Polyethylene Glycol–Induced Systemic Allergic Reactions (Anaphylaxis)

Priya Sellaturay, MRCP, Shuaib Nasser, FRCP, and Pamela Ewan, FRCP *Cambridge, United Kingdom*

Polyethylene glycols (PEGs) or macrogols are hydrophilic polymers found in everyday products such as foods, cosmetics, and medications. We present 5 cases of confirmed PEG allergy, which to our knowledge is the largest case series to date. Four of the 5 cases developed anaphylaxis to medications containing PEGs, with 1 near-fatal case resulting in cardiac arrest. Skin tests were undertaken to the index medications and to PEGs of different molecular weights. Three were confirmed with positive skin prick test result to PEG, 1 confirmed with a positive intradermal test result, and 1 confirmed after positive oral challenge. Two patients developed anaphylaxis following intradermal test to PEG and 1 a systemic allergic reaction (without hypotension or respiratory distress) following PEG skin prick tests. Before diagnosis, all 5 patients were mislabeled as allergic to multiple medications and their clinical management had become increasingly challenging. An algorithm is proposed to safely investigate suspected PEG allergy, with guidance on PEG molecular weights and skin test dilutions to minimize the risk of systemic allergic reaction. Investigation carries considerable risk without knowledge and informed planning so should only be conducted in a specialist drug allergy center. **(J Allergy Clin Immunol Pract 2021;9:670-5)**

Key words: *PEG allergy; Drug allergy; Skin test to PEG and anaphylaxis*

INTRODUCTION

Polyethylene glycols (PEGs) or macrogols are hydrophilic polymers used widely in pharmaceuticals. They are also used in medical products (eg, wound dressings and hydrogels), household products (eg, detergents and polishes),[1] food (eg, preservatives to food supplements),[2] and cosmetic products (as emollients and emulsifiers) due to their water-soluble properties.

PEGs have molecular weights (MWs) between 200 and 35,000 kDa. PEGs with a low MW (<400) are usually clear viscous liquids, but those with a high MW (>1000) are usually opaque solids and powders. Products with a MW more than 100,000 are referred to as poly(ethylene oxide).[3] Pharmaceutical products such as laxatives and bowel preparations (lavage solutions used for whole-bowel irrigation before colorectal surgery)[4] often contain PEG 3350 or PEG 4000. PEGs are found in tablet binders, parenteral liquid preparations, suppositories, and skin lubricants.[1] Also, pegylation (coating the surface of nanoparticles) improves systemic drug delivery. Similarly, PEGs are present in cosmetics, for example, creams, facial products, and baby wipes. MW labeling of PEGs for pharmaceuticals versus cosmetic products differs. The numerical value in cosmetic products refers to the average number of ethylene oxide units, whereas in medications, it refers to the average MW calculated by multiplying the number of ethylene oxide units by its atomic mass (44 Da). For example, PEG 75 is approximately the same weight as macrogol 3350 ($44 \times 75 = 3300$).[1]

There is increasing awareness of systemic allergic reactions (SARs) to PEGs, which can vary from mild SARs to life-threatening anaphylaxis. PEG can be referred to as "a hidden allergen." A reported death following PEG-induced anaphylaxis was reported in Dublin, Ireland. A 24-year old man was originally given a glucocorticoid injection containing PEG and developed urticaria. A year later, he was given a second glucocorticoid injection and died from anaphylaxis.[5]

Our experience and that of other authors[1] has shown that PEGs' potential to cause anaphylaxis increases with higher MWs and concentration. Therefore, when PEGs or macrogols are listed as drug excipients unless the MW and amount of PEG are stated it can prove frustratingly challenging to investigate suspected allergic reactions.

Four cases of anaphylaxis, as defined by the National Institute of Allergy and Infectious Disease, and 1 case of a SAR (without hypotension and respiratory distress)[6] to PEG were confirmed by skin tests, the largest case series to date.

An algorithm to investigate suspected PEG-induced SARs is proposed and includes the source of reagents, skin test dilutions, and methods used to grade the skin test results.

CASE 1—SKIN PRICK TESTS CAN CAUSE A SYSTEMIC REACTION

A 51-year-old woman with a history of contact dermatitis to cosmetics presented following anaphylaxis to medroxyprogesterone acetate (containing PEG 3350 and polysorbate 80) (Depo-Provera; Pfizer, Kent, UK) and a SAR to the laxative

Department of Allergy, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication May 17, 2019; revised September 7, 2020; accepted for publication September 13, 2020.

