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.

60, female	(1) Docetaxel (PS 80) (2) Paclitaxel (macrogolglycerol ricinoleate) (3) TriamHEXAL (PEG 4000, PS 80) and MepiHEXAL (4) Colon cleansing solution (PLENVU (=PEG 3350) (5) Contrast media	(1) Generalized itching (2) Nausea, clouding of consciousness, rash (3) 10 min after injection generalized itch, rise in blood pressure, sensation of heat (4) Generalized urticaria (5) After 20 min generalized urticaria, sensation of heat	SPT: negative to PEG 2000, 4000, 6000, 3350, PS 80, Comirnaty, Spikevax, Vaxzevria, Vaccine Janssen, TriamHEXAL, Gadotersäure (Dotagraf), Gadoxetsäure (Primovist), Gadobutrol (Gadovist)	IDT: positive to Comirnaty Negative to PEG 2000, 4000, 6000, 3350, PS 80, Spikevax Vaxzevria, Vaccine Janssen, TriamHEXAL, Gadotersäure (Dotagraf), Gadoxetsäure (Primovist), Gadobutrol (Gadovist)	BAT: positive to DMG-PEG (BühlMann), Comirnaty, Spikevax Borderline positive to PEG 2000 (BühlMann), PEG 2000, 4000, 6000, 3350, PS 80 Vaxzevria, Vaccine Janssen Negative to PEG 200	Tolerated OPT with PEG 4000 up to 900 mg. Systemic reaction at OPT with PEG 3350 at 38 g (tolerated up to 13 g of PEG 3350): urticaria, tingling of fingertips, shivering, nausea, stomach/ abdominal cramps	No vaccination

BAT, Basophil activation test; *IDT*, intradermal test (wheal ≥5 mm); *OPT*, oral provocation test; *NTX*, not tested, *PEG*, polyethylene glycol; *PS*, polysorbate; *SPT*, skin prick test (wheal ≥3 mm).

Reply to "Variability of eliciting thresholds in PEG allergy limits prediction of tolerance to PEG-containing mRNA COVID vaccines"

To the Editor:

We thank Mathes et al[1] for their correspondence regarding our article "Safety of COVID-19 vaccination in patients with polyethylene glycol allergy: a case series."[2] The authors raise the interesting issue that some polyethylene glycol (PEG)-allergic patients with low reaction thresholds and systemic reactions to PEG skin testing could be at risk of reacting to messenger RNA (mRNA) COVID-19 vaccines, which contain very small amounts of PEG 2000 linked to a lipid. Although this hypothesis is plausible, we would like to point out that the only mean of ascertaining this risk is to vaccinate these patients with an mRNA vaccine.

In our case series,[2] we identified 3 patients with a positive skin test to an mRNA vaccine who then tolerated the vaccine (one of them—patient 1—in a single dose on 2 occasions). This patient also had a low reaction threshold as he was positive on skin prick testing (SPT) to PEG 3350 at a concentration of 0.7 mg/mL.

Since the publication of the case series, we evaluated 2 other patients with a positive SPT to PEG 3350 (Table I). One accepted vaccination and tolerated an mRNA vaccine in a single dose. In addition, 1 patient (patient 6) from the original case series with a positive SPT to PEG 3350 tolerated an mRNA vaccine in a single dose, which she received as a booster after receiving the AstraZeneca vaccine for her initial immunization (Table I). Hennighausen et al[3] recently published a case report showing tolerance to an mRNA vaccine (in divided doses and with antihistamine premedication) in a patient with a positive basophil activation test to the vaccine and to the PEG 2000 lipid component. Taken together, these findings argue that skin testing and/or a basophil activation test to PEG of any molecular weight or to the vaccine itself does not reliably predict reactivity on vaccine inoculation.

As pointed out by Kelso in a recent review article,[4] important lessons can be learned from the egg allergy and influenza vaccine story: before an allergy to a vaccine constituent is considered a contraindication to this vaccine, allergists need to thoroughly evaluate this risk, which entails provocation testing.

In conclusion, given the high benefits of COVID-19 vaccination, especially with mRNA vaccines, and the reassuring data on their safety,[5,6] even in patients with a documented PEG allergy,[2,3,7] we would encourage allergists to offer supervised administration of mRNA vaccines to PEG-allergic patients either in a single or divided doses.

