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Fatal Food Anaphylaxis – registering a rare outcome

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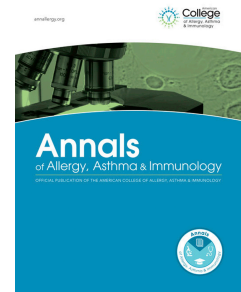
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Title Page

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Fatal Food Anaphylaxis – registering a rare outcome

Deaths due to food allergy are incredibly rare (1), but it is now understood that food is the most commonly identified trigger of anaphylaxis (2). In the United States, deaths from food anaphylaxis are broadly estimated to occur at a rate of 5-200 cases per year (3).

Theoretically, food allergy fatalities are preventable with avoidance measures, immediate use of epinephrine in case of accidental ingestion and could be made less likely with aid from immunotherapy (4). Risk factors associated with a higher chance of fatal food anaphylaxis, such as teen years, delayed epinephrine administration and history of asthma have been established. (5) Despite knowledge of these risk factors and subsequent educational efforts on allergen avoidance and rapid management of anaphylaxis, deaths continue to occur.

Due to its rarity and sudden occurrence in virtually any setting, fatal anaphylaxis to food is notoriously difficult to study. This has impeded a comprehensive approach to its evaluation. Therefore, we sought to clarify the scope of fatal food anaphylaxis in the United States, and to identify potential targets for future intervention.

Since fatal food-induced anaphylaxis can only be studied retrospectively, a focused, permanent, IRB approved registry called The National Food Allergy Death Registry (<https://www.nationalfoodallergydeathregistry.org/>) has been created to monitor and document these fatalities in the United States. This registry seeks to create a single database whereby the

epidemiology of fatal food anaphylaxis can be better understood. To date, the registry constitutes over 100 cases of fatal food anaphylaxis documented from 1983 to present. Each case is identified through national media searches, voluntary submissions and word of mouth, after which it is evaluated for authenticity through a systematic review of available details. The family of the deceased patient is contacted to obtain consent for inclusion in the registry. When consent is obtained, they are interviewed, and a review of the available medical record is completed.

Of 70 cases of fatal food anaphylaxis reported to the registry in the past 10 years, 33% were among females, and 67% were among males. The average age of fatal food anaphylaxis patients was 18 with a range of 2-44 years. During the past 10 year, an average of 7 cases of fatal food anaphylaxis were reported to the registry per year, along the lower limits of the reported 5-200 cases considered to occur annually in the US. During the highest year, 2013, the registry captured 12 cases, during the lowest year, 2009, the registry captured zero cases.

Foods currently reported to have caused fatality in the registry include peanuts, tree nuts, milk, shellfish, fish, wheat and unknown (with a history strongly supporting a food allergen). No cases of fatal anaphylaxis to egg, soy or sesame have been captured in the registry to date. Of the 70 fatalities captured by the registry in the past decade, just over half were caused by peanut (51%, 36/70 cases). Where details are available, most fatal cases had underlying asthma and delayed or no epinephrine use.

Although many cases in the registry can be considered 'typical' meaning the individual understood they had a food allergy, had an accidental consumption of their allergen, and had delayed or no use of epinephrine, there are several unique cases. These uncommon cases appear to contain valuable teaching points. For instance, the majority of cases were between 11-20 years old. There were only 3 children under 5 years old captured in the registry and only 3 adults over 30 years old during the past 10 years. No cases under 2 years old or over 45 years old were recorded. There was a single case of fatal fish anaphylaxis (believed to have been aerosolized), a single case of fatal wheat anaphylaxis and only 2 cases of fatal shellfish anaphylaxis. An unusual 'food' item, toothpaste containing milk, was identified to have caused fatal anaphylaxis in a single case.

In the registry, only 9% (6 /70) of accidental ingestions leading to fatality occurred at home. Most cases of fatal anaphylaxis occurred outside the home, making a strong argument for public access to epinephrine. The most commonly identified location for an accidental ingestion leading to fatal food anaphylaxis was restaurants (19%, 13/70 cases). Unusual locations for fatal food anaphylaxis such as jail, a bar and a school bus were captured. There were no fatalities captured by the registry on an airplane. No cases were reported without a preceding oral ingestion except for the aerosolized fish exposure.