Available online October 1, 2020.

Corresponding author: Priya Sellaturay, MRCP, Department of Allergy, Cambridge University Hospitals NHS Foundation Trust, CB2 0QQ Cambridge, UK. E-mail: priya.sellaturay@addenbrookes.nhs.uk.

2213-2198

https://doi.org/10.1016/j.jaip.2020.09.029

Abbreviations used
IDT- Intradermal test
IM- Intramuscularly
IV- Intavenous
MW- Molecular weight
PEG- Polyethylene glycol
SAR- Systemic allergic reaction
SPT- Skin prick test

Moviprep (PEG 3350, ascorbic acid; potassium chloride; sodium ascorbate; sodium chloride and sodium sulfate) (Norgine, Middlesex, UK).

Within minutes of receiving medroxy-progesterone acetate, she became light-headed and developed generalized pruritus, swelling of her hands and feet, profuse vomiting, and profound hypotension. She received 0.5 mg adrenaline intramuscularly (IM) and recovered. On another occasion, she developed generalized erythema and pruritus and mouth angioedema immediately following 4 sips of Moviprep and was treated with intravenous (IV) hydrocortisone.

Skin prick tests (SPTs) were sequentially undertaken to PEG dilutions of PEG 200 (10%), 400 (10%), 3350 (50%), 4000 (10%) (Sigma-Aldrich, Dorset, UK), and 20000 (10%; Santa Cruz Biotechnology, Dallas, Tex) and Moviprep (10%; Norgine). SPT wheals took 15 to 30 minutes to develop and were strongly positive to PEG 3350 (50%) (wheal 10 mm/flare 30 mm), 4000 (10%) (wheal 8 mm/flare 30 mm), and 20000 (10%) (wheal 15 mm/flare 30 mm) and positive to Moviprep (10%) (wheal 6 mm/flare 25 mm).

Following the completion of all SPTs, she developed facial flushing and 6 urticarial lesions on her neck, back, and abdomen. She was treated with oral cetirizine syrup and then IV hydrocortisone and chlorpheniramine without further sequelae.

CASE 2—ALLERGIC PATIENTS MAY HAVE AN INDIVIDUAL MW THRESHOLD

A 42-year-old woman developed generalized urticaria and lip angioedema after 2 Gaviscon Double Action tablets (sodium alginate, sodium bicarbonate, calcium carbonate, and PEG 20000) (Reckitt Benckiser, Slough, Berkshire, UK). She was successfully treated with oral glucocorticosteroids and chlorpheniramine in an emergency department. She had previously tolerated Gaviscon Peppermint Liquid (sodium alginate, sodium bicarbonate, and calcium carbonate) (Reckitt Benckiser, Slough) but had never previously taken Gaviscon Double Action tablets. The only difference noted between the 2 medications is that Gaviscon Double Action contains PEG 20000, but the liquid version does not.

SPT and intradermal test (IDT) results to Gaviscon Peppermint Liquid (SPT undiluted; IDT 1:100) and Gaviscon Double Action tablets (SPT 25 mg/mL; IDT 1:100) were negative, and she passed oral challenge to Gaviscon Peppermint Liquid. She was then challenged with 2 Gaviscon Double Action tablets on another visit and within 1 hour became agitated and pruritic and developed urticarial wheals on her leg, facial flushing, and cough. She immediately received IM adrenaline, IV hydrocortisone, IV chlorpheniramine, nebulized salbutamol, and ipratropium bromide. Serum tryptase was normal. She tolerated an oral challenge with Movicol (potassium chloride, sodium chloride, sodium bicarbonate, PEG 3350; Norgine).

There was a delay of 1 year in confirming the MW of PEG in the tablets from Reckitt Benckiser. During this time she had a transient ischemic attack and was started on clopidogrel (PEG 4000; Teva, Eastbourne, East Sussex, UK) and atorvastatin 40 mg (PEG 8000; Ranbaxy, Hayes, UK), which she tolerated. However, she did react to bisacodyl 5 mg (PEG 6000; Dulcolax GR; Sanofi, Berkshire, UK), developing a cough, dyspnea, and pruritus, which resolved with an H1-antihistamine.

