Anaphylaxis: *A Life Threatening Allergic Reaction*

What is Anaphylaxis?

Anaphylaxis is a sudden, severe, and potentially fatal allergic reaction that can cause a wide range of symptoms, including breathing problems, fainting, rash, and nausea. The most severe type of anaphylaxis—***anaphylactic shock***—will usually lead to death in minutes if left untreated, due to a rapid constriction of the person's airway. The most common emergency treatment for severe anaphylaxis is epinephrine, which is the active ingredient of Twinject®.

Anaphylaxis is triggered when a person comes into contact with an allergen through skin contact, injection, swallowing, or breathing in fine particles. The immune system for people with anaphylaxis identifies a specific substance (for example, peanuts) to be an allergic trigger, or *allergen*, and then tries to protect the body from that allergen by creating specific chemicals called *antibodies*. The next time that person comes in contact with that same allergen, these antibodies identify the allergen, and the immune system responds with an allergic reaction.

More **than 40 million people in the United States are at risk for anaphylactic reactions** and annually, tens of thousands in the U.S. experience anaphylactic reactions, including one in every 3,000 hospitalized patients.[1]

Food-induced anaphylaxis, which is the most common form, leads to approximately 30,000 trips to the emergency room and causes between 150 to 200 deaths each year in the U.S. alone. Even eating a very small amount of a problem food may cause a reaction in some people. In rare cases, exercising within a few hours after eating a specific food may cause an anaphylactic reaction.

Who is at-risk?

Anaphylaxis can occur at any age, however, the incidence of food-based anaphylaxis is increasing at an alarming rate among children. Peanut and tree-nut allergies have emerged as the most prevalent and fastest-growing cause of food-related anaphylactic reactions in the country. Between 1997 and 2002, the documented rate of nut allergy in children doubled.

Cause of Reactions

A summary of published studies states that among documented reports of anaphylaxis treatments in the U.S., reactions were caused by:

- Food in 35% of cases
- Drugs and biological sources, 20%
- Insect stings, 20%
- Exercise, 5%

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[1] The Asthma and Allergy Foundation, National Institute of Allergy & Infectious Diseases, American Academy of Family Physicians

- Allergen desensitization therapy. 3%
- 20% of reported cases were idiopathic in nature.[2]

Treating Anaphylaxis

While prevention is the first line of defense against anaphylaxis, epinephrine is the preferred emergency treatment for severe anaphylaxis. Epinephrine, which is sometimes referred to as adrenalin, is administered by injection through the skin and into the muscle and begins working immediately.

Epinephrine has a suppressive effect on the symptoms of anaphylaxis. It immediately improves breathing by relaxing constricted airways in the lungs, and it also reverses dropping blood pressure by constricting small blood vessels.

The Need for a Second Dose

Some anaphylactic reactions can be so severe that a single dose of epinephrine is not enough. The need for a second dose is more common than might be expected and can be unpredictable. In fact, one in three people who have a reaction that requires a second dose of epinephrine within ten minutes.[4],[5] Since getting professional medical assistance can often take longer, it is recommended that anaphylaxis sufferers always have two doses of epinephrine readily available. A recent study, however, demonstrated that only 16 percent of patients actually do carry two single doses of epinephrine at all times.[3]

Symptoms of Anaphylaxis

Whatever the cause of anaphylaxis, it is important to recognize the symptoms quickly and administer epinephrine when necessary to avoid life-threatening complications. The first symptoms usually occur within minutes, but may not appear for up to 2 hours and can affect many parts of the body, including:

- Skin – A tingling or warm sensation, itching, hives (large, raised spots)
- Taste – A metallic taste in the mouth
- Respiratory – Wheezing, coughing, difficulty breathing, swelling of the mouth and throat
- Gastrointestinal – Vomiting, diarrhea, cramping
- Loss of consciousness due to a drop in blood pressure

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[2] Korenblat P, Lundie MJ, Dankner RE, Day JH. A retrospective study of epinephrine administration for anaphylaxis: how many doses are needed? *Allergy Asthma Proc.* 1999;20:383-386.

[3] Sampson HA, Mendelson LM, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med.* 1992;327:380-384.

[4] Golden DB. Patterns of anaphylaxis: acute and late phase features of allergic reactions. *Novartis Found Symp.* 2004;257:101-110; discussion 110-115, 157-160, 276-85. Review.

[5] Vargese M, et al., AAAAI Annual Meeting 2006, Miami, FL March 3-7, 2006

Additional information

Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of anaphylaxis: an updated practice parameter. *Allergy Clin Immunol.* 2005;115(3 Suppl):S483-S523.

Common allergens that can trigger severe anaphylaxis include:

- Food – Peanuts, tree nuts (walnuts, cashews, etc.), shellfish, fish, milk, eggs
- Insect Stings – Wasps, hornets, honeybees, bumblebees, fire ants, harvester ants
- Latex – A natural rubber product found in gloves, elastic bands, balloons, condoms, and certain medical supplies
- Medications – Penicillin, muscle relaxants, and aspirin

Being Prepared for Anaphylaxis

Verus Pharmaceuticals, Inc., a pediatric-oriented specialty pharmaceutical company, recently launched the **Twinject®** epinephrine auto-injector, the first successful innovation in epinephrine auto injectors in more than 20 years. Twinject Auto-Injector (epinephrine injection, USP 1:1000) is the only available product approved by the United States Food and Drug Administration (FDA) that contains two doses of epinephrine in a single, compact device. This is an important feature, as published studies demonstrate that more than one dose of epinephrine may be required for approximately one in three patients to properly address the allergic reaction, with the second dose often needed within 5-10 minutes after the first.[4,5] Furthermore, a recent study demonstrated that only 16% of patients carry two single-dose auto-injectors at all times.[3] More information about anaphylaxis and Twinject is available on the Verus Twinject website at www.twinject.com. For information about using a Twinject is available at www.twinjecttraining.com.

