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Factors that Influence the Formation of Peanut Allergies in Children

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FACTORS THAT INFLUENCE THE FORMATION OF PEANUT ALLERGIES IN CHILDREN

by

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ABSTRACT

Allergies have the potential to be a life-long debilitating fight, especially the severe reactions from allergies such as anaphylaxis. Peanut allergies tend to be both common and severe, and they happen to be found hiding in many food products. People can have allergic reactions to food products that were made in the same facility as peanut products, that is why it is so important to be aware of the products that are being consumed. The incidence of peanut allergies has increased in the last decade, which is why it is crucial to study these allergies. This thesis looks at when the best time is to introduce peanut products to young children and the common risk factors that are associated with peanut allergies in children. The risk factors that are being looked at include: genetics, socioeconomic status, and ethnicity. This thesis also investigates a couple of treatment options for if your child develops a peanut allergy.

DEDICATIONS

I'd like to dedicate this to my family, nursing friends, and nursing professors. This year has been a challenging one, and I could not have done it without everyone's love and support. You have molded me into the hardworking person I am today. Thank you.

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INTRODUCTION

Peanut allergies are very common and widely misunderstood. “The Center for Disease Control and Prevention reports the prevalence of food allergy in children has increased by 50% between 1971 and 2011” (Food Allergy and Research Education, 2017, p. 1). In fact, studies have shown the number of peanut allergies has tripled in the past decade, evident in both Western and developing countries (Fleischer et al., 2015). Peanut allergies are a well-known topic of research because the reactions related to them are very severe. According to Anvari et al. (2017), “peanuts account for the most food-induced anaphylaxis and fatal reactions” (p. 77). As a result, parents are becoming increasingly worried about their children potentially developing this life-threatening allergy. This is leading to many research studies being conducted to link certain risk factors with the development of peanut allergies. Over the years, the recommendations and guidelines developed by the American Academy of Pediatrics (AAP) have changed drastically regarding peanut exposure. In less than a decade the guidelines have completely shifted.

Due to the severity of peanut allergies, many parents have stopped introducing peanuts into their children’s diet and decided to wait years for their children to come into contact with peanuts (Anvari et al., 2017). The 1999 AAP guidelines recommended that parents delay introducing peanuts to their children. There were also recommendations that associated maternal exposure to these allergens with an increased incidence of peanut allergies in children. Therefore, parents were hoping that by avoiding peanuts in the womb, early infancy, and childhood they would reduce the chances of their child becoming intolerant to peanuts.

Unfortunately, the result of this practice led to a rapid increase in peanut allergies. In 2008, new guidelines from the AAP recommended introducing peanuts during early infancy. As a result, there have been studies conducted to reinforce these new guidelines. Studies conducted since the introduction of these guidelines suggest there is no relationship between maternal exposure and the risk of peanut allergy in children (Anvari et al., 2017).

Genetics also appears to play a role in the formation of peanut allergies in children. First-degree relatives are very genetically similar and carry similar risks for many health concerns. If someone in a family is genetically predisposed to acquiring a peanut allergy, are the remaining family members at risk? Children are considered as "high risk" for acquiring an allergy if a first-degree family member has an allergy to the nut (Anvari et al., 2017). A study conducted by Bégin, Graham, Killer, Paradis J, Paradis L, and Des Roches (2016) linked the siblings of children to peanut allergies with a higher risk of developing a serious reaction to peanuts. It also concluded that due to one child in the family having an allergy, the parents neglected the introduction of the allergen to the rest of the siblings. This resulted in the allergy being more severe due to the delayed introduction. According to another study by Lavine, et al. (2014), parents neglected to introduce the siblings of children with a peanut allergy to peanuts under the assumption they would also have a sensitivity reaction. This was especially prevalent in families that had a subsequent child after the original diagnosis of a peanut allergy in their older child. This further contributes to the increase in prevalence of peanut allergies due to these parents delaying the children's exposure to peanuts.

