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The Gravity of Weight

The Brittle World of Peanut Allergy

Navigating the daily potentially life-threatening challenges of food allergies

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Posted Nov 24, 2016

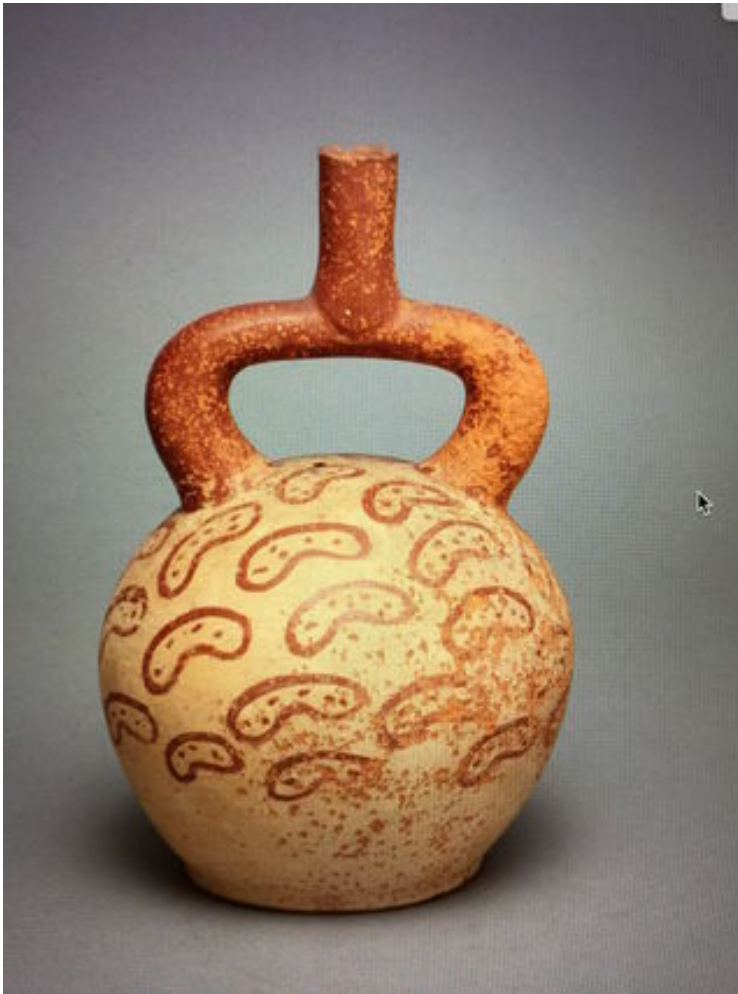


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The peanut has been cultivated worldwide for centuries and has been a decorative motif in art in civilizations as diverse as South America and China. There are, for example, images of peanuts on pottery that dates back from the 5th to 7th centuries A.D. from the Moche civilization of northern Peru. The Moche culture was known for its pyramid-like architectural mounds, ceramic stirrup-spouted pots, and metal works, as well as for an extensive irrigation system for agriculture. These people, though, were hardly peaceful farmers: we have anthropological evidence that they engaged in human

sacrifices that involved mutilation of bodies. There are ceramics with residues of human blood as well as others indicating the earthenware had contained peanuts.

Technically, the peanut is not a nut but rather a legume that belongs to the bean or pea family *Fabaceae*. (van Erp et al, *Current Treatment Options in Allergy*, 2016) Peanuts can be eaten raw or after boiling or roasting; they can be used in recipes and made into solvents, oil, medications, textile materials, and of course, peanut butter. (Praticò and Leonardi, *Immunotherapy*, 2015) Peanut cultivation requires a southern climate, and today Alabama and Georgia are the most common regions for its U.S. cultivation.



Stirrup Spout Vessel Depicting Diagonal Rows of Peanuts, Moche civilization, northern Peru, 250/500 A.D.

