A Rarely Adverse Reaction Case of Combined Diphtheria, Tetanus, Pertussis (DTP) Vaccination

Author's Details: ⁽¹⁾ Ning Tang ⁽²⁾ Bing Zhang Rui

⁽¹⁾ Corresponding author: Department of Public Health, Flinders University, Australia ⁽²⁾ Co-author: Center for Disease Control and Prevention, Yunyang, Chongqing, China

Abstract

A rarely adverse reaction case of combined diphtheria, tetanus, pertussis (DTP) vaccination was reported. The injection site in the arm of a two-year-boy presented swelling and redness, and itching four hours after having given the second dose of DTP vaccine. Meanwhile, he showed drowsiness, non-stop crying and fretfulness, and felt severe pain and soreness or tenderness in the arm. Then, his arm displayed local edema and scattered rash. The boy had a low-grade temperature fever, and came out mucous blisters in the arm, allergic rash or hives (urticatria) and angioneurotic edema one day later. However, his symptoms and conditions alleviated and improved gradually after the combined treatment of anti-infection, anti-allergy and local wet compress of a week. The recovered child fully one week later. Key Words: DTP Vaccination, Adverse Reaction, Symptom, Allergy, Treatment, Recovery.

Introduction

Vaccines are intended to produce active immunity to specific antigens in children and adults. Modern vaccines are safe and effective, but an adverse event or an undesirable side effect could occur after a vaccination [CDC 1996, Kroger 2011]. Adverse events of combined diphtheria, tetanus, pertussis (DTP) (adsorbed) vaccine could occur after injection, but they are uncommon [WHO 2014]. The adverse reactions of DTP vaccination at the injection site may be mild, moderate and severe [GC 2016, Melanie 2016, WHO 2017]. Redness, swelling and pain are the most common adverse reactions or side-effect to childhood DTP vaccination [CDC 2016, GC 2016, Melanie 2016]. Other mild problems include low fever (at least 100.4°F or 38°C), irritability, fussiness, tiredness, nausea, chills, headache, body aches, sore joints, stomach ache, poor appetite, diarrhea, vomiting, itching (pruritus), swollen glands [Liese 2001, CDC 2015, GC 2016, Melanie 2016]. Moderate reactions following DTP vaccine are pain, redness, fever (over 102°F or 38.9°C), headache, nausea, vomiting, diarrhea, stomach ache, abscess, swelling of the entire arm, rash [Rennels 2000, CDC 2015, GC 2016]. However, the moderate problems are rare [CDC 2015]. Severe adverse events of DTP vaccine show redness, significant swelling, severe pain, bleeding, high fever (over 104.9°F or 40.5°C), non-stopping or persistent crying, seizure or convulsion, hypotonic-hyporesponsive episode (HHE), encephalopathy, Dravet's syndrome, anaphylaxis or severe allergic reactions (i.e. hives or urticaria, angioneurotic edema [Blumberg 1993, PHAC 2005, Rüggeberg] 2007, GNBC 2011, WHO 2014, CDC 2015]. Nevertheless, the serious problems are very rare [Kroger 2011, WHO 2014, Staff 2015].

Case Report

A two-year-boy was given the second dose of DTP vaccine of 0.5 ml at a local town hospital in Yunyang county according to the regular vaccination plan. The injection site in the arm of the boy presented swelling and redness, and raised mucous blisters four hours after the vaccination. Meanwhile, he showed drowsiness, non-stop crying and fretfulness, and felt severe pain and soreness or tenderness in the arm. Then, his arm displayed local edema (5 x 6cm in injection site) and scattered rash. He had a low-grade temperature fever of 38.3°C one day later, and came out systemic rash and mucous blisters in injection arm, which were diagnosed as allergic rash or hives (urticatria) and angioneurotic edema. The symptoms and conditions of the boy alleviated and improved gradually after the combined treatment of chlorpheniramine, intravenous penicillin, dexamethasone, vitamins C and magnesium sulfate wet compress of a week. The child recovered fully one week later.