Results of SPT performed to PEG 200, 400, 3350, 4000, 20000, and polysorbate 80 (dilutions of 0.01%, 0.1%, 1%, and 10%) were negative. PEG IDT (0.01%) results were also negative.

However, 30 minutes after completing the IDTs she became agitated and developed a cough, urticaria on her upper extremities, and hypotension (systolic 80 mm Hg). She was treated with IM adrenaline, IV chlorpheniramine, and hydrocortisone. Her observations improved quickly, and tryptase levels measured immediately and at 1 hour and 1.5 hours were 5, 4, and 4 ng/mL, respectively (baseline 3.2 ng/mL).

CASE 3—AMOUNT OF PEG EXPOSURE AS WELL AS MW DETERMINES THRESHOLD FOR ALLERGIC REACTIONS

A 52-year-old woman had 3 reactions to medications. The first occurred when she immediately developed angioedema of her face, lips, and hands with dyspnea after taking an unknown tablet (not aspirin) before coronary angiography.

The second episode occurred on day 4 of taking Malarone (atovaquone, proguanil hydrochloride, PEG 400 and 8000) (GlaxoSmithKline, Middlesex, UK) when she developed nausea, facial erythema, bilateral hand angioedema, and dyspnea. The third reaction followed IM methylprednisolone acetate (Depo-Medrone, PEG 3350) (Pfizer), with immediate rhinitis, flushing, and pruritus of her palms and feet and light-headedness. She required 2 doses of 0.5 mg IM adrenaline, hydrocortisone, and chlorpheniramine. She gave a prior history of allergic conjunctivitis to certain moisturizers (although we were unable to establish whether they contained PEG).

SPTs were undertaken to methylprednisolone acetate (40 mg/mL; Pfizer), Malarone (250 mg/mL; GlaxoSmithKline), and PEG 200 (10%), 400 (10%), 3350 (50%), 4000 (10%), and 20000 (0.001%).

SPT results were positive to Malarone (250 mg/mL) (wheal 6 mm/flare 20 mm), PEG 3350 (50%) (wheal 3 mm/flare 6 mm), 4000 (10%) (wheal 4 mm, flare 16 mm), and 20000 (0.001%) (wheal 5 mm, flare 30 mm).

CASE 4—FATAL REACTIONS CAN OCCUR IN THOSE ALLERGIC TO PEG

A 20-year-old man presented following near-fatal anaphylaxis after taking Gaviscon Double Action tablets (PEG 20000). Thirty minutes after taking 2 Gaviscon Double Action tablets, he developed periorbital swelling and nasal congestion followed by generalized urticaria, dyspnea, and cardiac arrest in hospital. He was successfully resuscitated and taken to the intensive care unit for further monitoring.

He regularly takes mesalazine MR (PEG 6000) (Octasa; Tillotts Pharma, Lincolnshire, UK) without reaction.

TABLE I. Summary of investigations in 5 cases of PEG allergy and causative drugs

Case	Age (y)/sex	Index reaction to drug	Drug(s) cause	SPT	IDT	GR to skin test	
						SPT	IDT
1	51 F	Anaph	Medroxy-progesterone acetate (PEG 3350, Polysorbate 80) Moviprep (PEG 3350) Cosmetic	+ 3350 + 4000 + 20k + Moviprep	ND	+ U, E, Pr	ND
2	42 F	SR	Gaviscon Double Action (PEG 20k) Bisacodyl (PEG 6000)	− 200 − 400 − 3350 − 4000 − 20k	−200 −400 −3350 −4000 −20k	−	+ Anaph
3	52 F	Anaph	Unknown Malarone (PEG 400 & 8k) Methylprednisolone acetate (PEG 3350) Cosmetic	+ 3350 + 4000 + 20k + Malarone	ND	−	−
4	20M	Near- fatal anaph; cardiac arrest	Gaviscon Double Action (PEG 20k)	+ 20k	ND	−	−
5	70 F	Anaph	Moviprep (PEG 3350) Phenoxy-methylpenicillin (PEG 6000) Clopidogel (PEG 6k) Aspirin (NK)	− Penicillins − RCM − 4000 − 20k	+ 20k	−	+ Anaph

Anaph, Anaphylaxis; *E*, erythema; *F*, female; *GR*, generalize reaction; *k*, thousands; *M*, male; *ND*, not done; *NK*, not known; *Pr*, pruritus; *RCM*, radiocontrast media; *SR*, systemic reaction (without cardiac and airway compromise); *U*, urticaria; +, positive; −, negative.
MW above 4000 expressed as thousands.