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TABLE I. Patients with confirmed PEG allergy evaluated for COVID-19 vaccination since publication of the case series

Patient*	Age	Sex	PEG product causing reaction	Clinical manifestations of PEG allergy	Diagnostic tests for PEG allergy	COVID-19 vaccination
6	70	F	PEG 3350 and electrolyte solution (PegLyte) for bowel cleansing before colonoscopy	Lip and tongue angioedema and diffuse urticaria within minutes after ingesting between 3 and 6 g Five years before vaccination	Tested 1 wk before the first dose of AstraZeneca vaccine: PEG 3350 (Lax-A-Day): SPT + (500 mg/mL) (size: 7/7)	Tolerated Pfizer-BioNTech vaccine in a single dose (0.3 mL) Had previously received 2 doses of AstraZeneca vaccine without any reaction
13	39	F	Skin care products containing PEG (MW not specified)	Localized skin pruritus and erythema in contact with product. Dyspnea sometimes associated with skin symptoms Several years before allergy evaluation	At the time of allergy evaluation: PEG 3350 (Lax-A-Day): SPT + (70 mg/mL) (size: 10/30) Pfizer-BioNTech: SPT + (undiluted) (6/15) IDT + (1:100) (15/30)	Refused vaccination to mRNA and AstraZeneca vaccines in a single or divided doses
14	39	F	PEG 3350 and electrolyte solution (PegLyte) for bowel cleansing before colonoscopy	Oral pruritus, diffuse skin pruritus with hives, and mild dyspnea Three years before vaccination	Tested on day of vaccination: PEG 3350 (Lax-A-Day): SPT + (500 mg/mL) (7/25) Pfizer-BioNTech: Not tested	Tolerated Pfizer-BioNTech vaccine in a single dose (0.3 mL). Had previously received 2 doses of AstraZeneca vaccine without any reaction
			Methylprednisolone acetate (Depo-Medrol) intralesional	Diffuse urticaria within minutes of injection Eight years before vaccination	Tested 1 mo after vaccination: Methylprednisolone acetate (Depo-Medrol): SPT + (40 mg/mL) (6/17) Methylprednisolone succinate (Solu-Medrol): SPT- (40 mg/mL) and IDT- (4 mg/mL) Triamcinolone: SPT- (40 mg/mL) and IDT- (4 mg/mL)	

Patients 13 to 14 were evaluated after the publication of the case series.
Size of skin test: first number refers to wheal and second number to flare (mm); when only 1 number is shown, it refers to wheal, and flare was not recorded.
IDT, Intradermal test; *MW*; molecular weight; *PEG,* polyethylene glycol; *SPT*: skin prick test.
*Patient numbering refers to the published case series: Picard et al.[2]

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Anti-IL5/IL5R switching between biologics in patients with severe eosinophilic asthma

To the Editor:

We read with great interest the original article titled as "Long-term therapy response to anti-IL-5 biologics in severe asthma—a real-life evaluation" by Eger et al.[1] We would like to share our opinions on this study.

There is a great need for such studies, and it is a study that will fill the gap in the literature. We would like to thank Eger et al for their contribution to the literature with such a valuable study. Some points mentioned in the article drew our attention. First of all, we think that the criteria for the definition of super-responder are debatable. For example, when a patient with oral corticosteroid (OCS)-dependent asthma has the following criteria, this patient is not considered a super-responder according to the authors' definition:

- The patient's baseline forced expiratory volume in 1 second (FEV1) is low before biological therapy (eg, FEV1: 68%); although there is improvement in FEV1 (eg, FEV1: 78%) after biological therapy, the FEV1 may not rise above 80%, but the need for OCS may disappear completely and Asthma Control Questionnaire (ACQ) <1.5.

Or

- In a patient who initially received 20 mg maintenance prednisolone treatment and had an FEV_1 >80% and ACQ <1.5 in the second year of biological treatment, the maintenance prednisolone dose may be reduced to 4 mg but may not be completely discontinued. On the other hand, according to the authors' definition of super-responder, for example, a patient who was already on low-dose OCS (eg, 4 mg prednisolone) treatment at the beginning and whose prednisolone was discontinued at the end of 2 years after the addition of biological therapy and fulfilling the other super-responder criteria could be considered a super-responder. Considering all these, we think that the super-responder criteria should be more standardized and suitable for daily practice. Another point that draws our attention is that after 2 years of treatment in the super-responder group, it was stated in Table I that comorbidities of chronic rhinosinusitis, nasal polyposis (NP), chronic otitis, and allergic rhinoconjunctivitis were under control with these biologics; however, the control criteria were not defined in this article.

An important finding presented by the authors is that 31% of those with super-responders were shown to be super-responders when they switched from the first biological to another biological. How many of these transitions were partial responder or nonresponder before switch? If it is nonresponder with the first biological but becomes super-responder after switching to the second biological, this will be significant in emphasizing the importance of the transition between anti-IL5/IL5R biologicals.

Another important result in this study is the demonstration that patients in the super-responder group were associated with the absence of NPs, although statistically insignificant. However, some studies have shown that the presence of comorbid NP predicts that severe asthma may respond well to anti-IL5/IL5R monoclonal antibodies.[2-5] In addition, in the Global Initiative for Asthma report, NP is included in the criteria for good response to anti-IL5/IL5R in patients with eosinophilic severe asthma.[6]

Finally, the authors also stated that anti-IL5/IL5R was discontinued in 3 patients because of adverse effects. However, mentioning the adverse effects leading to discontinuation would have been very helpful to the readers.

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