Discussion

The symptoms of the boy showed that he had mild, moderate and severe adverse reactions after DTP vaccination of the second dose, which included local, systemic or allergic reactions. Therefore, it was a very rare case in vaccination [Kroger 2011, GNBC 2011, WHO 2014]. In particular, occurring time of adverse reaction of DTP vaccination in the case was different with that in other reported cases. Many of case reports reveal the adverse reactions occur more often after the 4th and 5th doses of the DTaP series than after earlier doses, and usually occur 1-3 or 4 days after the shot, lasting 1-7 days [Rowe 2005, Staff 2015, CDC 2015, CDC 2016, Melanie 2016]. However, some of mild, moderate and severe adverse reaction symptoms of the boy were similar to those of many of reported cases, such as there are similar swelling in injection site [GNBC 2011, CDC 2015, WHO 2014, CDC 2016, Melanie 2016]. For example, the case reports expose that local swelling or edema in injection site was 2.5 to 5 or over 5 cm diameter [Bell 1999, Liese 2001, Rowe 2005, Rennels 2008].

Anaphylaxis is a severe, acute and potentially life-threatening medical condition caused by the systemic release of mediators from mast cells and basophils [Liberman 2008, Cheng 2011]. In infants, symptoms of anaphylaxis may include fussiness, irritability, drowsiness or lethargy, and etc [GC 2016]. The reported case reveals that DTP vaccination could arouse allergic reaction or anaphylaxis of the boy. However, allergic reactions or anaphylaxis is a rare complication of immunization [GC 2016], in particular, severe or serious allergic reactions from a vaccination are very rare [Staff 2015, CDC 2015], which was estimated at fewer than 1 in a million doses, and would happen within a few minutes to a few hours after the vaccination [CDC 2015, CDC 2016]. Nevertheless, a study displays that DTP vaccination appeared to increase the risk of allergies in children and adolescents [Hurwitz 2000]. Meanwhile, neurological complications of immunisation could occur after DTP vaccination, but are rare too. A case report reveals that neuroallergic reaction occurred 5 days after receiving the second course of DTP vaccine [Wierzba 2000].

Usually, adrenaline (epinephrine), antihistamines and corticosteroids are used in treatment for anaphylaxis or allergy [ASCIA 2016, Cheng 2011]. Epinephrine is the undisputed initial therapy for anaphylaxis [Liberman 2008, Laemmle-Ruff 2013], additional interventions such as oxygen therapy, fluid resuscitation, beta-agonists, antihistamines, and corticosteroids should be strongly considered [Liberman 2008]. H(1)- and H(2)-antihistamines (i.e. chlorphenamine, diphenhydramine, ranitidine) are effective for treatment of acute urticaria or rhinoconjunctivitis [WGRC 2008, Norred 2012, Ring 2014], and commonly used as an adjuvant therapy or second line treatment choice in the treatment plan of anaphylaxis [Lin 2000, Sheikh 2007, WGRC 2008]. Moreover, Corticosteroids (i.e. glucocorticosteroids, dexamethasone, hydrocortisone) play a minor role in the acute phase of anaphylaxis treatment [Wierzba 2000, Choo 2010, Simon 2012, Laemmle-Ruff 2013].