Results of SPTs undertaken to PEG 400, 3350, 4000 (dilutions 0.1%, 1%, and 10%), PEG 20000 (0.1% and 1%) and polysorbate 80 and poloxamer 407 (10%; Sigma-Aldrich) were positive only to PEG 20000 at 1% dilution (wheal 4 mm, flare 16 mm).

As he tolerates medications with PEG 6000 following the reaction, this was established as the threshold level and he has avoided medications with PEG MW above 6000.

CASE 5—EXTREME CAUTION IS ADVISED WITH SKIN TEST TO PEG ESPECIALLY IDTs

A 70-year-old woman had 4 reactions to different medications. The first occurred after taking Moviprep (Norgine, Middlesex, UK). She took 3 sips and immediately developed plantar and groin pruritus and dyspnea, and became light-headed; no treatment was given.

Within 30 minutes of the first tablet of a course of penicillin, she developed plantar and groin pruritus, then generalized pruritus. She stopped the penicillin.

Her most severe reaction occurred during admission with chest pain and dyspnea. A computed tomography pulmonary angiogram with iohexol contrast (Omnipaque; GE Healthcare, AS, Oslo, Norway) was normal. She was treated for an acute coronary event with 75 mg clopidogrel (Sanofi, Paris, France) and fondaparinux (Aspen, Dublin, Ireland). Ten minutes later she became flushed and developed generalized pruritus and urticaria on the trunk and groin. No treatment was given. Two days later she had a computed tomography angiogram and immediately after iohexol developed plantar pruritus, generalized pruritus, dyspnea, profound hypotension (systolic 35 mm Hg), and tachycardia of 200 bpm. She was treated with IM adrenaline, IV hydrocortisone, chlorpheniramine, and fluids. She was successfully resuscitated and transferred to the intensive care unit for monitoring. An immediate tryptase was 32 ng/mL (baseline 10 ng/mL).

SPTs were undertaken to undiluted concentrations of benzyl penicilloyl-polylysine (SPT/IDT: 0.04 mg/mL), minor determinants mixture (SPT/IDT: 0.5 mg/mL) (major and minor determinants of penicillin, respectively) (Allergy Therapeutics, Worthing, UK), amoxicillin, (SPT: 200 mg/mL, IDT: 20 mg/mL; Wockhardt, Wrexham, UK), benzypenicillin (SPT: 150 mg/mL, IDT: 15 mg/mL; Genus, Berkshire, UK), flucloxacillin (SPT: 50 mg/mL, IDT: 5 mg/mL; Fresenius Kabi, Cheshire, UK), co-amoxiclav (SPT: 200 mg amoxicillin, and 40 mg clavulanic acid/mL, IDT: 20 mg amoxicillin, and 4 mg clavulanic acid/mL; Bowmed Ibisqus, Wrexham, UK), iohexol (Omnipaque SPT: 300 mg/mL, IDT: 30 mg/mL; GE Healthcare), iodixanol (Visipaque SPT: 270 mg/mL, IDT: 27 mg/mL; GE Healthcare), iopamidol (Niopam SPT: 370 mg/mL, IDT 37 mg/mL; Bracco, High Wycombe, UK), iomeprol (Iomeron SPT: 300 mg/mL, IDT 30 mg/mL; Bracco), and PEG 4000 and 20000 (SPT/IDT: 1%). All SPT results were negative, and therefore IDTs were undertaken to these agents, resulting in a positive reaction to PEG 20000 (1%). An hour after IDT she developed generalized pruritus, chest tightness, and dyspnea. She was treated with IM adrenaline and oral cetirizine and admitted overnight for observation. An immediate tryptase level was raised at 36 ng/mL.

