic rash or hives (urticaria) were observed. He was diagnosed as adverse or allergic reaction of tetanus antitoxin. However, the symptoms of the patient were gradually alleviated and improved, and his condition was stabilized thirty minutes after combined treatment of diphenhydramine (200mg), fluoxetine (10 mg: intramuscular injection), glucose (5%: 1000mg), vitamin C (3.0 g), hydrocortisone (100mg: intravenous infusion). The hives disappeared four hours later.*

*A twenty-two-year-man with an injury in one finger of his right hand was prescribed intramuscular tetanus toxoid (TT) desensitization injection after intra dermal sensitivity test at Yejin Hospital, Xingtai. The patient felt dizziness, nausea, palpitations, breathing with difficulty, itching on upper body, rash or hives (urticaria) several minutes after the booster. On examination, his blood pressure was 16/8kPa (Kilopascal). The patient was diagnosed as adverse or allergic reaction of tetanus antitoxin. Nevertheless, all of the symptoms of the patient were gradually improved and his condition was stabilized thirty minutes after oxygen administration and combined treatment of adrenaline (0.5 mg: subcutaneous injection), diphenhydramine (200mg), fluoxetine (10 mg), glucose (5%: 1000mg), vitamin C (2.0 g), hydrocortisone (200mg: intravenous infusion). His symptoms disappeared and the hives vanished two hours later.*

### Introduction

As with any medications, all of vaccines have the potential to cause side effects or adverse or allergic reactions [Zent 2002, Wood 2008, Fritsche 2010]. The variety of reported vaccine-related adverse events is broad. Most frequently, reactions to vaccines are limited to the injection site and result from a non specific activation of the inflammatory system [Fritsche 2010]. The common side effects include fever, redness, swelling around the injections, and soreness or tenderness around the injection site [Wikipedia 2017]. Tetanus toxoid (TT) is a commonly used vaccine for active immunization against *Clostridium tetani* and prevent tetanus [Fauci 2008, WHO 2017]. Although tetanus toxoid is a safe vaccine, its injection is sometimes followed by an adverse reaction [White 1973, Cunha 2016]. The side effects of tetanus toxoid vary from mild to severe reactions and are related to dose and type of toxoid, number of prior doses of toxoid received and method of injection [Stratton 1994, WHO 2017]. Most of mild adverse reactions of tetanus toxoid are generally associated with redness, mild pain or discomfort, mild swelling or irritation, mild fever and drowsiness around or near the injection site [GC 2016, NHA 2017, MDH 2017]. The side effects usually fade after a few days or weeks [MDH 2017]. Rarely, a tetanus toxoid shot leads to moderate adverse reactions, such as irritation of stomach or vomiting, nausea, fever, extremely tired, itching, muscle aches, diarrhea, sore lymph nodes [NHA 2017]. However, the moderate adverse reactions need being treated [WHO 2017]. Very rarely, an immunization with tetanus toxoid brings severe adverse or allergic reactions, such as swelling of face, lips and limb, difficulty in breathing or swallowing, cardiovascular symptoms (i.e. faintness, syncope, palpitations and hypotension), anaphylaxis (i.e. urticaria, angioneurotic edema), shock and Lyell syndrome, coma, seizures or brain damage, neurologic complications (i.e. cochlear lesions, brachial plexus neuropathies, paralysis of radial nerve, paralysis of recurrent nerve, accommodation paresis, Guillain-Barré syndrome (GBS), EEG disturbances with encephalopathy, and relapsing neuropathy) [Frank 1974, NCIRD 2011, TFSI 2012, MC 2017, NAS 2017, NHA 2017]. In extremely rare cases, patients may suffer from blood in the urine or stool and pneumonia after tetanus

shot [MDH 2017]. Very seriously, tetanus vaccination could lead to death [Staak 1973]. Yet, immediate severe or systemic allergic reactions after the vaccination are very rare [Zent 2002, NHA 2017]. Overall, adverse or allergic reactions are less common in adults than adolescents and children [GC 2016].

