

Online Supplement Table I: Reported cases* of anaphylaxis associated with the live attenuated Oka strain zoster vaccine in patients with coexisting beef, pork, gelatin, or alpha-gal allergy

Case (Year)	Reaction	Associated Allergy	Location
76 Year Old Female (2007)	20 minutes after vaccine receipt at a pharmacy developed anaphylaxis, admitted for overnight hospital stay. Description of the event is limited. Diagnosed as anaphylaxis by treating physician.	Positive specific IgE to Beef, pork, bovine gelatin, porcine gelatin, titers not reported. Reported negative alpha gal sIgE.	Maryland
70 Year Old Female (2008)	Developed life threatening hypotension, shortness of breath, angioedema shortly after vaccine receipt, with overnight hospital stay, treatment not reported. Diagnosed as anaphylaxis by treating physician.	Clinical report of preexisting beef, pork, dairy allergy. sIgE testing and titers not reported. Alpha-gal status and sIgE testing not reported	Arkansas
70 Year Old Female (2009)	Patient developed immediate severe allergic reaction upon receipt of vaccine in a pharmacy. Was taken to the emergency room, received epinephrine for treatment of hypotension. Diagnosed as anaphylaxis by treating physician.	Report of positive testing to gelatin, not reported if testing was skin or sIgE testing. Beef, pork, alpha-gal allergy status, sIgE testing and titers not reported.	Location not reported
61 Year Old Male (2013)	Patient developed disseminated rash shortly after vaccine receipt at a pharmacy. Returned to pharmacy and was given diphenhydramine 25mg. After 10 minutes of observation, patient developed dizziness and syncope. IM epinephrine was administered, and patient was transferred by EMS to hospital. Vital signs not reported.	Clinical report of preexisting beef and pork allergy. Results of sIgE testing and titers not reported.	Virginia
63 Year Old	5 minutes after vaccine receipt, patient developed generalized	Beef, pork, alpha-gal allergy reported.	Maryland

Male (2015)	itching followed by generalized hives and throat discomfort, resolution with diphenhydramine in the emergency department. Diagnosed as anaphylaxis by treating physician.	Reported sIgE porcine gelatin=0.58 kU/L, bovine gelatin <0.10kU/L, alpha-gal=3.70 kU/L	
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***Case Definition:**

1) a provider diagnosis of anaphylaxis or 2) use of published criteria for defining cases of vaccine-associated anaphylaxis when provider diagnosis was not reported.¹

Supplemental References:

A previous report indicates an increased likelihood of gelatin hypersensitivity when alpha-gal allergy is present.² Parenteral route of administration was also reported to increase the likelihood of allergic response, and alpha-gal was detected in gelatin colloids.² In studies of Japanese Encephalitis Virus Vaccine, reductions in gelatin content reduced the likelihood of anaphylaxis.³ In reviewing the original randomized controlled trial of zoster vaccine, there was one episode of an anaphylactic event in a patient who received the gelatin placebo.⁴

An important question is whether there is a reactivity threshold that can be tested to predetermine the likelihood of anaphylaxis to zoster vaccine in patients with alpha-gal allergy. Our patient had high titer alpha-gal IgE antibody and anaphylaxis. In contrast, administration of zoster vaccine without any adverse reaction has been reported in an alpha-gal allergic patient with a lower titer of alpha-gal IgE (alpha-gal sIgE = 6.0 kU/L).⁵

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2. Mullins R, James H, Platts-Mills T, Commins S. Relationship between red meat allergy and sensitization to gelatin and galactose- α -1,3-galactose. *J Allergy and Clin Immunology* 2012; 129:1334-42.
3. Nakayama T, Aizawa C. Change in gelatin content of vaccines associated with reduction in reports of allergic reactions. *J Allergy and Clin Immunology* 2000; 106:591-2.
4. Oxman M, Levin M, Johnson G, Schmader K, Straus S, Gelb L, et al. A Vaccine to Prevent Herpes Zoster in Older Adults. *New England Journal of Medicine* 2005; 352:2271-84.
5. Pinson M, Waibel K. Safe administration of a gelatin-containing vaccine in an adult with galactose- α -1,3-galactose allergy. *Vaccine* 2015; 33:1231-2.