



Community Pharmacist Role in Managing Anaphylaxis

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- Upon successful completion of this article, the pharmacist should be able to:
1. Discuss the pathophysiology of an anaphylactic reaction.
 2. Evaluate risk factors for patients with anaphylaxis and identify goals of treatment.
 3. Describe the role of current therapies and rationale for product selection.
 4. Identify adverse effects caused by anaphylaxis therapy and appropriate monitoring parameters.
 5. Educate patients on strategies to prevent anaphylaxis and appropriate techniques for using an auto-injector.

At the conclusion of this activity, the pharmacy technician should be able to:

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2. Identify risk factors for patients with anaphylaxis.
3. Describe the role of current therapies and rationale for product selection.
4. Identify adverse effects caused by anaphylaxis therapy.

INTRODUCTION

Anaphylaxis is becoming a commonly occurring concern in the community setting, evident through increasing prevalence, particularly in the younger population. Factors such as under-diagnosis, underreporting, and variability in defining anaphylaxis, make it difficult to

put an exact number on the prevalence of cases. However, clinical studies have estimated a lifetime incidence in the United States between 0.05–2 percent. There is no universal clinical definition for anaphylaxis but it is generally characterized as a serious allergic reaction of rapid onset which may result in death. The most common triggers to commence an anaphylactic reaction include various foods, medications, and insect stings. According to the Centers for Disease Control (CDC), food allergies cause 30,000 cases of anaphylaxis, 2,000 hospitalizations, and 150 deaths annually.

The most common organ systems involved are the cutaneous, respiratory, cardiovascular, and gastrointestinal systems. Gastrointestinal complaints comprise the most nonspecific symptoms of anaphylaxis, such as diarrhea, vomiting, abdominal pain, and nausea. These nonspecific symptoms should be taken into consideration with respect to differential diagnosis of anaphylaxis as these symptoms can present even when an allergen is not ingested. A complete anaphylactic reaction can result in urticaria, angioedema, hypotension, bronchospasm, and potentially, cardiovascular collapse. Because of the seriousness and quick onset of these symptoms, anaphylaxis is deemed a medical emergency, which should be identified and treated immediately. Clinical outlook of anaphylaxis is on an individual patient case basis, according to the severity of the reaction and response to treatment.

Lack of patient knowledge and poor adherence to trigger avoidance affords an opportunity for the community pharmacist to take a role in education and management. Taking into account the ease of accessibility, a community pharmacist is uniquely positioned to provide counseling on self-management strategies, such as

avoiding common anaphylactic allergens and proper administration techniques for epinephrine auto-injector devices. Additionally, pharmacists can impact long-term management of anaphylaxis by providing critical risk assessment and reduction through evaluating patient specific risk factors, which include comorbidities and concurrent medications. Supporting patients in the development of a written anaphylaxis emergency action plan is another fundamental management strategy for the pharmacist to utilize. This article will focus on the etiology and basic pathophysiology, treatment, and educational strategies for the pharmacist in the management of patients with anaphylaxis.

ETIOLOGY

A focus on risk assessment and risk reduction should be a critical component for health care professionals with regard to prevention and long-term management in those patients who have experienced anaphylaxis. There are a variety of different types of anaphylaxis which generally are categorized as either immunologic or non-immunologic, based on whether or not the underlying mechanism is mediated by IgE. A third type is IgE-independent anaphylaxis, whose triggers result in the activation of a complement cascade. This type of reaction can often be referred to as an anaphylactoid reaction, to distinguish the absence of IgE involvement.

Anaphylaxis can also be considered idiopathic, where the underlying mechanism is unknown. There are many risk factors which can cause IgE-mediated anaphylaxis, the most common of which include foods, cer-

tain medications such as antibiotics, and bee stings. Immunizations rarely cause anaphylaxis, but pharmacies should have a plan to respond when a patient has a reaction in the store. According to the CDC, about 3.3 million Americans are allergic to peanuts or tree nuts, and 6.9 million are allergic to seafood. The CDC also documents that an estimated 3–10 percent of Americans have experienced an allergic response to penicillin that is mediated by IgE. Anaphylaxis can also be triggered in some patients by immunologic mechanisms which do not involve IgE, such as blood products and some medications. Exercise or physical factors can cause anaphylaxis directly, instead of through immunologic mechanisms. Table 1 compares the most common triggers for the various forms of anaphylaxis.