## Case Report

A forty-year-old man presented with a cut injury in his left hand. After clinical examination, surgical debridement and suturation, and intra dermal sensitivity test, he was prescribed intramuscular tetanus toxoid (TT) desensitization injection at Yejin Hospital, Xingtai. The patient did not show any adverse reaction ten minutes after the shot and left the hospital. However, the patient felt itching on upper body, dizziness, nausea, vomit, abdominal pain, diarrhea thirty minutes after arriving home. Then, he returned to the hospital. On examination, his blood pressure and pulse were respectively 16/11kPa (Kilopascal) and 90 beats per minute, and systemic rash or hives (urticaria) were observed. The patient was diagnosed as adverse or allergic reaction of tetanus antitoxin, because he neither took any food and medicine nor was exposed to any allergic substances during the period. Immediately, the patient was treated with 200 mg and 10 mg intramuscular injection of diphenhydramine and fluoxetine, 1000mg, 100mg and 3.0 g intravenous infusion of glucose (5%), hydrocortisone and vitamin C. His symptoms were gradually alleviated and improved, and his condition was stabilized thirty minutes after the combined treatment. The hives disappeared four hours later.

A twenty-two-year-old man presented with an injury in one finger of his right hand. After clinical examination, surgical suturation and intra dermal sensitivity test, he was prescribed intramuscular tetanus toxoid (TT) desensitization injection at Yejin Hospital, Xingtai. Nevertheless, the patient felt dizziness, nausea, palpitations, breathing with difficulty, itching on upper body, rash or hives (urticaria) several minutes after the booster. On examination, his blood pressure was 16/8kPa (Kilopascal). The patient was diagnosed as adverse or allergic reaction of tetanus antitoxin, because he neither took any medicine nor was exposed to any new chemicals for the first time on that day. Immediately, the patient was treated with 0.5 mg subcutaneous injection of adrenaline, 200 mg and 10 mg intramuscular injection of diphenhydramine and fluoxetine, 1000mg, 200mg and 2.0 g intravenous infusion of glucose (5%), hydrocortisone and vitamin C. All of his symptoms were gradually improved, and his condition was stabilized thirty minutes after the combined treatment. The symptoms disappeared and the hives vanished two hours later.

## Discussion

The symptoms of the two patients in the case report showed that they had mild to severe adverse or allergic reactions after tetanus toxoid shot [CDC 2017, WHO 2017]. However, the two side effect cases were rare in tetanus vaccination [WHO 2017]. It has been known that the most important goals of post-exposure prophylaxis after minor wounds are removing the source of toxin production and neutralizing any toxin which may have been released. The first goal is best achieved by timely, thorough wound cleaning. The second goal is achieved by providing or inducing high circulating concentrations of tetanus antibody - tetanus toxoid booster [GC 2016]. Nevertheless, the immune complex formation between antibodies and antigen after the tetanus vaccination could cause local or systemic adverse reactions. In rare cases, it is possible that the immune complexes may form in the circulation, deposit in tissues, and activate complement. Moreover, this would result in the clinical syndrome of serum sickness.

Generally, the adverse reactions to TT vaccine are mostly mild and limited to the injection site [Mayorga 2003]. The most common adverse reactions include local edema and tenderness, fever and anaphylactoid response [Jacobs 1982]. Therefore, most of adverse reactions of the two patients in the case report were mild. However, they occurred systemic rash or hives (urticaria) after tetanus toxoid (TT) booster, which was severe adverse or allergic reactions [NHA 2017, CDC 2017]. Many of case reports reveal that the patients after tetanus toxoid vaccination experienced a severe anaphylactic reaction [Staak 1973, Bellioni 2001, Das 2012, TFSI 2012], because TT may induce allergic reactions, the potential causative agents can be TT antigens, aluminum

phosphate or thimerosal preservative [Mayorga 2003]. Some of cases show that some patients developed immediate or delayed urticaria after Tetanus toxoid vaccine [Bellioni 2001, Mayorga 2003], other patients occurred oedema or angioedema or erythema [Bellioni 2001], a few patients presented both urticaria and angioedema or erythema [Bellioni 2001]. Two patients in the case report only came out urticaria, did not occurred angioedema, which showed that they could have different hypersensitivity responses to tetanus toxoid as compared with other patients. Some of researchers indicate that there was a “probable” relationship between administration of TT and occurrence of anaphylaxis [Gaublomme 2010, Das 2012], because allergic reactions after tetanus vaccination could occur due to hypersensitivity to any of the components of the vaccine [Gaublomme 2010], and tetanus toxoid booster might cause delayed hypersensitivity responses with leukocyte migration inhibition [Johnson 1983]. Fortunately, the two patients in the case report did not appear neurologic complications. Nevertheless, some of clinical observations reveal that some patients, who occurred severe adverse reactions after tetanus toxoid immunization, developed neurologic symptoms, such as demyelinating neuropathy [Pollard 1978], polyradiculoneuritis and myelitis [Fenichel 1983], acute midbrain syndrome [Schwarz 1988]. It has been known that the adverse reactions of tetanus toxoid vaccination may be caused by immune complex formation between antibodies and antigen, but it is likely that other factors such as toxoid variables, adjuvants, dose, and host factors may also play a role in the development of adverse reactions [Stratton 1994, NAS 2017].

