

Polyethylene glycol: A hidden allergy risk?

Severe hypersensitivity reactions to polyethylene glycol are an emerging concern in health care and have been increasingly recognized as a cause of systemic allergic reactions that vary from mild to life-threatening anaphylaxis. It's essential for nurses to be knowledgeable about this potential allergen, to be able to identify high-risk patients, and to be prepared to initiate treatment to ensure best patient outcomes.

By Joan M. Zaloom, MA, RN-CNE and Mary Shannon, MSN

CG is a 39-year-old female with a history of familial dilated cardiomyopathy (FDCM), diagnosed at age 25. She is asymptomatic, and her FDCM is well controlled on carvedilol. (See *What is familial dilated cardiomyopathy?*) As part of her annual cardiac workup, CG presents today for her routine annual contrast echocardiogram at the medical center affiliated with her

cardiologist. The addition of utilizing an ultrasound contrast agent for a contrast echocardiogram enhances the image quality.³ Standard preprocedural protocols were followed: obtaining informed consent and verifying that CG has no allergies. An intravenous (IV) line was established, and cardiac and oxygen saturation monitoring was applied.



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Shortly after administration of the contrast agent, CG begins feeling very different than during previous tests. She reports to the nurse that she feels “very warm all over, itchy” and that “my throat is closing.” Recognizing the signs of a possible anaphylactic reaction, the nurse immediately flushes the IV line and administers IV epinephrine. A second dose of epinephrine is administered because of persistent symptoms without improvement. CG senses a rush of medical staff coming into the room and medical orders being shouted out. She begins to panic as she feels herself losing consciousness.

CG was in anaphylactic shock that wasn’t responding to the standard treatment of epinephrine, diphenhydramine, corticosteroids, and fluid resuscitation. Her palpable blood pressure was 60 mm Hg; she was in sinus tachycardia and becoming increasingly unresponsive. A repeat non-contrast echocardiogram revealed a severely reduced ejection fraction (EF) of 15%, indicating acute heart failure. CG’s EF prior to this echocardiogram was consistently approximately 45%. The decreased EF, in conjunction with persistent hypotension and poor perfusion, signaled the onset of acute cardiogenic shock, likely precipitated by the anaphylactic event.

Vasoactive infusions of dopamine, dobutamine, and norepinephrine were initiated. Because of minimal improvement

in CG’s hemodynamic status and cardiac function, the decision was made to urgently transfer her to the Cardiothoracic Intensive Care Unit.

The following interventions were initiated immediately:

- insertion of an intra-aortic balloon pump (IABP) for mechanical circulatory support;
- placement of an arterial line for continuous blood pressure monitoring and arterial blood gas sampling; and
- insertion of a central venous catheter for central venous pressure monitoring and administration of vasoactive medication administration.

It took several days for CG’s vital signs to stabilize and for her to be weaned off the vasopressors. It would be another week before the IABP could be removed. Upon discharge, CG’s vital signs were stable, and her EF was 35%. During her hospitalization, diagnostic testing was performed and proved to be inconclusive as to the cause of her anaphylactic reaction. On recommendation from her cardiologist, CG was evaluated by an allergist after discharge. Comprehensive testing for multiple allergens revealed that CG was allergic to polyethylene glycol (PEG), which was the likely cause of her anaphylaxis.

What is PEG?

PEG is a versatile polymer that was first created in 1859 and initially used

What is familial dilated cardiomyopathy?

Familial dilated cardiomyopathy (FDCM) is an inherited disease of the heart muscle characterized by enlargement and dilation of one or both of the ventricles, resulting in impaired contractility and a left ventricular ejection fraction (LVEF) <40%. It’s a major cause of heart failure and sudden cardiac death in young adults and has a prevalence of 1:250. Forty percent of all cases have a genetic cause, with more than 60 genes identified as being associated with FDCM.

Diagnosis is made by physical exam, electrocardiogram, echocardiogram, and genetic testing. Patients may or may not have symptoms. Typical symptoms include shortness of breath, fatigue, chest pain, and palpitations.