Along with these common triggers, there are a variety of patient-specific factors such as age and comorbidities that can place the patient at an increased risk of anaphylactic reaction. Age is an important risk factor to consider for anaphylaxis, because often anaphylaxis may be unidentified in infants due to their inability to describe their symptoms. Also, some common anaphylactic symptoms could emulate those experienced in a healthy state with this age group, such as flushing or loose stools. Additionally, the risk for the teenage population can be increased due to unpredict-

Table 1: Common Anaphylaxis Triggers and Causative Agents		
IgE-Mediated Immunologic	IgE-Independent Immunologic (Anaphylactoid)	Non-Immunologic
Foods (milk, eggs, peanuts, tree nuts, shellfish, fish, soy, and wheat)	Blood products (IV immunoglobulin)	Exercise (food dependent or food independent)
Medications (beta-lactam antibiotics, monoclonal antibodies,vaccines, NSAIDs)	Medications (dextran, ACE inhibitors, ARBs protamine)	Medications (opioids, muscle relaxants)
Insect sting venom (yellow jackets, honeybees, wasps, hornets)	Radiocontrast dye	Physical factors (cold, heat, sunlight)
Natural rubber latex		Ethanol
Occupational allergens		
Animal dander		

Adapted from: Kemp S, Lockey R. Anaphylaxis: A review of causes and mechanisms. Journal of Clinical Immunology. 2002; 110(3):341–346. Estelle F, Simmons R. Anaphylaxis: Recent advances in assessment and treatment. Journal of Clinical Immunology. 2009; 124(4):625–636.

able behavior with respect to avoiding their triggers for anaphylaxis. This barrier relates to the tendency for teenage patients to deny experiencing any anaphylactic-related symptoms. Denial often results in poor self-management through continued use of or exposure to triggers that commonly initiate a reaction and refusal to carry emergency auto-injectors.

Elderly patients are at increased risk for fatal anaphylaxis because of the presence of multiple comorbid disease states. These include asthma, COPD, cardiovascular diseases, allergic rhinitis, and eczema. Concomitant psychiatric disease can make it difficult for patients to recognize anaphylaxis symptoms. Pregnancy can place the mother and baby at an increased risk for fatality from anaphylaxis. Along with the medications that can trigger anaphylaxis, beta blockers can increase the severity of anaphylaxis or possibly make it more difficult to treat. Beta blockers can interfere with treatment by decreasing the patient's response to the beta agonist effects of epinephrine therapy. Additionally, clonidine, substances with CNS effects such as ethanol, and other drugs with hypotensive or anti-muscarinic side effects can potentially make it more difficult to recognize symptoms of anaphylaxis when they occur.

CLINICAL PRESENTATION

Anaphylaxis is a condition which presents with rapid onset and is often unpredictable, making early sign and symptom recognition of crucial importance. Anaphylaxis affects multiple organ systems and as a result can present with a diverse set of symptoms specifically related to these organ systems. Most anaphylaxis reactions involve the skin or mucous membranes and involve a combination of symptoms such as flushing, pruritus, urticaria, erythema, and angioedema. The respiratory system is also very frequently involved in anaphylaxis. Patients experience symptoms such as nasal congestion, rhinorrhea, sneezing, pruritus and tightness in the throat, dysphonia,

hoarseness, shortness of breath, coughing, chest tightness, and bronchospasm.

Anaphylaxis symptoms can also relate to the cardiovascular symptoms which include chest pain, palpitations, tachycardia, dizziness, hypotension, and cardiac arrest. The other major organ system involved in anaphylaxis is the gastrointestinal system. Gastrointestinal symptoms include nausea, cramping, abdominal pain, vomiting, and diarrhea. Due to the multisystem nature and overlapping symptoms, it is also important to consider other conditions that may resemble anaphylaxis in clinical presentation. Table 2 addresses some of these other conditions that present with symptoms which may be confused as anaphylaxis.

Table 2: Differential Diagnosis of Anaphylaxis

Hypotension	Cardiogenic shock Vasovagal reaction Hypovolemic shock Septic shock Capillary Leak Syndrome
Flushing	Carcinoid Red-Man syndrome Postmenopausal hot flashes Autonomic epilepsy
GI-related symptoms	Sulfites Monosodium glutamate Scombroid fish poisoning
Respiratory	Asthma or COPD exacerbation Foreign body aspiration Vocal cord dysfunction
Cardiovascular	Myocardial infarction Pulmonary embolism
Mixed symptoms	Panic disorder Non-allergic angioedema Mastocytosis

Adapted from: Estelle F, Simmons R. Anaphylaxis. Journal of Clinical Immunology. 2010; 125(2):S161–S181.

PATHOPHYSIOLOGY

Having an understanding of the underlying pathophysiology of anaphylaxis will provide the pharmacist with the resources to better evaluate the disease state and apply it to a determination of which medications are appropriate for optimal management of individual patient conditions. Anaphylactic reactions primarily occur as a result from a release of chemical mediators from mast cells and basophils. These chemical mediators include histamine, tryptase, cytokines, heparin, leukotrienes, and prostaglandins. After exposure to an allergen, IgE

antibodies are synthesized and subsequently become bound to high affinity receptors for IgE on the surface of mast cells and basophils. Re-exposure to the allergen activates the mast cells and basophils and causes release of the chemical mediators which propagates an anaphylactic reaction. Other immunologic mechanisms exist which lead to activation of mast cells and basophils such as IgG-antigen complex, and cytotoxins, as well as through activation of the complement and coagulation systems. The non-immunologic factors such as exercise and physical factors can cause an anaphylactic reaction through directly activating mast cells and basophils.

