

Near fatal anaphylaxis from orally administered gelatin capsule

Michael H. Land, MD^a, Mark D. Piehl, MD, MPH^b, and
A. Wesley Burks, MD^c

Clinical Implications

- Gelatin is a collagen-derived protein that is a common ingredient in many foods, medications, and vaccines.
- A case of near fatal anaphylaxis from a gelatin capsule in a patient with multiple food allergies is reported.

TO THE EDITOR:

Gelatin is a collagen-derived protein and common food ingredient in jellies, gummy candies, frozen desserts, marshmallows, deli meats, and beverages such as juices and wines. In addition to foods, it can be found in cosmetics and pharmaceutical products, including vaccine stabilizers, suppositories, plasma expanders, surgical sponges, and medication capsules. Gelatin is often derived from bovine or porcine sources but may originate from fish. Allergic reactions to gelatin have been reported in the literature, but, given the widespread exposure in everyday foods, the prevalence of true IgE-mediated gelatin allergy is thought to be quite low.

Cases of gelatin-associated anaphylaxis and/or urticaria have been reported from intravenous fluid used as a volume expander,^{1,2} gummy candies,^{3,4} erythropoietin,⁵ vaccinations,⁶ suppositories,⁷ and surgical sponges.⁸ No cases of confirmed allergic reactions from gelatin-containing medication capsules have been reported that we are aware of, although one report suspected gelatin but did not demonstrate sensitization.⁹ We report a patient with multiple food allergies who experienced near fatal anaphylaxis from a gelatin-containing capsule.

The patient is a 6-year 11-month-old girl who has a known history of peanut, tree nut, and shellfish allergy as well as persistent asthma that has been suboptimally controlled. She had pollen-food allergy syndrome from melons and bananas. She developed a febrile illness approximately 24 hours before the reaction occurred, which prompted administration of antipyretics. Her mother noted that ibuprofen had been given numerous times throughout her life (at least 40 times) in tablet form, and she had no history of reactions to medications. On the day of the reaction, she received ibuprofen in tablet form at approximately 5 PM in the afternoon. Because of her illness, she had decreased fluid intake but otherwise did not have other complaints or any asthma symptoms. The child went to sleep that evening but awoke with a tactile fever at 2 AM. She was given 2 Advil Liqui-gels containing ibuprofen 200 mg each (Wyeth, Madison, NJ) for the first time. Within 30 seconds, she complained of oral pruritus, scratching at her mouth. She vomited and then had a syncopal episode. She became flushed and irritable, continued to vomit, and then was limp and cyanotic. She was unresponsive for 3 to 4 minutes, and her pulse weakened until it was not palpable. Her mother, a physician, recognized this as anaphylaxis. Because of her history of food allergy, an

epinephrine auto-injector was available and administered. Her pulse immediately returned. Emergency services arrived at that point and stabilized the patient with intravenous fluids and intravenous diphenhydramine. She was noted to have angioedema of the lips and around the eyes on arrival at the emergency department. After stabilization at the emergency department, she was admitted overnight on diphenhydramine, famotidine, prednisone, and amoxicillin (to treat strep pharyngitis, the cause of her fever). The next day, she was discharged in stable condition.

Her past medical history was significant for shortness of breath and tightness of the chest immediately after the influenza vaccination on 2 occasions, at age 3 and age 4. She had avoided gummy candies and other foods containing gelatin because she disliked them.

The patient was referred to our service for evaluation a week after the event, and a prick-prick skin test was negative to the contents of the gelatin capsule when pricked through the coated surface. A bovine gelatin IgE level returned with a result of 26.4 kU/L, and the diagnosis of gelatin allergy was made. An oral food challenge was deferred, given the severity of the initial reaction. The patient's mother called the pharmaceutical company and discovered that the gelatin used in the product was bovine in origin.

She returned to the clinic 8 months after the initial visit for more complete skin tests but also to provide additional history of another reaction. Two weeks before the follow-up, she had another episode of strep pharyngitis and was complaining of a sore throat. Her mother was avoiding ibuprofen and accidentally gave her a Popsicle (Unilever, London, UK) brand "Slow Melt Mighty Mini" that contains gelatin to delay melting. Within seconds of the first bite, she complained of oral and pharyngeal pruritus and stopped eating the Popsicle. Oral diphenhydramine was given and the symptoms subsided. Skin prick testing was performed in the clinic to 6 gelatin-containing substances, dissolved in 15 mL of warm water (the Popsicle was melted without addition of water). Skin prick tests were positive in 5 of 6 substances as follows: Advil Liqui-gel, 10 × 10-mm wheal (30-mm flare); Knox gelatin (Kraft, Northfield, Ill), 10 × 7-mm wheal (27-mm flare); generic gummy candy, 6 × 5-mm wheal (22-mm flare); Haribo brand (Haribo, Bonn, Germany) Gummi Bears, 12 × 6-mm wheal (34-mm flare); Starburst (Mars, McLean, Va) fruit chew, 10 × 5-mm wheal (34-mm flare); melted Popsicle, negative. Controls were adequate with a negative saline and a histamine with a 5 × 3-mm wheal (30-mm flare).

To our knowledge, this report is the first case of anaphylaxis from ingestion of an oral medication containing gelatin. Allergic reactions to gelatin in foods, cosmetics, pharmaceutical products, and medications are rarely reported complications, given the relatively widespread use of gelatin-containing products and possibly from the low prevalence of true gelatin allergy. Other factors that may influence the incidence of clinical reactions may include differences in allergenicity of the protein due to dose, processing of the allergen, genetic background of the patient, gelatin type (bovine, porcine, or fish origin), and differences in reporting of adverse events (especially from vaccines). The previous reactions to the influenza vaccine could have

represented mild reactions, because some forms of the influenza vaccine can contain as much as 250 μg of gelatin.³ Her underlying illness with fever, fluid hydration status, and history of asthma could have contributed to the severity of her reaction and/or lowered her reaction threshold. Regardless of the cause, the patient's mother correctly identified an allergic reaction and administered epinephrine when the patient became pulseless. We advised the patient to continue avoidance of all types of bovine- and porcine-derived gelatin because of cross-reactivity. Gelatin allergy is an uncommon but real type of food allergy and may present at any time. When considering allergic reactions to medications, it is crucial to also consider food components of the medication that may be the cause of the reactions. With the current rise in the prevalence of atopic disorders and specifically food allergies, we may begin to see more patients with gelatin allergy.

^aDuke University School of Medicine, Durham, NC

^bWakeMed Health and Hospitals, Raleigh, NC

^cUniversity of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

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Corresponding author: Michael H. Land, MD, Southern California Permanente Medical Group, 7060 Clairemont Mesa Blvd, San Diego, CA 92111. E-mail: michael.h.land@kp.org.

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