It has been known that DTP vaccination led to urticarial rash and angioneurotic edema of the boy in the reported case. Clinical observations show that urticarial rash (i.e., hives or urticaria), an allergic reaction or anaphylaxis at the injection site, is a transient erythematous swelling of the skin, associated with itching, which usually resolves within 24 hours, and can occur after a vaccine shot [Kaplan 2014, GC 2016]. Meanwhile, clinical analysis reveals that angioneurotic edema or angioedema is a non-pitting edema which is characterized by swellings caused by edema in the deeper dermal, cutaneous and sub-mucosal tissue (i.e. mucous membranes of the face and upper aerodigestive tract) [Zanoletti 2003, Shafer 2012, Kaplan 2014]. Both of urticaria and angioedema are important components of systemic anaphylaxis which is an acute life threatening condition [Prasad 2001, Chaitra 2012]. Some of clinical reports show that urticaria and angioedema could occur lonely, but half of all patients with urticaria or more have angioedema [Finn 1999, Kaplan 2014, UMMC 2016]. Frquently, urticaria is associated angioedema in children [Kaplan 2002, Tuncer 2004, Leech 2011]. Antihistamines (i.e. chlorphenamine, loratadine or desloratadine, levocetirizine, cetirizine) could be used to treat or control urticaria and angioedema [Ring 2001, Agostoni 2001, Staevska 2010, Powell 2016], because they are the mainstay of treatment for children with urticaria [Leech 2011, Powell 2015]. Meanwhile, corticosteroid (i.e. prednisone) could be added to standard treatment with H1antihistamines for the management of acute urticaria and angioedema in outpatients [Pollack 1995, Powell 2015]. Nevertheless, some of studies reveal that epinephrine, steroids and antihistamine have not been proven to be efficacious for treatment of some

angioedema, in particular, inhibitor-induced angioedema [Gaboriau 1997, Peltekis 2009, Vasekar 2012]. On the contrary, they are effective for immunologic or allergic angioedema [Kaplan 2008, Wllkerson 2012].

On the other hand, medical practices reveal that some of herbs can be helpful for treatment and prevention of urticaria and angioedema, such as goldenseal (hydrastis canadensis) may be used to prevent or reduce allergic reactions, Licorice root (Glycyrrhiza glabra) has been used traditionally to reduce inflammation in the allergic reaction, and Chamomile (Matricaria recutita) has been employed customarily to treat hives [UMMC 2016]. Furthermore, some of studies show that magnesium sulfate wet compress could be used effectively to treat swelling or edema, and reduce inflammation and pain [George 2015, D'souza 2016, Chi 2016]. Additionally, ice may reduce swelling [PHAC 2005].

Therefore, the combined treatment of chlorphenamine, dexamethasone and magnesium sulfate wet compress for urticaria and angioneurotic edema of the boy was a suitable therapy in the reported case.

Conclusion

Adverse reaction of DTP vaccination of the child was a very rare event. Though the combined treatment was effective and successful, it is necessary to improve appropriately treatment for adverse reactions of the vaccination and to reduce side effect of vaccine for protecting children's health. Meanwhile, vaccines and vaccination should be administered systematically and strictly; adverse events after DTP childhood immunisation should be carefully monitored and punctually reported; and practicable treatment plans should be made, and treatment medicines should be used appropriately and effectively [WHO 2014, GC 2016]. Furthermore, allergic reaction cases of vaccination should be analyzed and evaluated completely [Franceschini 2015].

Competing interests

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

Acknowledgement

The authors appreciate support of doctors, nurses and health professionals at the town hospital in Yunyang county and Yunyang Center for Disease Control and Prevention, Chongqing, China.

Reference

Agostoni A, Cicardi M. Drug-Induced Angioedema without Urticaria Incidence, Prevention and Management. Drug Safety, 2001, 24 (8): 599-606. Access: <u>http://link.springer.com/article/10.2165/00002018-200124080-00004</u>.

Australasian Society of Clinical Immunology and Allergy (ASCIA). HC Guidelines - Acute management of anaphylaxis. 2016. Access: <u>http://www.allergy.org.au/health-professionals/papers/acute-management-of-anaphylaxis-guidelines</u>.

Bell F, Heath P, MacLennan J, Shackley F, Shearstone N, Diggle L, Thornton C, Griffiths H, Moxon ER, Finn A. Adverse effects and sero-responses to an acellular pertussis/diphtheria/tetanus vaccine when combined with Haemophilus influenzae type b vaccine in an accelerated schedule. European Journal of Pediatrics, 1999, 158 (4): 329-336. Access: <u>http://link.springer.com/article/10.1007/s004310051083</u>.