Obviously, the patients who occurred adverse or allergic reactions after tetanus toxoid vaccination should be punctually treated and their symptom should be controlled and alleviated effectively [CDC 2017, WHO 2017]. Firstly, the local mild adverse reactions, such as soreness, redness, itching, or swelling at the injection site, can be treated with cool compresses for the first hours after symptoms appear or with acetaminophen or nonsteroidal antiinflammatory drugs (NSAIDs) if pain or swelling is troublesome [NCIRD 2011, IAC 2014]. Usually, the first and most important acute management or therapy in anaphylaxis is intramuscular epinephrine, especially for respiratory or cardiovascular symptoms, or other signs or symptoms of anaphylaxis. Meanwhile, other related therapies, including H1 antihistamine, H2 antihistamine, glucocorticoid, corticosteroid, glucagon, vasopressor and etc, were also frequently used in clinical practice [Bellioni 2001, IAC 2014, CDC 2017]. Moreover, the counter medications like acetaminophen, ibuprofen, Benadryl or aspirin can lessen pain, itching fever and inflammation [NHA 2017]. If hypotension is present, the patient should be placed in a recumbent position with the legs elevated. Furthermore, maintenance of airway, oxygen administration, and intravenous normal saline might be necessary [DEI 2010, CDC 2017]. Therefore, the combined treatment of adrenaline, diphenhydramine, fluoxetine, glucose, vitamin C, hydrocortisone for the two patients in the case report was appropriate and effective.

## Conclusion

Tetanus toxoid vaccination has the potential to cause an adverse reaction. In order to minimize adverse reactions, patients should be carefully screened for precautions and contraindications before and after the vaccine is administered [IAC 2014]. While severe allergic reactions are rare, the development of a painful, swollen area and other mild adverse reactions after immunization is usually able to occur. However, it should not deter people from accepting the vaccine [White 1973]. Because anaphylaxis may occur after the vaccination, post-immunization monitoring in a medical facility for a period (tens of minutes to several hours) should be advised, even after the complete resolution of symptoms and signs. Particularly, health care providers should bear in mind the possibility of occurrence of hypersensitivity reaction for the vaccine, make emergency programs or strategies for occurrence of the allergic reactions of the vaccination, and provide punctual and effective treatment for the patients who occur adverse reactions [CDC 2017, WHO 2017]. Moreover, physicians, nurses and health practitioners should ascertain whether the allergic reaction was caused by the vaccine itself or other factors [Chung 2014]. Furthermore, health care providers and health professionals should provide consultation and advice of adverse reactions for the people who are given the vaccine [CDC 2017].

## Competing interests

All of the authors declare that they have no conflict of interests.

## Acknowledgement

The authors appreciate support of doctors and nurses in Yejin Hospital, Xingtai, Hebei, China.

## Reference

Bellioni BB, Paganelli R, Bruno G, Grossi O, Di Rienzo A, Businco L. Allergy to tetanus toxoid vaccine. *Allergy*, 2001, 6(7): 701-2. Access: <https://www.deepdyve.com/lp/wiley/allergy-to-tetanus-toxoid-vaccine-Z0B2f2QKW0> .

Centres for Disease Control and Prevention (CDC). Diphtheria, Tetanus (tetanus toxoid), and Pertussis: Recommendations for vaccine use and other preventive measures. *MMWR* 40: No. RR-10, 1991. Access: <https://www.cdc.gov/mmwr/preview/mmwrhtml/00041645.htm> .

Centres for Disease Control and Prevention (CDC). Vaccine Recommendation and Guidelines of the ACIP: Preventing and Managing Adverse Reactions. 2017. Access: <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/adverse-reactions.html> .

Chung EH. Vaccine allergies. *Clin Exp Vaccine Res.* 2014, 3(1): 50–57. Access: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3890451/> .