The third aspect of peanut allergies this literature review is going to address is the characteristics of the children that are most commonly seen with peanut allergies. Do children of a certain race, ethnicity or socioeconomic status have a higher incidence of peanut allergies? Hannaway, Connelly, Cobbett, and Dobrow (2005) conducted a study in Massachusetts where they collected data on who they were administering the most epinephrine injections for certain allergies based on three school districts one urban and two affluent suburban districts. They found that Caucasian students from kindergarten to fifth grade had the most epinephrine injections over the course of the year (Hannaway et al., 2005), suggesting a higher prevalence of allergies in Caucasian children of higher socioeconomic status. Another study by Leickly, Kloepfer, Slaven, and Vitalpur (2013) looked into the epidemiology of children that had a hypersensitivity to peanuts. This study followed over 1070 children that showed peanut sensitivity signs. Over the course of the two-year study, the researchers noted that children that had an allergy were "predominantly male (63%), Caucasian (78%), and had private health insurance (80%)" (p. 253). They also concluded that children experiencing anaphylaxis reactions to peanuts had higher IgE levels in their blood.

The last aspect this literature review will focus on are the most effective treatments for children that have already established a peanut allergy. The most important method for managing peanut allergies is prevention. It is extremely important to be aware of products that contain peanuts, especially products that have less visibility such as sauces, ice creams, and chilis. Another treatment that has been effective is early oral therapy. Vickery, Berglund, and Berk (2018) looked at oral therapy treatment for children with peanut sensitivity or allergy. They

introduced low dose peanut protein to these children over a certain amount of time, and followed their IgE levels throughout the study and concluded this is an effective way to desensitize children and allow them to build up a tolerance. Another treatment that Jones, Sicherer, and Burks (2017) studied was epicutaneous immunotherapy among children allergic to peanuts. This study consisted of three groups: one placebo and two independent groups receiving different dosages of peanut proteins through a patch on their arm. The study was conducted over fifty-two weeks, and the participants were able to tolerate higher doses as the study went on. The treatment had higher success among younger participants in the study.

BACKGROUND

Most people refer to peanuts as a tree nut, but that is not true. According to Food Allergy Research and Education (2018), peanuts come from the ground and are members of the legume family. In addition, an allergy to peanuts does not make someone any more susceptible to acquiring another legume allergy. When someone reacts to peanuts, they are told to avoid them, but there are other specific products the person needs to avoid. Products or ingredients such as peanut oil, groundnuts, peanut flour, and nutmeat consist of peanuts and can cause someone to produce an allergic reaction. It is important to read food labels closely to determine if the food product contains remnants of peanuts or was produced in a facility near products containing peanuts. Peanuts are present in many products or produced in factories that also produce other food products. Therefore, it is important that people with peanut allergies are aware of these risks and conscientious of the products they are consuming.

PURPOSE

The main issue with peanut allergies is they tend to be very severe and common. "Pediatric hospitalizations for food allergies tripled between the late 1990s and mid-2000s. Between 2004 and 2006, an average of 9,500 people/children received hospital care for food allergies each year" (FARE, 2017, p. 2). This literature review is proposing to identify the risk factors that are associated with long-term childhood peanut allergy development. It will also identify any developing patterns with the new increasing prevalence of allergies to peanuts such as time of introduction, SES, and genetics. It will evaluate a variety of treatment options that are available to reduce the severity of the peanut allergy once it is established. Lastly, the final literature review will examine these factors and go into depth regarding the findings of the studies listed. It will also highlight the most effective treatments and the newest guidelines by the American Academy of Pediatrics regarding peanut allergies in children. The purpose of this literature review is to identify high-risk groups, target these populations, and find out why this is occurring and find a solution to the problem.