Epinephrine auto-injectors became commercially available in 1987 allowing patients access to life-saving medication in any location. Despite this availability, low carriage rates and low use of epinephrine autoinjectors during anaphylaxis (5) argues that much is still needed in the way of educating patients. Only a few states (California, Nevada, Utah, Arizona, Nebraska,

Connecticut, New Jersey, Delaware, Maryland, Virginia, North Carolina and Michigan) currently require epinephrine to be stocked in schools, but 49 states have laws that allow it through the School Access to Epinephrine Act. Some EMTs may not be equipped with epinephrine or may only be able to assist with the individual's own epinephrine auto-injector. A national shortage of epinephrine auto-injectors has further reduced access with spot shortages, intermittent backorders and a constrained supply of epinephrine auto-injectors ongoing since 2018. In addition, the price of auto-injectors is reported to have increased 400% from 2007 to 2018.

While awareness of food-induced anaphylaxis has improved over time, it is clear from registry data that fatal food anaphylaxis continues. Prevention strategies, including early introduction of allergenic foods into an infant diet, will hopefully reduce the number of individuals affected by food allergies. In addition, there is a robust pipeline of potential food allergy therapies that may improve outcomes and decrease the risk of food-induced anaphylaxis. A significant weakness in the registry data is the reliance on national media searches and self-reporting. Like the most recent published data on fatalities due to food allergy, the registry does not represent a formal epidemiologic study (5). Still, we perceive that a careful examination of factors that led to fatal food anaphylaxis has already yielded surprising insights.

In conclusion, despite our understanding of the key risk factors so far identified, fatal anaphylactic reactions to foods continue to occur. Tracking and understanding each case is a crucial exercise in order to better learn how we can prevent these tragedies. By doing so, we can better protect the patients we care for every day, as well as honor the patients we have lost.

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References:

1. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal anaphylaxis: mortality rate and risk factor, JACI in Practice, 2017 Sep - Oct;5(5):1169-1178. doi: 10.1016/j.jaip.2017.06.031.
2. Michelson KA, Dribin TE, Vyles D, Neuman MI. Trends in emergency care for anaphylaxis, J Allergy Clin Immunol in Practice, 2019 Aug 8. pii: S2213-2198(19)30636-1.
3. Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, et al. Food Allergy: A practice parameter update – 2014. J Allergy Clin Immunology. 2014 Nov;134(5):1016-25.e43.
4. Vickery BP, Vereda A, Casale TB, Beyer K, Du Toit GD, et al. AR101 oral immunotherapy for peanut allergy. N Engl J Med 379:21 November 22, 2018: 1991-2001
5. Bock SA, Munoz-Furlong A, Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001-2006. J Allergy Clin Immunol, April **2007**, 1016-1018

Table I

From the National Food Allergy Death Registry, 2013, highest year recorded

Year of death	Age, years	Sex	Presumed Causative Foods	Location of ingestion	Epi prescribed?	Epi used prior to EMS?	Asthma?
2013	11	M	Unknown	Home	Unknown	Unknown	Yes
2013	13	F	Peanut	Camp	Yes	Yes, x 3	Yes
2013	17	M	Milk	Park	Yes	No	Yes
2013	15	F	Milk	Hotel	Yes	Yes, x 2	Yes
2013	6	F	Peanut	Unknown	Unknown	Unknown	Unknown
2013	11	F	Unknown	Unknown	Unknown	Unknown	Unknown
2013	14	M	Peanut	Home	Yes	No	Yes
2013	11	M	Peanut	Unknown	Unknown	Unknown	Yes
2013	11	M	Peanut	Friend's home	Unknown	No	Yes
2013	8	M	Milk	Restaurant	Unknown	Unknown	Unknown
2013	19	M	Peanut	Home	Yes	No	Yes
2013	2	F	Peanut	Daycare	Yes	Yes, x 3	Unknown