



Cracking the Shell on Egg-Hypersensitive Patients and Egg-Containing Vaccines

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Hens' eggs are a common food in the American diet. They are consumed as a primary food source and added as an ingredient to other foods. In individuals who are hypersensitive to eggs, egg-containing foods can cause mild to severe allergic reactions if ingested. These individuals may also have adverse reactions to vaccines produced on egg media. Vaccines that are created on egg media include those for measles, mumps, and rubella; rabies; yellow fever; and influenza. The authors discuss recent developments in the use of egg-containing vaccines in hypersensitive patients.

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In vaccine manufacturing, enriched media must be used to grow the virus that will be used in the vaccine. A hen's egg or its components are typically used as the enriched medium for growing the viruses that cause measles, mumps, and rubella (MMR); rabies; yellow fever; and influenza. Each virus grows best in a certain area of the egg or in an embryonic culture. When the virus is injected into the egg, the subsequent hole is sealed with gelatin. By growing this infectious pathogen in an egg, the virus becomes less pathogenic to humans,

and its replication rate slows—resulting in a decrease in disease manifestation in the host but still allowing for a host immunogenic response.¹

When the virus is collected from the egg or culture, picogram to microgram amounts of the egg are collected as well. During this process, egg allergen gets introduced into the vaccine, making the vaccine capable of causing allergic reactions, which may be as subtle as a mild local reaction requiring only a topical or oral antihistamine or as severe as anaphylaxis requiring intramuscular epinephrine.² In the present article, we describe the recently updated recommendations for using some of these vaccines in egg-hypersensitive patients.

Measles, Mumps, and Rubella

The MMR vaccine contains attenuated virus that has been grown in chick embryonic fibroblast cell cultures. This vaccine contains picograms to nano-

grams of egg. Most sources agree that the amount of egg in the MMR vaccine is not enough to cause allergic reactions in egg-hypersensitive patients.³

There is the potential for allergic reactions to the MMR vaccine caused by other contents of the vaccine—in particular, gelatin and neomycin. Gelatin may be present in this vaccine at concentrations of 14,500 µg per 0.5 mL of vaccine.⁴ Physicians administering this vaccine should have the best available knowledge, medication, and equipment to manage any allergic reactions that develop in patients.

Rabies

The rabies vaccine contains attenuated virus that has also been grown in chick embryonic fibroblast cell cultures. The vaccine contains micrograms of egg. Although we know of no reliable safety data on the use of the purified chick embryo cell (PCEC) rabies vaccine in egg-hypersensitive patients, this vaccine is contraindicated in patients who are hypersensitive to eggs.⁵

If a rabies vaccine is needed for an egg-hypersensitive patient, alternative vaccines—human diploid cell vaccine (HDCV) or purified Vero cell rabies vaccine (PVRV)—that contain no egg components may be administered.

A patient may be tested for egg hypersensitivity by means of a prick test to observe if there is a cutaneous response. If the test has negative results, the PCEC rabies vaccine may be administered in a graded manner in a setting in which anaphylaxis can be readily recognized and managed. It should be kept in mind that all rabies vaccine formulations may contain as much as 12,000 µg of gelatin per 1 mL of vaccine.⁴ Thus, patients with a history of gelatin hypersensitivity should be evaluated by an allergist or immunologist before administration of this vaccine.

Yellow Fever

The yellow fever vaccine contains a live attenuated yellow fever virus. The virus is grown in chick embryos, and the vaccine may contain micrograms of egg. This vaccine is contraindicated in patients with egg hypersensitivity.

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Testing for a cutaneous response may be performed with the yellow fever vaccine, and the vaccine may be administered in a graded manner. Physicians should be aware of the risk of anaphylaxis and the treatment for this condition (eg, epinephrine should be available). Another concern is the amount of gelatin present in this vaccine—7500 µg per 0.5 mL of vaccine.⁴ As with the rabies vaccine, the yellow fever vaccine requires evaluation for allergic reactions before administration in gelatin-hypersensitive patients.

Influenza

The influenza vaccine contains an inactivated live influenza virus. The virus is grown in chick extraembryonic allantoic fluid. The greatest amount of egg measured in the influenza vaccine is 0.7 µg per 0.5 mL of vaccine.⁶ Most manufacturers list the content of ovalbumin in the package insert. However, the concentration of ovalbumin may differ from year to year and from 1 brand of vaccine to another (Figure).^{6,7} On the basis of results in previous studies, vaccine lots containing less than 1.2 µg/mL of ovalbumin have been tolerated well by egg-hypersensitive individuals. Data regarding the least concentration of egg in the influenza vaccine that will cause an adverse reaction remain unclear.

Recent recommendations by the US Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP) state that the influenza vaccine can be administered to egg-hypersensitive patients without any precautions.⁸ If the patient can ingest lightly cooked eggs (eg, scrambled eggs) without reaction, he or she may receive the vaccine per usual protocol. If the patient develops hives only after ingesting eggs or egg-containing products, they may receive the vaccine but with a 30-minute observation period after the immunization. If any systemic events occur after the ingestion of egg, the patient should be referred to a physician with expertise in managing allergic conditions for further evaluation before immunization. The ACIP recommendations differ from those made by other organizations—including the American Academy of Allergy, Asthma, and Immunology; the American College of

Allergy, Asthma, and Immunology; the Joint Council of Allergy, Asthma, and Immunology; and the National Institute of Allergy and Infectious Diseases—which recommend using split dosing in patients who have had anaphylactic events after ingesting eggs.^{8,9}

The influenza vaccine administered nasally contains 2000 µg of gelatin per 0.2-mL dose, compared to 250 µg of gelatin per 0.5-mL dose when administered intramuscularly.⁴ Physicians administering this vaccine should be aware of the signs and symptoms of anaphylaxis and have appropriate medications available for treatment.

General Precautions

Regardless of recommendations, the potential of any vaccine antigen to trigger anaphylaxis must be respected in susceptible patients. The information on package inserts must be read carefully to determine the amount of ovalbumin present in a vaccine. In patients who are egg-hypersensitive, the vaccine containing the least amount of ovalbumin is recommended.

Anaphylaxis may occur with any antigen. Reaction severity can be influenced by the patient’s sensitivity to the allergen and the amount of allergen administered. When any antigen is administered subcutaneously or intramuscularly in the office, the patient should be kept in the office for at least 30 minutes for observation.⁹ Medical offices and clinics should develop protocols for handling an anaphylactic event. Epinephrine should be readily available.

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Vaccine	Ovalbumin Amount per Package Insert, µg/0.5 mL
Afluria (Merck; Whitehouse Station, NJ)	<1
Agriflu (Novartis; Basel, Switzerland)	<0.4
Fluarix (GlaxoSmithKline; Middlesex, England)	<0.05
FluLaval (GlaxoSmithKline)	<1
FluMist (MedImmune; Gaithersburg, MD)	NA
Fluvirin (Novartis)	<1
Fluzone (Sanofi Pasteur; Lyon, France)	NA

Figure. Concentration of ovalbumin in various influenza vaccines for the 2010 and 2011 seasons.^{6,7} Abbreviation: NA, not available.