On review of each of her reactions, we concluded that PEG caused the first reaction involving Moviprep, containing PEG 3350. General practitioner summary records confirmed that the second reaction was triggered by phenoxymethylpenicillin (Sandoz, Surrey, UK), which contains PEG 6000. The third reaction following clopidogrel and fondiparanux was felt to be secondary to clopidogrel, because the Sanofi brand of clopidogrel contains PEG 6000, whereas fondiparanux does not. Finally, the reaction during computed tomography angiogram could have

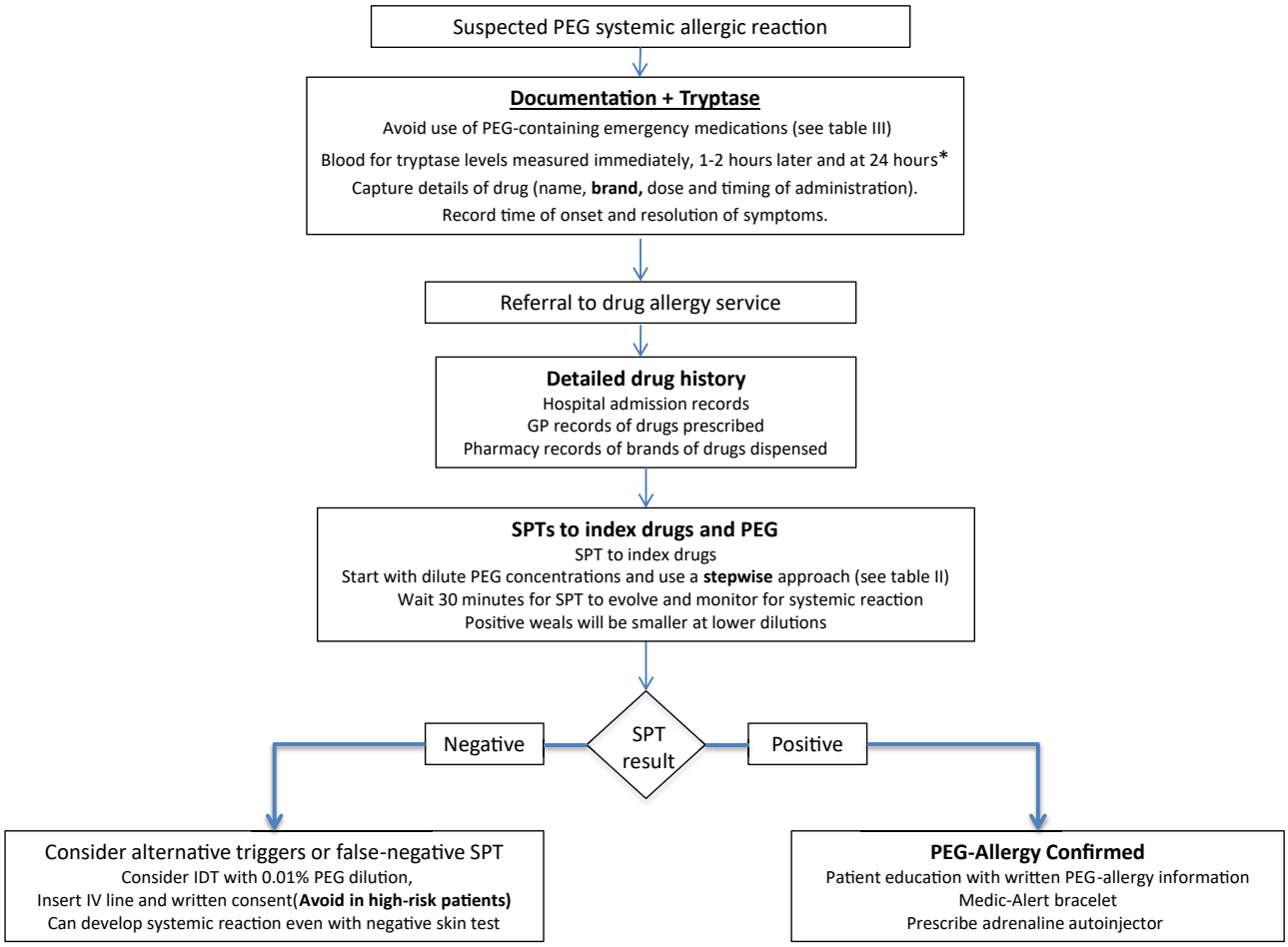

FIGURE 1. Algorithm for the investigation of suspected PEG SARs. *Twenty-four-hour sample can be done by allergy clinic.

been caused by aspirin 300 mg because some brands of aspirin 300 mg contain PEG 6000; however, the hospital was unable to confirm the brand of aspirin given to the patient. No other agent administered contained PEG and SPT and IDT results to other agents were negative.