The treatment depends on symptoms and may include beta-blockers, angiotensin-converting enzyme inhibitors, an implantable cardioverter-defibrillator, a left ventricular assist device, or a heart transplant. A patient’s prognosis will vary as it depends on the patient’s overall health.^{1,2}

in industrial applications. Its pharmaceutical potential began to emerge in the 1960s when scientists Frank Davis and Abraham Abuchowski made a groundbreaking discovery. They conjugated PEG to an animal protein, hypothesizing that it would shield the protein from the human immune system, preventing it from being recognized as a foreign substance. Their hypothesis proved correct, leading to the creation of the first PEGylated therapeutic agent approved by the United States Food and Drug Administration (USFDA).³

This innovation sparked a rapid increase in the development of PEGylated pharmaceuticals (see *What is PEGylation?*).³ PEG's ability to improve drug solubility, extend circulation time in the bloodstream, and slow renal clearance made it a valuable tool in enhancing therapeutic efficacy. It became widely used in medications for autoimmune disorders, cancer treatments, and hemophilia. Although PEG had long been a staple in pharmaceuticals, it gained unprecedented global attention in 2022, when it was used in some mRNA COVID-19 vaccines administered to more than 250 million people. This use brought the polymer into the spotlight, highlighting its critical role in modern medicine.⁴⁻⁶

At the same time, scientists began incorporating PEG into a wide range of consumer goods, including cosmetics, food items, household items, and other health-related products. In pharmaceuticals, PEG was used in tablet formulations to create a smooth coating and bind ingredients into easy-to-swallow pills. In cosmetics, food, and household products, it's added as an emulsifier, emollient, or as a vehicle to deliver a product into the skin. PEG can be found in wound dressings, bone cement, and synthetic surgical sealants.^{3,7-11}

PEG typically is assigned a numeric value, which refers to the ethylene

What is PEGylation?

Coating the surface of nanoparticles with PEG is a commonly used approach for improving the efficiency of drug and gene delivery to target cells and tissues. PEG creates a barrier around the nanoparticles, which renders them invisible, thereby increasing their circulation time and preventing them from being destroyed by the body's immune system.

oxide units or to the molecular weight (MW). The lower MW PEGs are found in personal products, whereas the higher MW PEGs are found in pharmaceuticals. PEG has numerous derivatives, which may not always be labeled explicitly as PEG or polyethylene glycol on an ingredient list. It's currently the most widely used "stealth" polymer because of its ability to produce a surface barrier around nanoparticles that renders them invisible to the immune system, therefore avoiding destruction. PEG has been classified as Generally Recognized as Safe (GRAS) by the USFDA since the 1970s.^{3,6,7,10,12}

Historically, PEG was well tolerated, with few reported allergic reactions. However, recent concerns have emerged because of 2 primary factors: increased awareness and identification of hidden allergens such as PEG, and the growing use of PEG-containing nanoparticles in products like contrast agents and certain mRNA vaccines. The widespread administration of these vaccines during the pandemic led to an increase in reported allergic reactions to PEG, ranging from mild symptoms to life-threatening anaphylaxis. The true prevalence of PEG allergy is unknown but is suspected to be significantly underreported.^{6-8,10,13-15}

What is a hypersensitivity reaction?

Hypersensitivity reactions are common and may present in a wide range of health care settings, from outpatient



Sometimes the body overreacts to a specific antigen, which results in an inappropriate and harmful reaction that manifests as a mild to life-threatening hypersensitivity reaction.

clinics to intensive care units. For nurses, having an understanding of the mechanisms behind allergic reactions is crucial. Early recognition of the signs and symptoms allows for prompt intervention, which can be lifesaving in severe cases such as anaphylaxis. This knowledge can equip nurses to monitor, manage, and educate patients effectively, ensuring safe and comprehensive care.

The body is exposed continuously to numerous invaders that have the capacity to destroy the body's vital tissues. It's the body's defense system against these invaders, or antigens, that maintains the integrity of all body systems. The largest defense system of the human body is antibody production. Antibodies are formed in reaction to an antigen. They are composed of immunoglobulins and lymphocytes and can render antigens inactive by neutralizing them so that they can be eliminated from the body. Sometimes the body overreacts to a specific antigen, which results in an inappropriate and harmful reaction that manifests as a mild to life-threatening hypersensitivity reaction.

