Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Table 1
Differential Diagnosis of Case Patient

Chronic spontaneous urticaria
Inducible urticaria (cold, solar, cholinergic)
Urticarial vasculitis
Autoinflammatory syndromes:
CAPS
Schnitzler's syndrome
Drug-induced lesions by recurrent exposure
Eosinophilic fasciitis/cellulitis/panniculitis
Interstitial granulomatous dermatitis
Mastocytosis (urticaria pigmentosa)
Infection (helminths)
Malignancy:
Cutaneous T-cell lymphoma
Non-Hodgkin's lymphoma
Solid organ tumor
Eosinophilic leukemia
Contact dermatitis (allergic vs irritant)

Abbreviation: CAPS, cryopyrin-associated periodic syndrome.

when there are atypical features, for example exotic travel history, association of elementary lesions (papules, crusts, scales, scarring), painful lesion, deep dermal findings, and poor response to antihistamine therapy, such as in our patient with our differential revealed in Table 1.

Loiasis is caused by an infection with the *L loa* filarial nematode that infects the lymphatic and subcutaneous tissue. It is a vector-borne infection that is introduced to the human host through bites of the *Chrysops* deerfly. These flies are native to West and Central Africa including Congo and Cameroon. A common cutaneous finding with loiasis is waxing and waning migratory edema of the subcutaneous tissue that is described as Calabar swelling. This is related to the migratory path that the filarial worm takes through the tissues and is usually found in the extremities adjacent to joints. *L loa* attempts to migrate to the subconjunctival tissue of the eye where it can be visualized and causes local symptoms including pain, pruritus, and photosensitivity. Diagnosis is made by the identification of an adult worm in the subconjunctiva or by Giemsa-stained smear of the plasma. Serologic tests specifically testing for the LISXP1 antigen are available through research laboratories. Although urticaria and other dermatologic findings have been reported in patients with filariasis,[2] this is less often reported with loaiasis.[3] The cutaneous lesions present in our patient did have findings that could be construed as urticarial in that excoriation and pruritus were present. However, the atypical degree of swelling, high-risk travel history, and presence of eosinophilia with significantly elevated total IgE in the absence of a strong history of atopic disease all suggested an alternative etiology. Filariasis infections are uncommonly found in many Western countries and can be challenging to diagnose. History is the most important tool to differentiate a rare diagnosis such as this from the more common conditions such as CSU followed by targeted laboratory evaluation as warranted.

Charles L. Dunn, MD*
Clinton P. Dunn, MD†
Andrew G. Ayars, MD†
*United States Air Force Medical Service Corps
Joint Base Elmendorf-Richardson
Anchorage, Alaska
†Division of Allergy and Infectious Diseases
Department of Medicine
University of Washington
Seattle, Washington
cpdunn08@uw.edu

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Hypersensitivity to different polyethylene glycol–containing products

As we prepare for large-scale vaccination in the middle of a roaring pandemic, we continue to face many challenges—more recently the reported allergic reactions to Moderna and Pfizer-BioNTech coronavirus disease 2019 vaccines containing 2-[(polyethylene glycol)-2000]-N. These reactions have highlighted the potential allergenicity of polyethylene glycol (PEG), a molecule generally considered inert. It is most typically found in laxatives, colonoscopic bowel preparation agents, ultrasonic gels, lubricants, cosmetics, and industrial products. It is also used as an excipient to enhance the chemical stabilization and half-life of a variety of medications, including chemotherapeutic agents.

We report a case of an 11-year-old girl with no previous allergy history who developed symptoms consistent with immediate, Immunoglobulin E (IgE)–mediated hypersensitivity reactions (anaphylaxis) to 2 separate PEG-containing products. The first reaction occurred at the time when she was undergoing chemotherapeutic treatment for T-cell lymphoblastic leukemia. The planned induction and consolidation regimen included intravenous pegaspargase. She tolerated the first 2 doses, given on day 4 and day 18 of the 35-day induction period, without any adverse reactions. However, a few minutes after infusion initiation, she developed diffuse facial flushing and nausea. The infusion was stopped, leading to the quick resolution of symptoms. On reinitiating the infusion, she rapidly developed facial flushing, angioedema, emesis, severe abdominal pain, and shortness of breath. The infusion was stopped, and she was treated with intravenous corticosteroids and antihistamines, leading to complete resolution of symptoms. Given this reaction, her next dose was given by a modified desensitization protocol, including premedication with cetirizine, prednisone, and famotidine, followed by the slow dosing with 1%, 9%, and 90% of pegaspargase. She tolerated this infusion without adverse reaction.