DISCUSSION

Wenande and Garvey[1] reviewed all the case reports of immediate hypersensitivity to PEG published between 1977 and 2016. Of the 37 cases reported, 76% met the criteria for anaphylaxis.[1] Patients report reactions to different brands of medications and some to cosmetics containing PEG.

Our cases demonstrate that each PEG-allergic subject has an individual threshold level dependent on MW in combination with the amount of PEG ingested.[1] For example, case 4 reacted to MW 20000, but tolerated medications containing PEG 6000 and was therefore advised to avoid medications with MW above 6000. Our cases also show that investigation carries a high risk of anaphylaxis. We were unable to determine the amount of PEG contained in each of the medications that gave rise to allergic reactions but consider it likely that the amount ingested as well as MW is an important factor determining whether an allergic reaction occurs. Tablets with PEG coating may be less allergenic, because there is a smaller amount ingested.

TABLE II. SPT protocol for PEGs

PEG MW	Step 1	Step 2	Step 3
400	0.5%		
3350	0.1%	1%	10%
4000	0.1%	1%	10%
8000	0.1%	1%	10%
20000	0.1%	1%	10%

PEG obtained from Sigma-Aldrich (diluent phenol saline). Each step carried out sequentially with intervals of at least 30 min.

The onset of SAR and anaphylaxis to PEG is typically rapid and severe. Common symptoms include pruritus, flushing, urticaria, and angioedema. Hypotension occurs in severe cases with airway symptoms of chest tightness and dyspnea.

Cases were listed in chronological order starting in 2016, and our method of investigation was modified after each case, culminating in the algorithm and skin test guideline provided. We have included a summary of the cases (Table I).

An algorithm is proposed to diagnose PEG allergy (Figure 1). This includes obtaining a detailed history of medications taken,

TABLE III. Emergency drugs containing PEG

PEG-containing drugs	Non–PEG-containing emergency drugs
Cetirizine tablets (4000)	Cetirizine syrup
Telfast tablets (400)	Chlorpheniramine tablets/syrup
Loratadine 10 mg Orodispersible tablet (Sandoz) (Polysorbate 80)	Hydrocortisone
	Soluble/nonsoluble prednisolone (excluding gastroresistant)
	Adrenaline
	Methylprednisolone
	Other forms loratadine tablets/syrup

Always check before giving rescue and new medications.

their brand and excipients, and MW of PEG. In many cases, it is necessary to obtain hospital and emergency department records to confirm time of administration of each drug, time course of onset, and resolution of symptoms and emergency treatment administered.[7] Tryptase levels should be measured within 30 minutes of the reaction and 1 to 2 hours later, with a baseline reading more than 24 hours later.[8] It is imperative to confirm the brand of the index drug causing each reaction to determine whether PEG is present and its MW. In addition, it is important to take a thorough drug history, confirming usual medications (including brands) taken and tolerated to determine, where necessary, each patient's individual MW threshold.

If PEG allergy is suspected, the patient should be referred to a specialist drug allergy service for SPT to PEG, because this poses a higher risk for SAR than do other types of drug allergy investigation.

From our experience, patients who are PEG allergic are at risk of systemic reactions to SPT (2 of 5 cases). This occurred with high concentrations of PEG and always with higher MWs. SPT wheals develop slower than biological wheals, and can take 30 minutes to evolve, and SPTs produce small wheals at lower concentrations. Therefore, skin prick testing should begin with dilute concentrations of PEG using a stepwise approach, and waiting at least 30 minutes before progressing to the next concentration to reduce the risk of a reaction. We have included guidance for SPT concentrations and MWs undertaken in our clinic (Table II).

IDTs in PEG-allergic patients who have negative SPT results can cause systemic reactions (as in 2 of 5 of our cases who underwent IDT) and therefore should be undertaken with considerable caution by starting with low MWs at low concentration. Patients should provide a formal consent, because the risk is similar to a challenge test, and patients should be cannulated before IDTs. IDTs should be avoided or undertaken only with special precautions in patients with cardiovascular risk, multiple comorbidities, older patients, as well as those who have had severe hypersensitivity reactions. Wenande and Garvey[1] recommend that intradermals if undertaken should be undertaken at 0.01% dilution. SPT and IDTs were undertaken in 4 control patients who were not allergic to PEG with negative results.