Hypersensitivity reactions are classified in 4 different ways:

1. Anaphylaxis is the most severe hypersensitivity reaction. It's characterized by being unexpected with a rapid onset. Chemical mediators that affect the skin, lungs, and gastrointestinal tract are released in the body in reaction to the antigen. The

symptoms manifested are edema of the larynx and cardiovascular collapse.

2. Cytotoxic reactions cause cell lysis and tissue damage. The most common cause is a hemolytic transfusion reaction caused by a patient mistakenly receiving a blood transfusion of the incorrect blood type. Symptoms include fever, chills, low back pain, chest tightness, dyspnea, and anxiety.⁵
3. Immune complex reactions are inflammatory reactions that are frequently associated with autoimmune disorders. Symptoms may include fever, rash, joint pain, or swelling.
4. Delayed reactions can occur 24-48 hours after exposure to an antigen. This type of reaction will be seen in a patient who has been exposed to *Mycobacterium tuberculosis* and has a positive purified protein derivative result manifested by erythema and induration at the site of injection.⁵

Pathophysiology of a PEG reaction

Hypersensitivity reactions to PEG and PEGylated products have been documented to occur primarily through 2 mechanisms. One common pathway involves the immune system producing antibodies against PEG after initial exposure. Upon reexposures to PEG or PEGylated compounds, these antibodies can trigger allergic reactions, which

often become more severe with repeated contact. This type of immune response is typically classified as an immunoglobulin E (IgE)-mediated allergy. In some individuals, anti-PEG antibodies have been detected.^{8,16}

The second mechanism is called a complement activation-related pseudoallergy (CARPA), a drug-induced hypersensitivity reaction that can occur with the first exposure to a specific allergen. No antibodies are produced by the body. Symptoms can mimic a true allergic response. Radiocontrast media and nanoparticle-containing drugs and biologicals can cause CARPA.^{8,14,17,18}

Diagnosis of a PEG allergy

Currently, there's no established international protocol for investigating and managing PEG hypersensitivity, despite increasing reports of severe reactions—including anaphylaxis—to PEG and PEGylated products. Diagnosis of PEG allergy is often delayed for several reasons. First, such reactions are rare, leading to limited clinical suspicion. Second, there's a general lack of awareness and understanding of PEG allergies among health care providers. Additionally, identifying PEG in product labels can be challenging because of its inclusion in numerous formulations under various names and synonyms. Although hypersensitivity can occur upon first exposure, it's often repeated exposures and multiple adverse reactions that eventually prompt diagnostic testing.^{16,19}

Although some testing protocols found in the literature are slightly different, all protocols include the following steps:

1. Conducting a focused clinical history.²⁰
2. Stepwise skin prick testing: When suspected, performing a skin prick test (SPT) with a panel of different MW PEGs is the recommended investigation, although systemic

Did you know?

Products containing PEG can be in your home right now, which can be serious or even deadly for a person with a PEG allergy. The following products contain PEG:

- laxatives
- eye drops
- hair conditioners
- toothpaste
- flavored popcorn
- detergents
- oral penicillin

reactions have been reported on SPT.²¹

3. Intradermal testing and graded challenge with PEG-containing products should only be performed with caution because of the relatively high risk of inducing anaphylaxis.
4. Drug provocation testing—supervised administration of a drug under controlled conditions as this poses considerable risk to the patient.^{11,22}

Who is most at risk of a PEG allergy?

Severe hypersensitivity to PEG has recently gained attention as a significant cause of systemic allergic reactions, including potentially life-threatening anaphylaxis. Given PEG's broad presence in medications and foods, nurses must be able to identify people who may be at increased risk for developing a PEG allergy.

- People with unexplained, multiple allergic reactions to different, unrelated medications (within minutes to hours of exposure) may be at higher risk.
- People who repeatedly use PEG-containing medications and products.
- Women are more affected than men, possibly because of frequent exposure from cosmetics and personal care products.^{1,19} (See *Did you know?*)



A nurse's timely recognition of a hypersensitivity reaction in the clinical area is crucial to providing the correct interventions that'll improve patient outcomes.