The chemical mediators released by mast cells and basophils are responsible for originating the common symptoms of anaphylaxis. Histamine activation of H1 receptors causes the pruritus, rhinorrhea, and bronchospasm, while activation of both H1 and H2 receptors cause headache, flushing, and hypotension that is characteristic of anaphylaxis. Prostaglandins and leukotrienes are responsible for the bronchospasm, vascular dilation, hypotension, and mucous secretion.

FOOD ALLERGIES

Allergies to certain foods were mentioned in the etiology of anaphylaxis as one of the most common triggers and ultimately an important public health issue. Therefore, it is imperative for pharmacists to have a good understanding of this condition, in particular, to adequately advise patients on proper prevention and management strategies. In most cases, if food allergies are appropriately recognized early or prevented, they will not progress to the severity of an anaphylactic reaction. This includes understanding aspects such as the different mechanisms of allergic responses to food and associated conditions, the difference between food allergies and food intolerances, risk factors, and the various adverse reactions or syndromes that can present as a result of a food allergy or intolerance.

Food allergens are components of food, often protein, that are recognized by specific immune cells which then cause an allergic response to develop. It is important to note that allergens can still cause hypersensitivity reactions despite proper cooking of the food, though allergens in fruits and vegetables can often cause allergic reactions when eaten raw. Food oils, depending on the level of protein retained from the food oil source, can

also potentiate an allergic reaction. Generally, the most common types of food hypersensitivities found in children include peanuts, eggs, cow's milk, and soy, and can be outgrown or clinically tolerated. With respect to cow's milk, the allergy is directed against one or both of the major milk proteins, namely casein and whey. With regard to the egg allergies, children may be allergic to the white, yolk, or both. Additionally, allergies to peanuts, tree nuts, shellfish, and eggs are the cases more commonly being seen in adults.

There are various factors that are important to keep in mind when assessing patient risk of food allergy. Clinical evidence suggests a strong genetic component associated with food allergies, most notably with peanut and gluten allergies. In regard to age and gender, male children tend to be more affected by food allergies, whereas females are more frequently affected amongst adults. Hypotheses currently exist regarding some dietary changes that have occurred in western society in connection with the recent rise in the prevalence of food allergy. These changes in diet which have been studied in association with an increase in food allergies include components such as abnormally high or low levels of vitamin D, increase in dietary fat, decrease in the consumption of fruits and vegetables containing vital antioxidants, and the increase of childhood obesity. Furthermore, the significant rise in celiac disease incidence in recent decades can be pointed to the genetic engineering of wheat, which has resulted in around a 500-fold increase in the gluten content of modern day wheat. In older individuals, certain factors such as exercise, alcohol consumption, and the use of NSAIDs should be considered as a potential corresponding risk, as some patients only develop allergies to food when it is consumed in combination with these factors. Hypersensitivity reactions to food are more prevalent when associated with other allergic conditions such as asthma, allergic rhinitis, atopic dermatitis, and eosinophilic gastrointestinal diseases.

The signs and symptoms associated with a normal food allergy generally involve the cutaneous symptoms discussed with the presentation of anaphylaxis. When the symptoms become more severe resembling angioedema, bronchospasm, and cardiovascular issues, it can indicate that the food allergy may have progressed into an anaphylactic reaction. Risk factors for progression into food-induced anaphylaxis include poorly controlled asthma, previous episode of anaphylaxis with the particular food, failure to recognize early symptoms of an allergic response to food, lack of skin symptoms, or a delay in the use of treatment. The timing of symptoms presenting from an allergic response to food can often distinguish the type of mechanism of the reaction. Immediate reactions occur within minutes to a few hours and typically they involve IgE-mediated mechanisms. Delayed reactions occur within several hours to even a few days and typically occur through cellular mechanisms.

Adverse reactions to food can be caused by a number of mechanisms, and depending on the mechanism, can result in a variety of clinical syndromes. Reactions which are caused through immune-mediated mechanisms are considered a food allergy. Those food components that induce adverse reactions which are not immune based, are considered food intolerances rather than food allergens. A classic example to illustrate this difference is seen with an individual who has an adverse reaction due to an immunologic response to milk protein compared with an individual who has abdominal pain and diarrhea because their body is unable to digest the lactose contained in the milk. The first case would be considered an allergy to milk because it is immune-based, whereas the second case is not and would therefore be considered intolerance to the lactose found in milk. The various immune-mediated mechanisms of adverse food reactions include IgE-mediated, non-IgE mediated, mixed IgE and non-IgE mediated, and cell mediated. Celiac disease is a com-

Table 3: Immune-Based Mechanisms of Adverse Food Reactions

IgE- mediated	Acute urticaria Oral allergy syndrome Immediate GI hypersensitivity
Non-IgE-mediated	Celiac disease Food protein induced enterocolitis syndrome Food protein induced enteropathy
Mixed IgE and non-IgE mediated	Eosinophilic esophagitis Eosinophilic gastroenteritis
Cell Mediated	Allergic contact dermatitis Dermatitis herpetiformis

Adapted From: Boyce et al. Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel. J Allergy Clin Immunol. 2010; 126(6):S9-S10.

mon syndrome that is a result of a non-IgE mediated immune response to the gluten protein that is found in grains. Some other clinical syndromes resulting from each of the different immune mediated mechanisms are described in Table 3.