Cunha JP. Tetanus Side Effects Center. RxList, 2016. Access: <http://www.rxlist.com/tetanus-side-effects-drug-center.htm> and <http://www.rxlist.com/tetanus-drug.htm> .

Das S and Monda S. Tetanus Toxoid Induced Anaphylaxis. *J Vaccines Vaccin*, 2012, 3 (1): 1-2. Access: <https://www.omicsonline.org/tetanus-toxoid-induced-anaphylaxis-2157-7560.1000126.pdf> .  
<https://www.omicsonline.org/tetanus-toxoid-induced-anaphylaxis-2157-7560.1000126.php?aid=4768> .

Division of Epidemiology and Immunization (DEI). Emergency Treatment for Vaccine Reactions. Massachusetts Department of Public Health, USA. 2010. Access: <http://www.mass.gov/eohhs/docs/dph/cdc/immunization/mso-emergency-treatment.pdf> .

Fauci AS, Braunwald E, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. *Harrison's Principles of Internal Medicine*, Vol: 17<sup>th</sup> ed. New York: McGraw-Hill, 2008. Access: <https://www.amazon.com/Harrisons-Principles-Internal-Medicine-Single/dp/0071466339> .

Fenichel GM. Neurologic Complications of Tetanus Toxoid. *Arch Neurol*, 1983, 40 (6): 390. Access: <http://jamanetwork.com/journals/jamaneurology/article-abstract/581927> .

Fritsche PJ, Helbling A, Ballmer-Weber BK. Vaccine hypersensitivity: update and overview. *Swiss Med Wkly.* 2010, 140: 238–246. Access: <https://www.ncbi.nlm.nih.gov/pubmed/20349363> .

Gaublomme K. Tetanus Toxoid Vaccination: An Overview. *International Medical Council on Vaccination.* 2010. Access: <http://www.vaccinationcouncil.org/2010/08/19/tetanus-toxoid-vaccination-an-overview/> .

Government of Canada (GC). *Canadian Immunization Guide: Part 4 - Active Vaccines: Tetanus Toxoid.* 2016. Access: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-22-tetanus-toxoid.html> .

Immunization Action Coalition (IAC). *Medical Management of Vaccine Reactions in Adult Patients.* [www.immunize.org](http://www.immunize.org) and [www.vaccineinformation.org](http://www.vaccineinformation.org) . 2014. Access: <http://www.immunize.org/catg.d/p3082.pdf> .

Jacobs RL, Lowe RS, Lanier BQ. Adverse reactions to tetanus toxoid. JAMA, 1982, 247 (1): 40-42. Access: <https://www.ncbi.nlm.nih.gov/pubmed/7053439> .

Johnson C, Walls RS, Ruwoldt A. Delayed hypersensitivity to tetanus toxoid in man: in vivo and in vitro studies. Pathology, 1983, 15 (4): 369-372. Access: <https://www.ncbi.nlm.nih.gov/pubmed/6674868> .

Johansson SG, Bieber T, Dahl R, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol, 2004, 113: 832. Access: <https://www.ncbi.nlm.nih.gov/pubmed?term=15131563> .

Kelso JM, Adkinson NF, Feldweg AM. Allergic reactions to vaccines. UpToDate. 2017. Access: <https://www.uptodate.com/contents/allergic-reactions-to-vaccines> .

Mansfield LE, Ting S, Rawls DO, Frederick R. Systemic reactions during cutaneous testing for tetanus toxoid hypersensitivity. Ann Allergy, 1986, 57(2): 135-137. Access: <https://www.ncbi.nlm.nih.gov/pubmed/3740557> .

Mayorga C, Torres MJ, Corzo JL, Alvarez J, Garcia JA, Rodriguez CA, Blanca M, Jurado A. Immediate allergy to tetanus toxoid vaccine: determination of immunoglobulin E and immunoglobulin G antibodies to allergenic proteins. Ann Allergy Asthma Immunol, 2003, 90 (2): 238-43. Access: [http://ssu.ac.ir/cms/fileadmin/user\\_upload/Moavenatha/MBehdashti/Pishgiri\\_Bimariha/0000tal2/35.pdf](http://ssu.ac.ir/cms/fileadmin/user_upload/Moavenatha/MBehdashti/Pishgiri_Bimariha/0000tal2/35.pdf) ; <https://www.ncbi.nlm.nih.gov/pubmed/12602673> .