Symptoms of a PEG allergy

Symptoms of PEG allergy are diverse and can occur immediately to minutes later, depending on the mode of delivery of the allergen and its MW and concentration. A nurse's timely recognition of a hypersensitivity reaction in the clinical area is crucial to providing the correct interventions that'll improve patient outcomes. These symptoms include:

- shortness of breath,
- angioedema,
- pruritus,
- urticaria,
- tongue and throat swelling,
- abdominal and back pain,
- hemodynamic instability,
- arrhythmias,
- hypoxia,
- rapid-onset sneezing,
- rhinorrhea,
- chest tightness, and
- biphasic urticaria.^{11,20,22}

Nursing implications

To be prepared for a potential hypersensitivity reaction in a patient, it's important that you, the nurse, take a comprehensive approach that includes performing a thorough patient interview. Questions you ask may include:

- Are you allergic to any medications, vaccines, foods, or cosmetics?
- Does anyone in your family have allergies? Do you have seasonal allergies?
- Are you allergic to latex?

- Have you ever had any allergic reactions before, during, or after any medical procedures or surgery?
- Can you describe the symptoms of the allergic reaction? How was the reaction treated?
- Did you take any medications?
- Did you go to an emergency department?
- How severe was the reaction?
- How long did the reaction last?
- Did you have allergy testing after the reaction to verify the allergen?

To provide the best patient outcomes if a patient experiences a hypersensitivity reaction, health care providers who administer contrast agents like those utilized in contract echocardiograms should receive specialized training. Additional training should include cardiopulmonary resuscitation (CPR) and instruction on the institution's protocols for treating hypersensitivity reactions. Having knowledge of where CPR equipment is located and how to call a rapid response is also essential.²⁰

Treatment of a hypersensitivity reaction to PEG

Hypersensitivity reactions to PEG can vary widely in severity and medical management and should be tailored according to the patient's symptoms and response to treatment. For instance, some mild to moderate reactions like urticaria can often be treated with oral diphenhydramine and/or corticosteroids. In contrast, severe reactions like

How to use an EpiPen

First step: After removing the autoinjector from its carrying tube, grasp the unit with the orange tip (injecting end) pointing downward. Form a fist around the unit with the orange tip down; with your other hand, remove the blue safety release cap.

Second step: Hold the black tip near outer thigh. Swing and jab firmly into the outer thigh until a click is heard with the device perpendicular (90° angle) to the thigh. Don't inject into buttocks.

Last step: Hold firmly against the thigh for approximately 10 seconds. Remove the unit from the thigh and gently massage the injection area for 10 seconds.

Call 911 and seek immediate medical attention. Carefully place the used autoinjector unit, needle-end first, into the device storage tube without bending the needle. Screw on the storage tube completely and take it with you to the hospital emergency room.⁵

anaphylaxis, as seen in CG's case, require more intensive interventions, including multiple doses of epinephrine, fluid resuscitation, and IV vasopressors to maintain blood pressure and normal hemodynamic status.

The type of hypersensitivity reaction a patient experiences will also determine a nurse's initial management and interventions. In a mild reaction, like a rash, the goal is to limit exposure to the allergen and provide comfort for the patient. In a more severe reaction like anaphylaxis, the nurse must implement action immediately to ensure the best patient outcome. Initial assessment of the patient's ABCs (Airway, Breathing, Circulation) will reveal the patient's condition and determine the nurse's action. Is the patient's airway patent, is the patient's breathing effective, and is their hemodynamic status stable? Observation of the patient is continuous to identify an increase in symptoms of increasing respiratory distress, hemodynamic instability, or edema. Other interventions include:

- Prompt notification of the rapid response team to alert staff and procure more personnel to assist.
- Initiate IV access.
- Administer supplemental oxygen.
- Prepare for possible intubation.
- Perform CPR if necessary.
- Eliminate or reduce the exposure to the allergen; for example, stopping

an IV medication if that medication is the cause of the reaction, and rapidly flushing the line with normal saline to dilute the allergen.