Blumberg DA, Lewis K, Mink CM, Christenson PD, Chatfield P, Cherry JD. Severe reactions associated with diphtheria-tetanus-pertussis vaccine: detailed study of children with seizures, hypotonic-hyporesponsive episodes, high fevers, and persistent crying. Pediatrics, 1993, 91: 6 (1158-1165). Access: https://www.ncbi.nlm.nih.gov/pubmed/8502521/.

Center for Disease Control and Prevention (CDC). Update: vaccine side effects, adverse reactions, contraindications, and precautions: recommendations of the Advisory Committee on Immunization Practices

(ACIP).MMWR,1996,45(No.RR-12).Access:https://www.cdc.gov/mmwr/preview/mmwrhtml/00046738.htm .

Center for Disease Control and Prevention (CDC). Vaccine Information Statement: Tdap (Tetanus, Diphtheria, Pertussis) VIS. 2015. Access: <u>http://www.cdc.gov/vaccines/hcp/vis/vis-statements/tdap.html</u> . .

Center for Disease Control and Prevention (CDC). Vaccines & Immunizations: Possible Side-effects from Vaccines. 2016. Access: <u>http://www.cdc.gov/vaccines/vac-gen/side-effects.htm</u>.

Chaitra TR, Ravishankar TL, Nalawade TM. Angioneurotic edema: report of two cases.

Braz J Oral Sci, 2012, 11: 4, on-line version ISSN 1677-3225. Access: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1677-32252012000400013.

Cheng A. Emergency treatment of anaphylaxis in infants and children. Paediatr Child Health, 2011, 16(1): 35–40. Access: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3043023/#b6-12957_chen</u>.

Chi Y, Wang D, Li HY. Herapeutic effect of wet compress of magnesium sulfate combined with vitamin B12 on chemotherapy-induced phlebitis in rabbits. Int J Clin Exp Med, 2016,9 (6): 12356-12360. Access: <u>http://www.ijcem.com/files/ijcem0021571.pdf</u>.

Choo KJ, Simons E, Sheikh A. Glucocorticoids for the treatment of anaphylaxis: Cochrane systematic review. Allergy, 2010, 65: 1205–1211. Access: <u>http://onlinelibrary.wiley.com/doi/10.1111/j.1398-9995.2010.02424.x/full</u>.

D'souza BL and Shivakumar. Effectiveness Magnesium Sulphate Crystal Fomentation Vs Paste Application for Phlebitis among Children Receiving Peripheral Infusion who are Admitted at Selected Hospital at Mangalore. Nitte University Journal of Health Science, 2016, 6 (1): 9-12. Access: http://www.nitte.edu.in/journal/march2016/o6.pdf .

Gaboriau HP, Solomon JW. Angioneurotic edema. J La State Med Soc, 1997, 149: 2 (50-52). Access: <u>https://www.ncbi.nlm.nih.gov/pubmed/9055526</u>.

Finn AF, Kaplan AP, Fretwell R, Qu R, Long J. A double-blind, placebo-controlled trial of fexofenadine HCl in the treatment of chronic idiopathic urticarial. Journal of Allergy and Clinical Immunology, 1999, 104 (5): 1071-1078. Access: <u>http://www.sciencedirect.com/science/article/pii/S0091674999700916</u>.

Franceschini F, Bottau P, Caimmi S, Crisafulli G, Lucia L, Peroni D, Saretta F, Vernich M, Dascola CP and Caffareli C. Vaccination in children with allergy to non active vaccine components. Clin Transl Med, 2015, 4: 3. doi: 10.1186/s40169-014-0043-0. Access: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4384976/</u>.