Mayo Clinic (MC). Drug and Supplements: Tetanus Toxoid (Intramuscular Route, Injection Route): Side Effects. 2017. Access: <http://www.mayoclinic.org/drugs-supplements/tetanus-toxoid-intramuscular-route-injection-route/side-effects/drg-20066243> .

Mayorga C, Torres MJ, Corzo JL, Alvarez J, García JA, et al. Immediate allergy to tetanus toxoid vaccine: determination of immunoglobulin E and immunoglobulin G antibodies to allergenic proteins. Ann Allergy Asthma Immunol, 2003, 90 (2): 238-243. Access: <https://www.ncbi.nlm.nih.gov/pubmed/12602673> .

National Academy of Sciences (NAS). Diphtheria and Tetanus Toxoids. 2017. Access: <https://www.nap.edu/read/2138/chapter/6#70> .

National Center for Immunization and Respiratory Diseases (NCIRD). MMWR Recomm Rep, 2011, 60 (2): 1. Access: <https://www.ncbi.nlm.nih.gov/pubmed?term=21293327> .

New Health Advisor (NHA). Tetanus Shot Reactions. 2017. Access: <http://www.newhealthadvisor.com/tetanus-shot-reactions.html> .

Pollard JD, Selby G. Relapsing neuropathy due to tetanus toxoid (tetanus (tetanus toxoid) toxoid): report of a case. J Neurol Sci, 1978, 37:113-125. Access: <https://www.ncbi.nlm.nih.gov/pubmed/308529> .

Rutledge SL, et al. Neurologic complications of immunizations. J Pediatr 109: 917-924, 1986. Access: <https://www.ncbi.nlm.nih.gov/labs/articles/3537247/> .

Schlenska GK. Unusual neurological complications following tetanus toxoid (tetanus (tetanus toxoid) toxoid) administration. J Neurol, 1977, 215: 299-302. Access: <https://link.springer.com/article/10.1007/BF00312502> .

Schwarz G, Lanzer G, List WF. Acute midbrain syndrome as an adverse reaction to tetanus immunization. Intensive Care Medicine, 1988, 15 (1): 53-54. Access: <https://link.springer.com/article/10.1007/BF00255639> .

Stratton KR, Howe CJ and Johnston RB. Adverse events associated with childhood vaccines. Evidence Bearing on Causality. Vaccine Safety Committee, Institute of Medicine. National Academy Press, Washington, DC, 1994. Access: <https://www.ncbi.nlm.nih.gov/books/NBK236291/> .

Staa M, Wirth E. Zur Problematik anaphylaktischer Reaktionen nach aktiver Tetanus-immunisierung. Dtsch Med Wschr, 1973, 98: 110-111.

Thermo Fisher Scientific Inc (TFSI). Tetanus toxoid: Allergen Exposure. 2012. Access: <http://www.phadia.com/da/Products/Allergy-testing-products/ImmunoCAP-Allergen-Information/Drugs1/Allergens/Tetanus-toxoid/> .

White WG, Barnes GM, Barker E, Gall D, Knight P, Griffith AH, Morris-Owen RM and Smith JW. Reactions to tetanus toxoid. J Hyg Camb, 1973, 71: 283 – 297. Access: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2130491/pdf/jhyg00080-0070.pdf> .

Wikipedia. Tetanus vaccine. 2017. Access: [https://en.wikipedia.org/wiki/Tetanus\\_vaccine](https://en.wikipedia.org/wiki/Tetanus_vaccine) .

Wood RA, Berger M, Dreskin SC, et al. An algorithm for treatment of patients with hypersensitivity reactions after vaccines. Pediatrics, 2008, 122: e771–e777. Access: <https://www.ncbi.nlm.nih.gov/pubmed/18762513> .

World Health Organization (WHO). Tetanus vaccines: WHO position paper – February 2017. Weekly epidemiological record, 2017, 92 (6): 53/76. Access: <http://apps.who.int/iris/bitstream/10665/254582/1/WER9206.pdf?ua=1> .

Zent O, Arras-Reiter C, Broeker M, Hennig R. Immediate allergic reactions after vaccinations: a post-marketing surveillance review. Eur J Pediatr, 2002, 161: 21–25. Access: <https://www.ncbi.nlm.nih.gov/pubmed/11808876> .