Source: Art Institute Chicago, used with permission, Art Resource (www.artres.com) for scholarly work

In the United States, peanuts were originally used to feed animals. Agriculturist, educator, and innovative researcher George Washington Carver, born a slave around the time of the Civil War, popularized their use for human consumption in the U.S. and laced his educational bulletins with his peanut recipes. Carver understood the need for crop rotation and the use of soil-enriching crops such as peanuts (and away from soil-depleting cotton.) (See the websites of Tuskegee Institute, Simmons College, and the National Park Service.)

In U.S. colloquial use for at least the past 150 years (*Oxford English Dictionary*), a “peanut” is a small or unimportant person, a small or insignificant amount of money, or even something that is trivial, worthless, or undersized. There is nothing trivial or insignificant, though, about peanut allergies that affect about 1 to 3% of children in westernized countries and have potentially deadly consequences in those particularly vulnerable. (Greenhawt, *Pediatric Clinics of North America*, 2015.)

Peanut allergies are not as prevalent as those to egg or milk, but they are less likely than milk, egg, soy, or wheat to be outgrown: (Syed, Kohli, Nadeau, *Immunotherapy*, 2013) fewer than 20% of cases resolve with age. (Greenhawt) Unintentional exposure is common enough since peanut products are found in many foods or processed in facilities where peanuts are found. Peanut proteins can be found in the dust in homes where peanuts have been consumed. (Benedé et al, *EBioMedicine*, 2016) As a result, a person’s (and entire family’s) quality of life can be severely compromised because there is the constant threat of exposure and the need for relentless



5th to 7th century, northern Peru, from Moche civilization, ceramic: Stirrup Spout Bottle with Peanut Figure.

Source: Metmuseum.org/open access for scholars/OASC

watchfulness. (Antolín-Amérigo et al, *Clinical and Molecular Allergy*, 2016) Moreover, those affected may suffer from allergies to many other foods as well, and there is the phenomenon of the so-called *atopic march* (Bantz et al, (*Journal and Clinical and Cell Immunology*, 2014), i.e., a progression from skin sensitivity such as atopic dermatitis (e.g. eczema) to food allergies.

The development of a food allergy is characterized by two stages: *sensitization* where an allergic reaction is established on first exposure and *elicitation* where the immune system produces an inflammatory response when the person is re-exposed to that particular allergen. Only a small number of foods actually induce allergies. Why this happens is not known. (Syed, Kohli, Nadeau, 2013.)

When there is a hypersensitivity reaction, though, patients may experience hives, wheezing, or vomiting that occurs after exposure to common allergens such as milk, peanut, or egg. (Benedé et al, 2016) For mild or moderate symptoms, anti-histamines are the first-line treatment.

Anaphylaxis, though, is an acute, life-threatening, medical emergency that involves two or more organ systems and usually occurs within minutes of exposure. Symptoms include vomiting, skin rash, rapid and weak pulse, abdominal pain, swollen throat and lips, trouble breathing or swallowing, diarrhea, and chest tightness. (Benedé et al, 2016) The current standard of care, though, is strict avoidance of the culprit food and readily available intramuscular injectable epinephrine, the only treatment for the most serious, potentially lethal reactions that occur after unintentional exposure. (Yu et al,



Peanut specimen of George Washington Carver, born in the 1860s; Carver was an educator, inventor, and agriculturist who had many recipes for peanuts in his educational bulletins.

Source: Wikimedia Commons/Public Domain



Peanut allergies can be deadly and even peanut dust can cause severe reactions in those vulnerable

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International Archives of Allergy and Immunology, 2012) It is no wonder there was such media uproar recently over the extraordinary price gouging from the manufacturer of the EpiPen. Nadeau and colleagues (Yu et al, 2012) note that peanut allergy is the leading cause of food-related fatal anaphylaxis in the U.S.