She did well until 5 days later when she acutely developed diffuse urticaria involving the face, legs, arms, back, and trunk. Thereafter, she developed marked lip swelling, severe abdominal pain, and scratchy throat. She received diphenhydramine orally and epinephrine intramuscularly, with subsequent improvement in symptoms. Two days after this event, she again developed intensely pruritic diffuse urticaria, skin flushing of face and extremities, and

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diarrhea. The symptoms improved with scheduled diphenhydramine. A thorough review of the patient's recent new food or medication exposure revealed that she took a dose of over-the-counter PEG-3350 (Miralax, Bayer) 4 hours before the onset of the first reaction, and again took it 2 hours before the onset of the second reaction. She was started on high-dose fexofenadine and instructed to discontinue this PEG-containing product. Serum asparaginase levels obtained revealed undetectable levels, consistent with the drug's typical half-life. After discontinuing PEG-3350, she did not have any recurrence of allergy-related symptoms. Skin prick testing was deferred because of the high potential for a false-negative test result given the recent mast cell degranulation during the acute reaction, and because she was actively undergoing chemotherapy.

The molecular weight of PEG can range from 200 to 35,000 g/mol.[1] The one used in Moderna and Pfizer-BioNTech vaccines has an average molecular weight of 2000 g/mol, whereas over-the-counter and generic PEG used for constipation measures 3350 g/mol and pegaspargase measures an average of 5000 g/mol. In recent years, there has been growing recognition of IgE-mediated, immediate hypersensitivity reactions to PEG.[1] Literature review by Wenande and Garvey[2] identified 37 case reports of an immediate hypersensitivity reaction to PEG-containing products, 28 (76%) of these reports were consistent with IgE-mediated anaphylaxis. Stone et al[1] reviewed the US Food and Drug Administration Adverse Event Reporting System database from 1989 through 2017 and noted 133 reported events of anaphylactic reaction or shock with PEG, and suggested an average of 4 cases per year of PEG-associated anaphylaxis with laxative use or colonoscopy preparation, highlighting that the incidence of these reactions is more common than recognized. When given intravenously, pegaspargase has an approximate half-life of 5.3 days and is recognized for a high incidence of drug-induced reactions.[3] A large trial reported that systemic hypersensitivity reactions occurred in 5.4% of intramuscular and 3.2% of intravenous infusion groups, with most reactions occurring during the second or third dose.[4]

Non–IgE-mediated mechanisms can also lead to anaphylaxis. One such important pathway described in animal models and clinical studies is the complement activation–related pseudoallergy to liposomal pegylated nanoparticle–based pharmaceutical preparations, in which anti-PEG IgM and IgG can trigger complement activation and production of C3a and C5a (anaphylatoxins), which then mediate a powerful immunologic response resulting in anaphylaxis.[5,6] Increasing seropositivity to PEG in healthy individuals and those with allergy has been reported in the literature, despite a lack of evidence that these antibodies lead to an immunogenic or anaphylactic response in all cases. To date, most commercially available anti-PEG assays have lacked specificity with minimal to no diagnostic use in clinical settings.[7] A recent case series proposed that individuals can develop a reaction to PEG from 1 molecular weight category but may be able to tolerate another. Moreover, progressive exposure to a similar molecular weight category may increase the risk of severe allergic reactions. Two of the 5 patients who underwent intradermal testing developed anaphylaxis, and 1 patient had a systemic reaction after skin prick testing, exhibiting the need for considerable caution when proceeding with skin prick and intradermal testing.[8]

This clinical case of an 11-year-old girl with anaphylaxis to 2 different PEG-containing medications, first given intravenously and second by the oral route, illustrates the potential for adverse reaction with different administration routes and molecular weights of PEG. As such, it highlights the importance of identifying previous potential hypersensitivity reactions to PEG-containing products when obtaining a history. This is of particular significance now, as PEG continues to be more frequently included in medication and vaccine development, coinciding with increasing reports of allergic or anaphylactic reactions. Furthermore, subsequent PEG exposures, such as repeated vaccinations, may increase sensitization, resulting in a higher risk for IgE-mediated hypersensitivity reaction.[1]

If a patient's clinical history is consistent with IgE- or non–IgE-mediated anaphylaxis to a PEG-containing product, we suggest the avoidance of pegylated drugs if a suitable alternative is available. If the patient's reported reaction is ambiguous, the medication or vaccine of concern should be given in a clinically monitored setting under the supervision of an experienced medical team, with full access to all appropriate anaphylaxis-related medications. This also underscores the need for a reliable and safe diagnostic tool to accurately identify PEG hypersensitivity.

Muhammad Bilal Khalid, MD*
Vanessa Bundy, MD, PhD†
*National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
†Department of Allergy and Immunology, Children's National Hospital, Washington, District of Columbia
muhammad.khalid@nih.gov

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Polyethylene glycol and polysorbate skin testing in the evaluation of coronavirus disease 2019 vaccine reactions

Early report

In December 2020, the US Food and Drug Administration (FDA) issued emergency use authorizations for coronavirus disease 2019 (COVID-19) vaccines from Pfizer-BioNTech and Moderna, and widespread vaccination is ongoing. Contraindications to

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