George SC, Tata SH. Effectiveness of Magnesium Sulphate Crystal Fomentation versus Glycerine Magnesium Sulphate Paste Application for Phlebitis among Children Receiving Peripheral Infusion in Krishna Hospital, Karad. International Journal of Science and Research, 2016, 5 (4): 515-518. Access: https://www.ijsr.net/archive/v5i4/NOV162619.pdf.

Government of Canada (GC). Canadian Immunization Guide: Part 4 - Active Vaccines. 2016. Access: <u>http://healthycanadians.gc.ca/publications/healthy-living-vie-saine/4-canadian-immunization-guide-canadien-immunisation/index-eng.php?page=15</u>.

Government of New Brunswick, Canada (GNBC). Adverse Events Following Immunization: Interpretation and Clinical Definitions Guide. 2011. Version 1.0. Access: <u>http://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/HealthProfessionals/AEFIsinterpretationandclinicaldefinitionsguide.pdf</u>.

Hurwitz EL, Morgenstern H. Effects of diphtheria-tetanus-pertussis or tetanus vaccination on allergies and allergy-related respiratory symptoms among children and adolescents in the United States. Journal of Manipulative and Physiological Therapeutics, 2000, 23: 2 (81-90). Access: http://www.sciencedirect.com/science/article/pii/S0161475400900721.

Kaplan AP. Clinical practice. Chronic urticaria and angioedema. N Engl J Med, 2002, 346 (3): 175-179. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed/11796852?dopt=Abstract</u>.

Kaplan AP. Angioedema. World Allergy Organization Journal, 2008, 1:103. Access: <u>https://waojournal.biomedcentral.com/articles/10.1097/WOX.0b013e31817aecbe</u>.

Kaplan AP. Urticaria and Angioedema: Synopsis. World Allergy Organization. 2014. <u>http://www.worldallergy.org/professional/allergic_diseases_center/urticaria/urticariasynopsis.php</u>.

Kroger AT, Sumaya CV, Pickering LK, Atkinson WL. General Recommendations on Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP). Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. MMWR, 2011, Vol. 60, No. 2. Access: <u>http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf</u>.

Laemmle-Ruff I, O'Hehir R, Ackland M, Tang MLK. Anaphylaxis: Identification, management and prevention.AustralianFamilyPhysician,2013,42(1):38-42.Access:http://www.racgp.org.au/afp/2013/januaryfebruary/anaphylaxis/.....

Leech S, Grattan C, Lloyd K, Deacock S, Williams L. The RCPCH care pathway for children with Urticaria, Angio-oedema or Mastocytosis: an evidence and consensus based national approach. Arch Dis Child, 2011, 96: i34-i37. Access: <u>http://adc.bmj.com/content/96/Suppl_2/i34</u>.

Liese JG, Stojanov S, Zink TH, Froeschle J, Klepadlo R, Kronwitter A, Harzer E, Jow S, Belohradsky BH. Safety and immunogenicity of Biken acellular pertussis vaccine in combination with diphtheria and tetanus toxoid as a fifth dose at four to six years of age. Munich Vaccine Study Group. Pediatr Infect Dis J, 2001, 20(10): 981-988. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed?term=11642633</u>.

Liberman DB, Teach SJ. Management of anaphylaxis in children. Pediatr Emerg Care, 2008, 24: 861–869. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed/19092569</u>.

Lin RY, Curry A, Pesola GR, et al. Improved outcomes in patients with acute allergic syndromes who are treated with combined H1 and H2 antagonists. Ann Emerg Med, 2000, 36: 462–468. Access: https://www.ncbi.nlm.nih.gov/pubmed/11054200.

Melanie W. Everything You Need to Know About Vaccines: Diphtheria, Tetanus, Pertussis and the DTaP Vaccine. Carrington College. 2016. Access: <u>http://carrington.edu/blog/medical/vaccines/diphtheria-tetanus-pertussis-and-the-dtap-vaccine/</u>.

Norred CL. Anesthetic-Induced Anaphylaxis. AANA Journal, 2012, 80 (2): 129-140. Access: <u>https://www.aana.com/newsandjournal/Documents/jcourse1-0412-p129-140.pdf</u>.