METHOD

The initial searches for the literature review were done by going online to the UCF library database. I searched for articles on CINAHL, EBSCOhost, Cochrane, and Medline databases using the terms PEDI* or PAED* or child* or children*, peanut allerg*, anaphylaxi*. For each point, I used the above criteria along with "genetics", "socioeconomic status", and "treatments". I also searched the above criteria with "treat*" or "cure" to find common ways to treat peanut allergy reactions. The articles were then narrowed down further by only using peer-reviewed articles that were written in English and published no earlier than 2010. Once several articles were viewed, assessed and deemed appropriate, they were placed and organized into a reference table based on the points they were used for and relevance to the literature review.

REVIEW OF LITERATURE

When to Introduce

In 1999 the AAP came up with their set of guidelines for peanut products they believed would reduce the incidence of peanut allergy formation in children (Anvari et al., 2017). These guidelines stated that in order to put children at less risk of developing peanut allergies, parents should delay the introduction of peanuts in infancy and early childhood. The incidence of peanut allergies began to rise (Anvari et al., 2017) studies have been done to determine why there is an increasing incidence of peanut allergies and new guidelines have been released to combat these allergies. A significant study was conducted in 2015 by the *New England Journal of Medicine* called the LEAP (Learning Early About Peanut Allergy) trial that looked more in-depth at when to introduce peanut products.

Lisette Hilton (2017) wrote a journal article that discussed several medical doctors' views on the ever-changing peanut guidelines. Bernard Cohen, an MD from John Hopkins University School of Medicine says, "Many of us were concerned about delaying exposure to all sorts of allergens, the idea being that, if kids are exposed early on, they become tolerant and do fine" (p. 36). Lawrence F. Eichenfield, MD specializes in pediatric dermatology and has noticed the connection between children who have atopic dermatitis and developing food allergies. He served on the board for the newest set of guidelines on behalf of the American Academy of Dermatology (AAD) and supported the notion that children with skin conditions should be

exposed early to certain foods prone to create severe allergies to minimize the risk of developing an allergy.

Eichenfield further discusses the best method for introducing peanuts to infants because there is a high aspiration risk if a child is simply given a peanut to chew on (Hilton, 2017). "Cohen recommends a product called Bamba, a snack made in Israel, by Osem Group, for safe exposure" (p. 38) An Israeli news source, *Haaretz*, wrote an article about Bamba. It discussed how Israeli children have a significant amount of less peanut allergies than Westernized children with similar ethnicities. "One reason could be early exposure to peanuts by eating (and teething on) Bamba, a peanut-flavored snack considered a staple of Israeli childhood" (p. 38). Cohen also states that many of these introductions should be done for the first time in a pediatrician's office to be monitored.

Peter Lio, MD is a slight critic of these new guidelines. He believes there needs to be more research done. The guidelines were based on the LEAP Trial and may not serve as the best recommendation for every child (Hilton, 2017). He also believes that one doctor's definition of "severe atopic dermatitis" may differ from another, making treatment regimens inconsistent.

In summary, current studies have shown favorable results regarding early introduction of peanuts in children. These new recommendations highly contradicted the previous guidelines, but had more research studies behind it backing it up. Hopefully, future studies will be done to further this research and will continue to reduce the numbers of peanut allergies in children.

Genetic Component

Another important factor to consider in the development of peanut allergies is a genetic component. It is important to recognize any similarities or patterns that evolve around a family unit regarding peanut allergies. If researchers can identify a genetic component between family members, it may lead to new advancements, which could reduce the overall peanut allergy prevalence in the population.

Lavine et al. (2014) conducted a study called the Canadian Peanut Allergy Registry (PAR). "This study looked at nine hundred and twenty-two siblings of children that have developed a peanut allergy" (p. 249-254). They sent these families a questionnaire based "on siblings' sociodemographic characteristics, exposure and reactions to peanut, confirmatory tests performed, and whether peanut allergy had been confirmed" (p. 249-254). "Of the peanut allergic siblings, 13.6% had never been exposed to peanut, 764 had been exposed, and 33 were uncertain. Among those never exposed, the majority (n = 88/125) was born after the diagnosis of peanut allergy (PNA) in the index child. Of the sibling group, 8.7% reported having been diagnosed with peanut allergy by a physician. Among these 80 children, 41 (51.3%) had reacted to peanut, 34 (42.5%) had never reacted, and in 5 children, the parents were not sure" (p. 249-254). The study showed that a significant number of children that were born after their sibling had been diagnosed with a peanut allergy, would be delayed the opportunity to try peanut products if the parents chose. The study concluded that siblings of children with peanut allergies have a slightly higher risk of developing a similar allergy (7%) verses children that do not have a sibling with a peanut allergy (1%).