Post care for a severe anaphylactic hypersensitivity reaction to PEG is a vital element for which nurses have responsibility. Continuous monitoring of vital signs is imperative, as well as maintaining IV access for fluid and medication, continuous hemodynamic monitoring to titrate vasopressors, and ongoing assessment to evaluate if treatment is successful. If a patient has been given epinephrine, they should be monitored in the emergency department for a minimum of 4-8 hours after the initial allergic episode. This is to monitor for a rebound or delayed reaction. As the nurse, you're responsible for accurate documentation of the event to avoid future exposures to the allergen. The patient should also be given proper follow-up instructions, including referrals.⁵

Patient education

Patient education needs to focus on preventing future exposure to PEGs and the subsequent recurring hypersensitivity reactions as well as what to do if a hypersensitivity reaction occurs. Because PEG is included in many everyday products, frequent and unexpected exposure to this allergen may be difficult to avoid, and a reaction may be unexpected when exposure does



PEG allergies have only recently begun to receive widespread, international attention as a cause of severe hypersensitivity reactions.

occur.^{7,16} To prevent future exposure and hypersensitivity reactions, patient education should include:

1. Epinephrine use: Patients and significant others should be instructed on how to self-administer an epinephrine injection. Videos and/or written material should be readily available to share with patients before they leave the emergency department (see *How to use an EpiPen*).⁵
2. Teach patients to consistently check the ingredient list for all prescribed and over-the-counter medications, household items, and personal care products.
3. Patients should be provided with information on apps like Yuka and CodeCheck, which can scan product barcodes or ingredient lists to provide information on ingredients in a product.
4. Maintain an up-to-date list of medications and allergies. This list should be kept in a place of easy access.
5. Encourage patients to wear an allergy alert bracelet.
6. Educate patients that the frequency of hypersensitivity reactions is rare—approximately 1 in 10 000 cases. This education is critical, as fear of an anaphylactic reaction can lead patients to delay or refuse necessary treatments. For example, patients like CG, who have a history of severe allergic reactions, may

experience heightened anxiety when faced with new medications or procedures. Without proper reassurance and guidance, this anxiety could result in postponing or avoiding essential care, potentially leading to suboptimal outcomes. Providing accurate risk information and emotional support can help patients make informed decisions and reduce the likelihood of treatment avoidance due to fear.^{10,13}

7. Encourage patient to inform their pharmacist about their PEG allergy to help prevent future prescriptions that contain PEG.¹³

Multidisciplinary collaboration

Proper communication between the health care team can be a significant factor in assuring patient safety, resulting in improved patient outcomes. Providing treatment for a patient with a PEG hypersensitivity can be very challenging and complicated. It's critical to have communication among multiple disciplines, as lack of knowledge on anyone's part can have a detrimental effect on the patient's outcome. The members of the health care team may include nurses, physicians, pharmacists, radiology department staff, psychologists, and social workers.¹³

Special considerations

Nurses in pediatric and oncology specialties are likely to witness

hypersensitivity reactions from chemotherapeutic agents. Many agents contain PEG, and all have the potential to cause a hypersensitivity reaction. Asparaginase or Peg-asparaginase is a commonly used, effective chemotherapeutic agent used to treat pediatric leukemia. These medications have the potential to cause mild to severe reactions in half of all pediatric patients. Symptoms include loss of appetite, nausea, vomiting, localized erythema, urticaria, and anaphylaxis.²³ It's important to note that diagnosing a hypersensitivity reaction in pediatric patients can prove challenging as signs and symptoms may present less clearly than in adults. For example, young patients may have difficulty articulating nausea, throat swelling, or difficulty breathing, and a health care practitioner may assess these symptoms and think the child is anxious and delay life-saving interventions.^{24,25} To provide the best outcomes, nurses in the pediatric setting should be educated on the unique presentations of hypersensitivity reactions in children, as well as the differences in dosing of commonly used medications such as epinephrine.

Growing awareness and advancing care

This article only highlights the important and timely issue regarding PEG allergies in multiple settings. PEG allergies have only recently begun to receive widespread, international attention as a cause of severe hypersensitivity reactions. As awareness grows, it's essential that new findings are effectively shared with the broader medical and nonmedical community. Although some progress has been made in understanding PEG-related allergic responses, significant knowledge gaps remain—particularly in identifying those patients who may be at risk, testing protocols, clinical intervention guidelines, and comprehensive patient education.

Nurses, who are on the front lines of patient care, play a vital role in recognizing and managing PEG allergies. Their involvement in both clinical practice and research is crucial to improving patient safety and outcomes. Nursing research focused on risk assessment, intervention strategies, and educational approaches will be instrumental in advancing care for individuals affected by PEG allergies. ■

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