Peltekis G, Palaskas D, Samanidou M, Fragakis A, Alexopoulos K, Kotsani A, Vogiatzis I and Kyrmizakis E. Severe migratory Angioedema due to ACE inhibitors use. Hippokratia, 2009, 13 (2): 122–124. Access: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2683457/.

Pollack CV, Romano TJ. Outpatient Management of Acute Urticaria: The Role of Prednisone. Annals ofEmergencyMedicine,1995,26(5):547-551.Access:http://www.sciencedirect.com/science/article/pii/S0196064495700021.

Powell RJ, Leech SC, Till S, Huber PAJ, Nasser SM and Clark AT. BSACI Guideline for the Management of Chronic Urticaria and Angioedema. Clinical & Experimental Allergy, 2015, 45: 547-565. Access: http://onlinelibrary.wiley.com/doi/10.1111/cea.12494/epdf.

Powell RJ, Du Toit GL, Siddique N, Leech SC, Dixon TA, Clark AT, Mirakian R, Walker SM, Huber PAJ, Nasser SM. BSACI guidelines for the management of chronic urticaria and angio-oedema. Wiley Online Library. 2016. Access: <u>http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2222.2007.02678.x/full</u>.

Prasad PS. Urticaria. Indian J Dermatol Venereol Leprol, 2001; 67: 1 (11-20). Access: <u>http://www.ijdvl.com/article.asp?issn=0378-</u> 6323;year=2001;volume=67;issue=1;spage=11;epage=20;aulast=Prasad.

Public Health Agency of Canada (PHAC). ARCHIVED - Interval Between Administration of Vaccines Against Diphtheria, Tetanus, and Pertussis. 2005. Access: <u>http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/05vol31/acs-dcc-8-9/9-eng.php</u>.

Rennels MB, Deloria MA, Pichichero ME, Losonsky GA, Englund JA, Meade BD, Anderson EL, Steinhoff MC, Edwards KM. Extensive swelling after booster doses of acellular pertussis-tetanus-diphtheria vaccines. Pediatrics, 2000, 105(1): e12. Access:

https://www.ncbi.nlm.nih.gov/pubmed?term=10617749.

Rennels MB, Black S, Woo EJ, Campbell S, Edwards KM. Safety of a fifth dose of diphtheria and tetanus toxoid and acellular pertussis vaccine in children experiencing extensive, local reactions to the fourth dose. Pediatr Infect Dis J, 2008, 27(5):464-465. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed?term=18398385</u>.

Ring J, Hein R, Gauger A, Bronsky E, Miller B, and the Desloratadine Study Group. Once-daily desloratadine improves the signs and symptoms of chronic idiopathic urticaria: a randomized, double-blind, placebo-controlled study. International Journal of Dermatology, 2001, 40(1): 72-76. Access: http://onlinelibrary.wiley.com/doi/10.1046/j.1365-4362.2001.00186.x/full.

Ring J, Beyer K, Biedermann T, Bircher A, Duda D, Fischer J et al. Guideline for acute therapy and management of anaphylaxis. Allergo J Int, 2014, 23: 96–112. Access: <u>http://www.awmf.org/fileadmin/user_upload/Leitlinien/061_D_Ges_fuer_Allergologie_und_klinische_Immuno_logie/061-025e_S2k_Akuttherapie_anaphylaktischer_Reaktionen_2013-12.pdf</u>.

Rowe J, Yerkovich ST, Richmond P, Surivaarachchi D, Fisher E, Feddema L, Loh R, Sly PD and Holt PG. Th2-Associated Local Reactions to the Acellular Diphtheria-Tetanus-Pertussis Vaccine in 4- to 6-Year-Old Children. Infection and Immunity, 2005, 73: 12 (8130-8135). Access: <u>http://iai.asm.org/content/73/12/8130.full</u>.