Risk assessment and patient education are the most important strategies in the management of patients with a potential food allergy. Proper risk assessment involves obtaining a thorough history consisting of a complete list of foods suspected to be causing the symptoms, details of how the food was prepared, how much of the food is needed to cause symptoms, past medical or family history of other allergic diseases, predisposing factors such as exercise or NSAID use, and most importantly, a detailed description of the reaction. Avoiding the allergen is the best approach to treatment of food allergies and, as a result, patients should be counseled on how to recognize these relevant food allergens that should be removed from their diet. Clinical guidelines also recommended that patients and caregivers are counseled on how to properly read food labels to identify ingredients which contain the pertinent allergens as well as encouraged to inquire about the presence of these ingredients when eating out and in medications. Due to lack of clinical evidence and the need for adequate nutritional status for development, it is no longer recommended that a mother restrict her diet during pregnancy as a way to prevent food allergies from developing in the child. Pharmacologic therapy for allergic reactions triggered by food consists of either antihistamines for non-severe reactions or

immediate administration of epinephrine if symptoms progress towards anaphylaxis.

ANAPHYLAXIS PREVENTION

Optimal long-term management of patients with anaphylaxis in a community setting is dependent on appropriate risk assessment and prevention strategies. Risk assessment and reduction of relative risk of morbidity and mortality resulting from exposure is an essential component of anaphylaxis prevention. It should be a primary focus of health care professionals—specifically pharmacists—in the community. The main components of risk reduction include identifying potential sources of triggers, avoiding triggers to prevent further episodes, evaluating comorbidities and concomitant medications, education to identify symptoms of allergic response that may progress to anaphylaxis, and emergency preparedness. Pharmacists should stress individualized lifestyle changes for patients that allow them to avoid certain triggers of anaphylaxis. This may involve such behaviors as using food substitutes, avoiding certain foods to which they are allergic, avoiding exposure to skin allergens such as latex, nickel and urushiol, and minimizing outdoor activities for patients allergic to insect stings.

Pharmacists can refer patients with food allergies to a dietician who can help them make appropriate food choices, and recognize foods and food ingredients which may trigger an anaphylactic reaction. Strategies for prevention of anaphylaxis induced by exercise include avoiding relevant co-triggers for at least four hours before exercise, and stopping exercise as soon as the patient experiences symptoms of anaphylaxis. Current literature states that premedication with agents such as antihistamines have not been shown to be effective in preventing anaphylaxis caused by exercise. Pharmacists have a role in risk assessment through screening patients for comorbidities or medications that can put them at an increased risk for anaphylaxis. Pharmacists should identify newly prescribed medications with a potential for allergy and counsel patients appropriately. Patients need to be informed of the potential for allergy in a manner that makes them aware but does not cause excessive worry or panic. Pharmacists should first consult with the patient to inquire about prior history of adverse drug reactions, disease history, and concur-

rent medication in order to help patients and prescribers weigh the risk of allergy with the benefit in managing their disease. If the pharmacist and patient together conclude that the potential risk outweighs the benefit, an offer should be extended by the pharmacist to consult the prescriber with a recommendation to switch medications to one that is better suited and safer for the patient's needs.

Recognizing the difficulty for most patients to be able to permanently eliminate or avoid allergens and triggers, makes emergency preparedness key to the prevention of anaphylaxis and proper emergency action. Emergency preparedness involves carrying at least one epinephrine auto-injector, having a written anaphylaxis emergency action plan, and the use of medical identification. Considering that often a reaction might be serious enough in nature to inhibit the patient from emergency self-treatment, additional people such as spouses, parents, caregivers, coworkers, coaches, and teachers should be trained on recognizing symptoms of a reaction and proper use of epinephrine auto-injectors. Pharmacists should ensure that patients who are at risk or have experienced an anaphylactic reaction are provided with an emergency action plan. These emergency action plans include the patient's name, what causes their anaphylaxis, common symptoms, describes the location and instructions for using their epinephrine auto-injector, and provides emergency medical numbers such as calling 911. These plans should also document patient comorbidities and concurrent medications as well as provide phone numbers and contact information for family members. These completed action plans should be kept at all places an individual might need to utilize it such as school, home, and work. Sufficient detail should be included for other individuals such as coworkers, coaches, or teachers to be trained on how to adequately respond to a situation of an anaphylactic reaction.