Patients diagnosed with PEG allergy will find it challenging to avoid PEG-containing products especially if their allergic threshold is at a low MW, because this increases the number of medications to be avoided. Therefore, it is vital to investigate for PEG allergy only if there is a high index of suspicion, rather than screening large numbers of patients, because this may adversely impact the vigilance required during investigation. Establishing PEG MW thresholds provides additional valuable information allowing individual risk-assessment.

Emergency medications used to treat anaphylaxis may contain PEG. We have compiled a list of emergency anaphylaxis medications that contain PEG (Table III) and that are safe to use; however, these are formulations of medications used in the United Kingdom and may differ around the world and require regular updating. As formulations change, it is important to check excipients before prescribing and not to use generic prescribing. Health care professionals may avoid prescribing "any" medication in these patients when they are confronted with a nonallergic emergency, resulting in inequitable access to health care. Therefore, each hospital should have a PEG-free emergency drug list, dependent on local availabilities, which should be regularly checked and updated.

Patient education is paramount; they need to be suspicious of all new medications prescribed and even new supplies of existing prescriptions. In our experience, when the diagnosis is confirmed, patients are scrupulous with new medications or brands. Patients should also be informed of their individual threshold level.

As PEG allergy is emerging, with little awareness among medical professionals, it is important to carefully manage these patients and prevent deaths. Emergency departments should be aware of PEG allergy and check medications before treating PEG-allergic patients in the acute setting. Written patient information should also be provided. General practitioners and pharmacists should also check the brands of medications that contain PEG before prescribing or dispensing medications to PEG-allergic patients. Electronic medical record developers will need to update their software to facilitate accurate PEG allergy recording and avoidance of PEG-containing drugs.

Once confirmed, details of the PEG allergy should be added to the electronic medical record, and a copy provided to the patient, and copied to the general practitioner.[7,8] This should identify the PEG MWs to be avoided and list the medications to which the patient has reacted. It should also highlight medications containing PEG (with MWs) that should not be used to treat acute allergic reactions and a list of medications that can be used safely. The patient should be given a copy of the clinic letter so this can be presented to physicians involved in their future management.

Normally, an adrenaline autoinjector is not indicated in drug allergy because the drug is avoidable.[7,8] However, PEG is not easily avoidable and therefore we recommend prescribing an adrenaline autoinjector in conjunction with a written emergency treatment plan.

This is the largest case series of PEG-allergic patients confirmed with skin tests. PEG is a high-risk "hidden" allergen, usually unsuspected, and can cause frequent allergic reactions due to inadvertent reexposure. Allergy investigation carries the risk of anaphylaxis and should be undertaken only in specialist drug allergy centers. Patients require detailed written information with instructions on how to keep them safe.

REFERENCES

1. Wenande E, Garvey LH. Immediate-type hypersensitivity to polyethylene glycols: a review. Clin Exp Allergy 2016;46:907-22.
2. EFSA Panel on Food Additives and Nutrient Sources added to Food (EFSA ANS Panel)Younes M, Aggett P, Aguilar F, Crebelli R, Dusemund B, et al. Refined

exposure assessment of polyethylene glycol (E 1521) from its use as a food additive. EFSA J 2018;16:e05293.
3. Bailey FE, Koleske JV. Poly (Ehtylene Oxide). New York: Academic Press; 1976.
4. Bowden TA, DiPiro JT, Michael KA. Polyethylene glycol electrolyte lavage solution (PEG-ELS): a rapid, safe mechanical bowel preparation for colorectal surgery. Am Surg 1987;53:34-6.
5. Roseingrave L. Verdict of medical misadventure in case of fatal allergic reaction. Available from: https://www.irishtimes.com/news/crime-and-law/courts/coroners-court/verdict-of-medical-misadventure-in-case-of-fatal-allergic-reaction-1.3324937. Accessed December 12, 2017.
6. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006;117:391-7.
7. Mirakian R, Ewan PW, Durham SR, Youlten LJ, Dugué P, Friedmann PS, et al. BSACI guidelines for the management of drug allergy. Clin Exp Allergy 2009;39:43-61.
8. Dworzynski K, Ardern-Jones M, Nasser S. Diagnosis and management of drug allergy in adults, children and young people: summary of NICE guidance. BMJ 2014;349:4852.