Rüggeberg JU, Gold MS, Bayas JM, et al. Brighton Collaboration Anaphylaxis Working Group. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine, 2007, 25: 5675-5684.

https://www.ncbi.nlm.nih.gov/pubmed/17448577 .

Shafer WG, Hine MK, Levy BM. Physical and chemical injuries of the oral cavity. A textbook of oral pathology. 7th ed. Philadelphia: W.B. Saunders; 2012. Access: <u>https://fr.scribd.com/doc/297276031/Shafer-s-Textbook-of-Oral-Pathology-7E-2012-PDF-UnitedVRG-pdf</u>.

Sheikh A, Ten Broek V, Brown SG, Simons FE. H1-antihistamines for the treatment of anaphylaxis: Cochrane systemic review. Allergy. 2007, 62: 830–837. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed/17620060</u>.

Simon FER, Ardusso LRF, Bilò MB, Dimov V, Ebisawa M, et al. Guideline for the assessment and management. World Allergy Organization. 2012. Access: http://www.bsaci.org/guidelines/wao_anaphylaxis_guideline_2012.pdf.

Staevska M, Popav TA, Kralimarkova T, Lazarova C, Kraeva S, Popova D, Church DS, Dimitrov V, Church MK. The effectiveness of levocetirizine and desloratadine in up to 4 times conventional doses in difficult-to-treat urticarial. Journal of Allergy and Clinical Immunology, 2010, 125 (3): 676-682. Access: <u>http://www.sciencedirect.com/science/article/pii/S0091674909027341</u>.

Staff H. Diphtheria, Pertussis, and Tetanus Vaccines. HealthLinkBC. 2015. Access: <u>https://www.healthlinkbc.ca/medications/zb1209</u>.

Tuncer A, Adalioglu G. The Etiology of Different Forms of Urticaria in Childhood. Pediatric Dermatology, 2004, 21 (2): 102-108. Access: <u>http://onlinelibrary.wiley.com/doi/10.1111/j.0736-8046.2004.21202.x/full</u>.

University of Maryland Medical Center (UMMC). Angioedema. 2016. Access: <u>http://umm.edu/health/medical/altmed/condition/angioedema</u>.

Vasekar M, Craig TJ. ACE inhibitor-induced angioedema. Curr Allergy Asthma Rep, 2012, 12 (1): 72-78. Access: <u>https://www.ncbi.nlm.nih.gov/pubmed/22127615?dopt=Abstract</u>.

Wierzba J, Irga N, Balcerska A, Borzych D. A severe adverse event after vaccine for diphtheria, tetanus, pertussis and poliomyelitis (DTP + polio) in a 4.5 month old infant. Przegl Lek, 2000, 57: (7-8) 436-8. Access: https://www.ncbi.nlm.nih.gov/pubmed/11109323.

Wllkerson, RG, Manlnl A, Scott J. Angioedema in the Emergency Department: An Evidence-Based Review. Emergency Medicine Practice, 2012, 14 (11): 1-24. Access: <u>https://umem.org/files/intl/Angioedema%20-%20Final%20copy.pdf</u>.

Working Group of the Resuscitation Council (WGRC). Emergency treatment of anaphylactic reactions: Guidelines for healthcare providers. Resuscitation Council (UK). 2008. Access: http://www.rcpch.ac.uk/sites/default/files/asset_library/Research/Clinical%20Effectiveness/Practice%20Statem ents/reaction.pdf .

World Health Organization (WHO). Information Sheet Observed Rate of Vaccine Reactions: Diphtheria,
Pertussis, Tetanus Vaccines. 2014. Access:
http://www.who.int/vaccine_safety/initiative/tools/DTP_vaccine_rates_information_sheet.pdf.

World Health Organization (WHO). Vaccine Safety Basics: Module 3: Adverse events following immunization – Vaccine reaction. 2017. Access: <u>http://vaccine-safety-training.org/vaccine-reactions.html</u>.