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Twinject® Epinephrine Auto-Injector For Severe Allergic Reactions

Twinject is a novel epinephrine auto-injector indicated for the emergency treatment of severe allergic reactions (anaphylaxis). Twinject is the only available product approved by the United States Food and Drug Administration (FDA) that contains two doses of epinephrine in a single device. This is an important feature, as published studies demonstrate that more than one dose of epinephrine may be required for approximately one in three patients to properly address the allergic reaction, with the second dose often needed within 5-10 minutes after the first.[4,5] Furthermore, a recent study demonstrated that only 16% of patients carry two single-dose auto-injectors at all times.[6]

Twinject was launched in the U.S. in August 2005 by Verus Pharmaceuticals, Inc., a pediatric-oriented specialty pharmaceutical company.

Prior to Twinject, people at risk for anaphylaxis had only one option for an epinephrine auto-injector and that product device carries only a single dose. Twinject is the first successful innovation in epinephrine auto injectors in more than 20 years.

Second Dose

The need for a second dose of epinephrine is more common than is expected and can be unpredictable.

- 35% of patients may experience anaphylactic reactions requiring additional epinephrine[1]
- Up to 20% of children with severe anaphylactic reactions will experience a secondary response[2]
- The more severe the initial reaction, the more likely there will be prolonged manifestations requiring additional treatment[7]
- Even when there are mild symptoms initially, the potential for progression to a severe and even irreversible outcome must be recognized

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[4] Korenblat P, Lundie MJ, Dankner RE, Day JH. A retrospective study of epinephrine administration for anaphylaxis: how many doses are needed? *Allergy Asthma Proc.* 1999;20:383-386.
[5] Sampson HA, Mendelson LM, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med.* 1992;327:380-384.
[6] Vargese M, et al., AAAAI Annual Meeting 2006, Miami, FL March 3-7, 2006
[7] Golden DB. Patterns of anaphylaxis: acute and late phase features of allergic reactions. *Novartis Found Symp.* 2004;257:101-110; discussion 110-115, 157-160, 276-85. Review.

Twinject Features

- Enables rapid, easy delivery of epinephrine
- Unique dual-dose design eliminates the need for two single-dose injectors
- Each Twinject comes with attached, easy-to-follow, step-by-step directions for use
- Slim, crush-resistant case protects Twinject in handbags, backpacks and travel kits
- Twinject is the smallest, lightest epinephrine auto-injector making it easy to carry[8]

Twinject is available in the following configurations:

Twinject 0.3 mg	Twinject 0.15 mg
Twinject 0.3 mg Two-Pack	Twinject 0.15 mg Two-Pack

Each Two-Pack configuration contains two devices for self-administration and a demonstrator for patient training purposes.

For full product and safety information and additional information about anaphylaxis, please visit Twinject's Web site at www.twinject.com. For more information about using Twinject, visit www.twinjecttraining.com.

About Verus

Verus Pharmaceuticals is dedicated to improving the lives of children and those who care for them. Verus is building a portfolio of products for the unmet medical needs of children through acquisitions and alliances, with an initial focus on the treatment of asthma, allergies, and related diseases and conditions. Verus is differentiated by its pediatric orientation and its strong financial position and experienced management team, which allows the company to capitalize on an extensive network to build its product portfolio and pursue complementary transactions. The company's rigorous, disciplined approach to strategic decision-making and core competencies in development and commercialization is expected to provide significant value to its partners. More information about Verus is available on the company's corporate website at www.veruspharm.com.

Twinject® and Verus® are registered trademarks of Verus Pharmaceuticals, Inc.

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[8] Kelso J, J Allergy Clin Immunol, Vol 117, No. 2, Feb 2006

Additional Information

Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of anaphylaxis: an updated practice parameter. *Allergy Clin Immunol.* 2005;115(3 Suppl):S483-S523.

MANAGING ANAPHYAXIS
CHECKLIST

☑ If someone has come into contact with a food allergen that causes an anaphylactic reaction, quickly determine his/her physical symptoms.

☑ If a person child is not having trouble breathing, but immediately has excessive rash or hives, these are symptoms of anaphylaxis.

☑ Do not hesitate to use an epinephrine auto-injector at the first sign of anaphylaxis, then immediately seek professional, emergency medical care. Too often people "wait and see" or try to use an antihistamine, which can mask symptoms.

☑ Be sure to schedule a follow-up appointment with an allergist or specialist after any reaction. For a first reaction, it is important to try to identify the allergen to avoid future exposure.

☑ Always have two injections of epinephrine available, since studies have shown that a second dose is often needed within five to 10 minutes after the first. A recent study demonstrated that only 16 percent of patients carry two single-dose auto-injectors at all times, while as many as 30 percent may need two doses.

☑ Communicate with schools, school nurses, teachers, camp directors etc. about a child's allergy. This will help protect against accidental exposures and ensure that everyone understands the symptoms of anaphylaxis, which vary from patient to patient.

☑ Double-check the expiration date of any epinephrine auto-injectors, and schedule a visit with an allergist the same time every year to get a prescription for a new auto-injector.

☑ As children become more independent during adolescents, it is particularly important that they understand how to protect themselves and share information with their friends, identifying foods that they must avoid, and the symptoms of a severe reaction.

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