The use of medical identification can be

a wallet card or medical identification bracelets. These bracelets can be as simple as a medical alert bracelet classifying the patient as anaphylactic or as advanced as tags that have storage capability to provide worldwide, 24 hour, 365 day access to a patient's medical record on a mini-USB. Provided the medical record is current, this allows all health care professionals in the chain of treatment to have information about the patient's triggers, comorbidities, and concurrent medications. Advise patients who are at risk of severe allergic reactions to program ICE (In Case of Emergency) numbers into their cell phones. This speeds identification of emergency contacts in case an anaphylactic reaction arises which requires emergency action. Early emergency action through medical identification and prompt treatment provides significant impact in evading the progression to serious complications such as anaphylactic shock.

EPINEPHRINE TREATMENT

The primary medication therapy available for the emergency treatment of anaphylaxis is epinephrine. Epinephrine can be used to treat all forms of anaphylaxis, including those cases which are idiopathic or exercise-induced. Epinephrine is beneficial in the treatment of anaphylaxis due primarily to its stimulatory effect on alpha adrenergic receptors, which can decrease vasodilation and increase vascular resistance. This action stops or slows the loss of intravascular fluid volume and hypotension which is problematic in anaphylaxis. The beta adrenergic agonist action of epinephrine relaxes bronchial smooth muscle to relieve respiratory symptoms of bronchospasm and dyspnea. Epinephrine also stimulates smooth muscle relaxation of other organs associated with anaphylaxis and as a result can alleviate pruritus, urticaria, angioedema, and gastrointestinal symptoms.

Epinephrine is delivered in the form of an auto-injector device. There are currently three brands of auto-injectors on the market, includ-

ing EpiPen®, Adrenaclick®, and Twinject®. There are currently no generic forms of epinephrine auto-injector on the market. Due to the Food and Drug Administration's rating of BX, none of these brand products are considered to be therapeutically equivalent and therefore cannot be automatically substituted for one another upon dispensing. The BX code indicates that there is insufficient data available for the FDA to determine therapeutic equivalence, and consequently the FDA presumes the specific drug products to be therapeutically inequivalent until it determines that the data is adequate enough to say otherwise. B ratings typically indicate different dosage forms or administration devices, rather than an issue with active ingredients.

EpiPen® and EpiPen® Jr is a single-dose auto-injector device. This cartridge-based delivery system is activated by removing device from the protective carrier tube and pulling the blue safety release while the device is held in a fist with the orange tip pointed downward. The orange tip is then to be pushed firmly against the outer thigh until it clicks and held in place for 10 seconds. The needle is designed to work through clothing. Appropriate dose is determined according to the weight of the patient. EpiPen® contains 0.3 mg of epinephrine, which is intended for injection in patients who weigh greater than or equal to 30 kg. EpiPen® Jr is available for the purpose of administering a dose of 0.15 mg to patients weighing between 15 kg and 30 kg. The recommended maximum single dose to be administered is 0.5 mg for adults and 0.3 mg in children.

Adrenaclick® is a single-dose auto-injector device. The device is activated by sequential removal of safety caps labeled "1" and "2". The red tip is then pressed firmly against the middle of the outer thigh and held in place for 10 seconds. The needle is designed to work through clothes. Patients should verify that the needle is visible when they remove the device from the thigh; this is indication that the medication was administered. Instruct patients to avoid contact with the red tip before administration to prevent early release of the medication. Appropriate dose is determined according to the weight of the patient. Adrenaclick® is available in two strengths; 0.3 mg for patients who weigh 30 kg or more, and 0.15 mg for patients who weigh between 15–30 kg.

Twinject® is a single-dose auto-injector with a second, back-up dose administered by syringe, accessed

through partial disassembly of the device. The device is activated by sequential removal of green safety caps labeled “1” and “2”. The red tip is then pressed firmly against the middle of the outer thigh and held in place for 10 seconds. The needle is designed to work through clothes. Patient should verify that the needle is visible when they remove the device from the thigh; this is indication that the medication was administered. Instruct patients to avoid contact with the red tip before administration to prevent early release of the medication. Advise patients to immediately prepare the second, back-up dose by unscrewing the red tip, grasping the newly exposed blue plastic to remove the syringe and carefully removing the yellow collar under the plunger. After administration of the first dose, the needle is exposed and patients or caregivers should handle with care. Patients should administer the second dose after 10 minutes if symptoms have not improved or have returned. This requires manual injection into the outer thigh. Appropriate dose is determined according to the weight of the patient. Twinject® is available in two strengths: 0.3 mg for patients who weigh 30 kg or more, and 0.15 mg for patients who weigh between 15–30 kg.