Food allergies affect roughly 15 million Americans (including 8% of U.S. children, Greenhawt, 2015) and 17 million Europeans, (Praticò and Leonardi, *Immunotherapy*, 2015) Anvari et al (*JAMA Pediatrics*, 2016) suggest that prevalence rates of reported peanut allergy have tripled in the ten years. The data on the epidemiology and natural course of food allergies, though, are not particularly accurate. (Savage and Johns, *Immunology and Allergy Clinics of North America*, 2015) Actual estimates vary widely because of differences in study methods, definitions of allergy, and different geographical areas. (Savage and Johns, 2015) Further, most statistical estimates are derived from self-or parent-report that can be notoriously inaccurate. Demographically, food allergies are more common in non-Hispanic blacks, Asians, and males; there is also a genetic predisposition, with specific genes likely involved. There are environmental factors: children with older siblings and those with pets are less likely, while those with vitamin D deficiency and those with atopy (e.g. asthma and atopic dermatitis), more likely. The most common age for presentation of peanut allergy is 18 months (Savage and Johns, 2015).

The mechanisms for food allergies are not well understood; it is not yet known whether these allergies represent pathological immune



Allergic skin reaction of hives

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responses in allergic children or the absence of protective mechanisms normally found in healthy children. Current diagnostic techniques emphasize the importance of clinical history, family history, presence of other allergic conditions, and the timing of allergic reactions after ingestion. When allergic patients are exposed to a potential allergen by skin prick, they develop a skin reaction called a “wheal.” While this test is usually safe, rapid, and highly sensitive, it does not provide specific information about severity, and extracts are often crude and unstandardized. (Syed, Kohli, Nadeau, 2013)

The gold standard for diagnosing a food, including peanut allergy, is the oral food challenge, but this has not been studied on a population level.

(Savage and Johns, 2015) For increased diagnostic accuracy, rather than relying on “crude peanut extract,” investigators use component-resolved diagnostics (CRD) to measure sensitization to purified or recombinant allergenic proteins within the peanut. Researchers can measure increases in levels of serum IgE antibodies when a patient is exposed to the specific peanut protein Ara h 2 that is pathognomonic for peanut allergy. (Syed, Kohli, Nadeau, 2013) CRD cannot be used to predict the risk of a severe allergic reaction. (van Erp et al 2016)

Why have rates of food allergies been increasing? The National Institute of Allergy and Infectious Diseases notes that there are insufficient data to suggest maternal diet, including during pregnancy, influences the development or course of food allergy in children. Studies from Israel where peanut allergies are significantly less common seem to indicate that early exposure to highly allergenic foods may even be preventive for food allergies. (Syed, Kohli, Nadeau, 2013)

The *hygiene hypothesis* suggests that changes in the pattern of the intestinal microbiome during infancy and decreased exposure to infectious agents in childhood are important factors in the development of allergic disease. (Syed, Kohli and Nadeau, 2013)

Prior to 2008, the American Academy of Pediatrics and others recommended delaying exposure to any peanut products in children before the age of three, especially for those at high risk (e.g. parent or sibling with family history or history of eczema in children) (Greenhawt, 2015) But international studies, including the LEAP Trial in England, confirmed that children at high risk of developing allergy to peanuts were actually more likely to develop a peanut allergy without any exposure than those exposed frequently as

early as six months, who had a “clear protective benefit;” exposure, though, “did not unequivocally prevent peanut allergy from developing” in some exposed children. (Greenhawt, 2015) This study had limitations: it did not address different doses of peanut required to maintain tolerance, the minimal duration of therapy necessary to achieve tolerance, or the potential risks of premature discontinuation or the sporadic feeding of peanut. (Anvari et al, 2016)

DuToit et al (*NEJM*, 2016) conducted a follow-up to the LEAP study, called the LEAP-ON, for those high-risk children exposed to peanuts in the first year of life and then throughout their first five years. The study did demonstrate a persistent reduction in the prevalence of peanut allergy in a significant number of children, even after a one-year peanut hiatus.