There are no absolute contraindications for the use of epinephrine administered from any type of auto-injector. Epinephrine from an auto-injector is recommended to be injected intramuscularly into the anterior lateral thigh and should never be injected into the buttock.

Even though all the doses of epinephrine in these auto-injectors are very similar, each auto-injector has unique features which the pharmacist should recognize and prepare to counsel appropriately. These differences are important to take into consideration for initial product selection as well as for patients who may have switched products. Give careful consideration to patient and caretaker ability to learn administration and dose verification techniques. Twinject® and Adrenaclick® are considered syringe-based injectors, while the EpiPen/EpiPen Jr is a cartridge-based design. An advantage seen with the cartridge delivery system over the syringe-based approach is that medication is not deployed until the needle has fully entered the patient's skin. This minimizes the loss of medication and ensures that the desired dose has been administered. The cartridge delivery system can also achieve deeper penetration through the skin because

its design is capable of applying more force during administration. Another major difference exists with the Twinject® containing the second dose of epinephrine. Patients who are willing to manually inject a second dose of epinephrine or who live and participate in outdoor activities in rural areas may benefit from this convenience. Another consideration is that the EpiPen has a 22-gauge needle, while the Twinject auto-injector needle is 25 gauge. Some patients may be comforted by having the smallest available needle size. Other minor differences exist between the products, including color and appearance of device components.

It is important for the pharmacist to instruct the patient that prompt administration of epinephrine is critical to treatment. It is also important for the patient to call 911 either before or immediately after administering the first dose of epinephrine. Second doses of epinephrine are often needed for optimal management to treat recurrent or biphasic reactions based on the patient's response to the medication or severity of their condition. Subsequent doses to treat biphasic reactions generally should be given every five to 15 minutes as necessary after 911 has been called or en route to the emergency room. For this reason it is appropriate for the pharmacist to convey the importance of having multiple auto-injectors at a time which are easily accessible.

ADVERSE EFFECTS

When administering medications such as epinephrine, attention should be paid to possible adverse effects that may result. Pharmacists should be aware of these adverse effects so that they may appropriately counsel patients on how to monitor for these and as a result are better able to manage them if they occur. Patients may experience adverse effects from epinephrine that range from anxiety, apprehension, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, or

respiratory difficulty. Patients with concurrent complications such as coronary artery disease can potentially experience arrhythmias or angina as a result of epinephrine therapy. The manufacturers provide a warning that accidental injection into the fingers, hands, or feet may result in a loss of blood flow to that area due to the vasoconstriction produced by epinephrine. Remind patients to avoid handling the orange or red tip of the device. Pharmacists should advise patients who experience any of these side effects should report them to their physician to determine patient follow up. Monitoring strategies that may be utilized for patients who experience more serious side effects such as respiratory difficulty and arrhythmias include pulmonary function tests and ECG respectively.

ADJUNCTIVE MEDICATIONS

In addition to epinephrine, other adjunctive therapies can be utilized to manage and relieve other symptoms caused by anaphylaxis. H1-antagonist antihistamines such as diphenhydramine are considered second-line to epinephrine in the treatment of anaphylaxis. They are slower in onset of action and are not considered to be life-saving but instead are utilized for cutaneous symptom relief. Consequently, these agents are primarily useful for the symptomatic relief of pruritus, flushing, urticaria, and angioedema. Diphenhydramine is recommended to be administered intravenously or intramuscularly for more serious symptoms or orally for mild symptoms at single doses of 25–50 mg for adults and 1 mg/kg up to 50 mg for children. These agents are most effective when also used in combination with H2-antagonist antihistamines such as ranitidine. H2 antihistamines can help to decrease hypotension, vasodilation, gastric acid and airway mucus secretion, vascular permeability, and potentially decrease cardiac effects such as tachycardia and inotropic activity. Antihistamines are generally recommended to be continued for two to three days after the acute reaction has been treated.

Fluid management is also important with anaphylaxis, and patients who remain hypotensive despite treatment with epinephrine should be hydrated with crystalloids or colloid liquids. If hypotension is still resulting, patients can be tried on therapy with vaso-pressors such as dopamine to induce vasoconstriction. Concurrent use of beta2 adrenergic agonists, such as albuterol, in patients experiencing anaphylaxis can be impactful in causing bronchodilation, which can decrease bronchospasms and associated wheezing, coughing, and shortness of breath. Corticosteroids can potentially have a benefit in treating idiopathic or biphasic anaphylaxis, but minimal evidence exists to confirm this. Other medications such as inotropes, glucagon, and oxygen therapy have also been tried as added treatment to control anaphylaxis.

PHARMACIST EDUCATION

To prevent and effectively manage anaphylaxis in the community setting, pharmacists should take a proactive role to ensure that patients are appropriately educated about their allergy; identifying trigger factors, signs of a severe reaction, proper techniques for administering an auto-injector, and lifestyle changes which can prevent them from experiencing a reaction. Proper counseling of patients starts with underscoring the seriousness and unpredictability of anaphylaxis as well as the importance of possessing and promptly using an epinephrine auto-injector. Optimal, emergency self-management of anaphylaxis through the use of an auto-injector requires that the patient is competent in the proper administration technique, providing another area of consultation for pharmacists. Studies have shown that for patients prescribed an epinephrine auto-injector, only about 30–45 percent can correctly demonstrate how to use them. Table 4 describes appropriate administration technique that pharmacists should make sure patients understand.

Anaphylaxis education provided by the pharmacist provides the patient with basic information related to the condition, strategies such as trigger avoidance for preventing anaphylaxis, and components of emergency preparedness. Pharmacists should also counsel patients to inspect their auto-injectors to verify that they are not outdated and are not exposed to extreme hot or cold conditions. A study from 2000 published in the *Journal of Clinical Immunology*

Table 4: Administration Techniques for Auto-injectors

Epi-Pen®/Epi-Pen® Jr.	1. Flip open case and remove injector. 2. Hold in dominant hand and make a fist keeping fingers away from ends. 3. Orange tip should be face downward and other hand should pull off the blue safety release. 4. Firmly press the orange tip onto outer, upper thigh muscle and hold for 10 seconds. 5. Remove the pen and if the dose was given correctly, the cartridge window will be obscured and the orange tip will move back over the needle.
TwinJect® and Adrenaclick®	1. Remove the injector from the case. 2. Pull off green cap which is labeled "1" to expose a red tip containing the needle. Keep fingers away from tip. 3. Pull off the green cap labeled "2". 4. Form fist around injector and face the red tip down. 5. Place red tip against upper, outer thigh and firmly press until the needle penetrates the skin and hold for 10 seconds. 6. Remove injector and examine the red cap to see if the needle is visible, which confirms that the dose was given.
TwinJect® Only	7. Immediately unscrew the red cap and remove the needle to prepare the second dose. Pull the blue syringe out of the barrel and slide yellow collar off plunger. Press needle firmly into your thigh muscle and push the plunger all the way down to inject the medicine.

Taken from: Patient information: Use of an epinephrine auto-injector. Up to Date. 2010.

evaluated the bioavailability and content of epinephrine in outdated EpiPens. This study determined the bioavailability of epinephrine to be significantly reduced in the outdated injectors compared with those that were in date.

Due to the seriousness of anaphylactic reactions and the necessity for a prompt, potent treatment dose, the authors recommend not using outdated epinephrine products. However, as long as the injector does not contain a precipitate or visible discoloration, they also deem the benefits of using an outdated one to outweigh the risks of using nothing if no other devices are available to the patient during a reaction. Patients taking epinephrine therapy should also be monitored for adverse effects that may result from the treatment.

Pharmacists need to assume responsibility for ensuring that all pharmacy staff is trained to identify and respond to possible triggers of anaphylaxis that exist in the community pharmacy itself. The pharmacy personnel may encounter an anaphylaxis situation in need of emergency medical treatment with patients receiving vaccinations, undiagnosed patients who are seeking help in selecting over-the-counter products, and pharmacy with food or snack availability.

CONCLUSION

Anaphylaxis should be of major concern in the community setting, and pharmacists are situated in a prime position to provide a positive impact toward prevention and management for patients experiencing a reaction. Pharmacists

can provide risk assessment by identifying triggers and evaluating comorbidities and concurrent medications that have the potential to cause an anaphylactic reaction. They can educate patients on being prepared for an emergency and lifestyle changes which the patient can make to lower their risk of a recurrent episode. Additionally, pharmacists can influence the management of anaphylaxis through demonstrating the correct way for patients to self-inject epinephrine. Having a comprehensive understanding of anaphylaxis and the implementation of these management strategies allows the pharmacist and other health care professionals to contribute to the effort to decrease the frequency and severity of anaphylaxis in the community. 

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Editor's Note: For the list of references used in this article, please contact *America's Pharmacist* Managing Editor Chris Linville at 703-838-2680, or at chris.linville@ncpanet.org.

CONTINUING EDUCATION QUIZ

Select the correct answer.

NC is a 29-year-old, 87 kg male who is a construction worker. While working at a construction site, the man encountered a beehive and was stung by a bee. Immediately after being stung, he commented to his coworkers that he did not feel very well. His symptoms consisted of pain of the bee sting, along with dizziness, substantial nausea, and a tight sensation in his throat.

1. Based on this information, what is the most likely pathological mechanism causing this patient's anaphylactic reaction?

- a. IgG-mediated
- b. IgE-mediated
- c. Direct activation of mast cells
- d. Idiopathic

2. The recommended dose of epinephrine to be administered to an individual weighing more than 30 kg (66 pounds) is?

- a. 0.15 mg
- b. 0.30 mg
- c. 0.50 mg
- d. 1 mg

The coworkers dial 911 and they realize that NC has an EpiPen® auto-injector in his possession for emergency situations such as this.