What about those who already have a potentially deadly food allergy such as to peanuts? There is no approved treatment for food allergies other than avoidance or emergency treatment when exposed. (Benedé et al, 2016) Clearly there is a need for “proactive therapies” since avoidance is hardly a foolproof, long-term solution. (Commins et al, *Current Allergy and Asthma Reports*, 2016)

Food allergy immunotherapy protocols have been tested in the past 25 years (Leung, Sampson, et al, *NEJM*, 2003) but to date, “it is not clear if this therapy is a myth or a reality.” (Praticò and Leonardi 2015) The main goal of immunotherapy is a permanent oral tolerance of the offending food (even after a hiatus of exposure) by causing a decrease in IgE-specific antibodies and a significant increase in IgG4 antibodies. Different from tolerance, desensitization involves only *transitory* changes in certain intestinal cells and the need for continuous exposure to that food. Further, any factor that that can affect the “intestinal barrier function” (e.g. exercise, gastroenteritis, stress) may cause a loss of protection to the previously tolerated dose, even after the end of immunotherapy, unless there is actual modulation of the pathological immune mechanisms. (Praticò and Leonardi, 2015)



Emergency intramuscular injections of epinephrine can prevent death when there is anaphylactic shock due to peanut ingestion in those with severe peanut allergies

Source: iStock.com/used with permission/MichelGuenette

Several techniques for food immunotherapy have been developed: sublingual immunotherapy (SLIT), oral immunotherapy (OIT), and epicutaneous (e.g. skin patch)(EPIT). (Benedé et al, 2016) A high percentage of those who achieve desensitization develop clinical reactivity when treatment is stopped. In all the protocols for immunotherapy, side effects are quite common. Initial phases are more likely to produce side effects, and rush protocols are usually more dangerous. A higher incidence of systemic reactions has been observed with OIT, while oral reactions are quite common with SLIT,

and SLIT has been found too dangerous to use with peanut allergies. (Syed, Kohli, Nadeau, 2013) Patients may also experience cutaneous symptoms (e.g. itching) and gastrointestinal (e.g. nausea, vomiting, abdominal pain) and respiratory symptoms (e.g. asthma) that can be severe and usually linked to withdrawal from the study or poor adherence to the protocol. (Praticò and Leonardi, 2015)

The use of the anti-IgE (omalizumab, brand name Xolair), together with oral immunotherapy, has recently been reported to improve the safety of OIT, (Benedé et al, 2016) but note that this medication has, to date, been approved for use *only* with patients with asthma or chronic urticaria. (Bauer et al, *Journal of Allergy and Clinical Immunology*, 2015.) Further, its administration must be done under strict medical supervision in case of potentially life-threatening anaphylactic reactions. Clearly, much more research with standardization of protocols is warranted. (Syed, Kohli, Nadeau, 2013)

In their provocatively entitled, “Oral Immunotherapy for the Treatment of Peanut Allergy: Is It Ready for Prime Time?” Wood and Sampson (2014, *Journal of Allergy and Clinical Immunology: In Practice*) caution the use of OIT based on their own years of clinical experience and a review of the current literature. They believe, “Claims that OIT is safe are potentially misleading,” and they strongly recommend that these experimental treatments be conducted under the oversight of institutional review boards and the U.S. Food and Drug Administration. Further, they note this treatment is not proven in either the short or longer-term, and patients may be living with a “false sense of security.”

Other researchers have noted it is “easy to understand the trepidation” of practitioners and patients to oral immunotherapy, especially for a peanut allergy, since it is responsible for more anaphylactic deaths than other allergens. (Yu et al, 2012) More recently, Nadeau and her group (Ryan et al, *Proceeding of the National Academy of Science, USA*, 2016) have also found a way to measure OIT success by tracking and monitoring changes in specific cells involved in our immune system.

Bottom line: Food allergies, and particularly peanut allergies, can be lethal. There is currently no standard treatment other than avoidance of the specific food or emergency epinephrine in case of unintentional exposure. Immunotherapy shows promise but is still considered experimental; investigative trials have involved small, select populations and adverse effects have been common.



Qing Dynasty (1644-1911), 18th century, China; Peanuts and Jujube Dates, on view at Metropolitan Museum of Art, NY, Gallery 222

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About the Author



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In Print: *The Gravity of Weight: A Clinical Guide to Weight Loss and Maintenance*

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