3. What action should the coworkers take?

- a. The coworkers should urge NC to immediately administer the epinephrine.
- b. The coworkers should only urge NC to administer the epinephrine if the 911 operator instructs them to do so
- c. The coworkers should wait for emergency personnel to arrive

4. Which is not an adverse effect of epinephrine?

- a. Hypotension
- b. Palpitations
- c. Anxiety
- d. Respiratory difficulty

AL is a 12-year-old female with a serious allergy to peanuts. She had her first anaphylactic reaction about a year ago after the consumption of peanuts, and her doctor placed her on emergency self-treatment epinephrine therapy at that time. She is 4-foot-9 and weighs 98 pounds. The patient's mother comes into the community pharmacy requesting a refill for her daughter's TwinJect® that she has been continuously receiving for the past year. At the drop-off counter the mother informs the pharmacist that her daughter has been recently having technical difficulties using the Twinject® device and asked the pharmacist to give her the EpiPen® 2-pack this time.

5. True or false? The pharmacist may grant the patient's mother her request and switch AL to the EpiPen® without consulting the doctor because all epinephrine auto-injectors are equivalent to one another.

- a. True—these products can automatically be switched by the pharmacist since they both contain epinephrine.
- b. False—these products have an FDA equivalency rating of “BX” and therefore the pharmacist should consult with the patient's physician to obtain a new prescription before switching epinephrine auto-injectors.

6. Which of the following may be AL's actual technical difficulties complaint for using the Twinject® device?

- a. AL is not willing to administer a manual injection if a second dose is needed.
- b. AL wants an auto-injector with a smaller needle than Twinject®.
- c. AL wants an auto-injector that works through clothing.
- d. These are all potential technical difficulties of Twinject®.

7. After AL's doctor authorizes the switch, her mother returns to pick up the prescription. What counseling should the pharmacist provide her?

- a. Communicate the importance that AL faithfully carries at least one EpiPen® with her at all times and to administer it at the first sign of symptoms which would indicate an anaphylactic reaction.
- b. Educate AL and her mother on proper administration technique of the newly prescribed EpiPen®, making sure they understand how to administer it, store it, and verify that the dose was given.
- c. Review the patient's emergency action plan and encourage some form of medical identification or assist the patient in obtaining medical identification.
- d. All of the above

To properly prevent future anaphylactic episodes in AL, the same pharmacist decides to perform risk assessment for this patient. The pharmacist inquires with the mother regarding whether AL has any other disease states and the mother reports asthma, ADHD, allergic rhinitis, and type 1 diabetes. AL's medication profile displays monthly prescriptions for an inhaled corticosteroid, albuterol inhaler, insulin, loratadine 10 mg, clonidine 0.2 mg, and extended-release mixed amphetamine salts 20 mg.

8. Which of the following are risk factors apply to AL that the pharmacist should focus on?

- a. Peanuts as a trigger
- b. Asthma and allergic rhinitis
- c. Clonidine
- d. All of the above

9. What effect does clonidine have on anaphylaxis risk?

- a. It is similar to albuterol, as it impairs response to epinephrine therapy.
- b. Clonidine masks the symptoms of anaphylaxis.
- c. None, as clonidine is adjunctive therapy for anaphylaxis.

10. Select the FALSE statement regarding anaphylaxis below:

- a. Repeat dosing of epinephrine should be given after 5–15 minutes if initial response is poor or symptoms progress.
- b. Inhaled Beta-adrenergic therapy (such as albuterol) may substitute for epinephrine in patients with asthma.
- c. An epinephrine auto-injector should be held against the outer thigh for 10 seconds to ensure proper dose of medication.
- d. Food allergens may trigger anaphylaxis whether cooked or uncooked.

Community Pharmacist Role in Managing Anaphylaxis

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Quiz: Shade in your choice

	a	b	c	d	e		a	b	c	d	e
1.	☐	☐	☐	☐	☐	6.	☐	☐	☐	☐	☐
2.	☐	☐	☐	☐	☐	7.	☐	☐	☐	☐	☐
3.	☐	☐	☐	☐	☐	8.	☐	☐	☐	☐	☐
4.	☐	☐	☐	☐	☐	9.	☐	☐	☐	☐	☐
5.	☐	☐	☐	☐	☐	10.	☐	☐	☐	☐	☐

Quiz: Circle your choice

- 11. Is this program used to meet your mandatory C.E. requirements?
a. yes **b.** no
- 12. Type of pharmacist: **a.** owner **b.** manager **c.** employee
- 13. Age group: **a.** 21–30 **b.** 31–40 **c.** 41–50 **d.** 51–60 **e.** Over 60
- 14. Did this article achieve its stated objectives? **a.** yes **b.** no
- 15. How much of this program can you apply in practice?
a. all **b.** some **c.** very little **d.** none

How long did it take you to complete both the reading and the quiz? _____ minutes