Bégin et al. (2016) conducted a similar double-blind study where fifty-four children that had older siblings with peanut allergies had skin testing done and then were introduced to peanuts. The results showed that "eight participants (5.2%) presented unequivocal IgE-mediated reactions to peanut upon introduction, including five anaphylaxes. These participants were significantly older compared to the rest of the cohort. The negative predictive value of skin prick test with peanut extract and peanut butter and of specific IgE was 99%, 100%, and 100%, respectively. Six peanut-tolerant participants had positive peanut allergy tests" (p. 1762-1771). The conclusions were similar to Lavine et al.'s (2014) study, where there is a higher risk of children with peanut allergic siblings to acquire a peanut allergy.

Common Characteristics of Children with Peanut Allergies

This component aims to identify common characteristics of children with peanut allergies. If these characteristics can be identified and proven, pediatricians can target these specific populations in hopes to reduce severe allergic reactions.

Hannaway et al. (2005) studied three suburban school districts. They collected data from these districts, specifically focusing on the number of times the school children were injected with epinephrine to combat an allergic reaction. They also looked at specific characteristics of the children: ethnic status, race, socioeconomic status. Of the 181 students that were injected with epinephrine over the course of the trial period, 118 of these were treated due to a tree nut/peanut allergy. In children that had the tree nut, or peanut allergy, there was a higher incidence of white males receiving the epinephrine injections. Further research needs to be done to see why this is the case. It may have something to do with a certain number underdiagnosed or untreated children, which could be affected by other factors such as socioeconomic status.

Leickly et al. (2018) conducted an epidemiological study that also included the same components. The sample consisted of children from 3 facilities in Indiana who had a peanut allergy or sensitization called the Riley Peanut Registry that began in 2011. “Peanut allergy was defined based on a convincing history of a reaction within 2 hours after exposure to peanut either by ingestion or by contact and the presence of a positive allergy test.” (p. 224) Sensitization to peanuts was defined as “having a skin prick test >3 mm bigger than the negative control. Or, for those children who were seen prior to adopting caliper measurements, a wheal of 3-4+ size and/or the presence of detectable IgE to peanut, but no clinical history of a reaction” (p. 224).

The Leickly et al. (2018) study showed that of the 1070 children that were in the study, 67% had an official allergy, and 33% had a sensitivity. This is a consistent ratio found in other studies. The results are shown in Table II. They indicate that peanut allergies are more common in males with skin reactions to the peanut being the most common finding. Also, peanut allergies are more common in siblings, Caucasians, and in children with private health insurance.

Figure 1

Table II. Demographics and other allergic associations

Demographics	Anaphylaxis (n = 248)	Other reactions (*n = 465)	P†	No reactions (n = 357)	P‡
Sex (male)	164 (66.1%)	284 (61.0%)	.18	235 (65.8%)	.26
Race			.31		.28
White	198 (79.8%)	361 (77.6%)		263 (73.7)%	
African American	30 (12.1%)	51 (11.0%)		41 (11.5%)	
Asian	8 (3.2%)	10 (2.2%)		18 (5.0%)	
Hispanic	0 (0%)	2 (0.4%)		1 (0.3%)	
Biracial	12 (4.8%)	39 (8.4%)		33 (9.2%)	
Other*	0 (0%)	2 (0.4%)		1 (0.3%)	
Insurance			.61		.41
Private	205 (82.7%)	371 (79.8%)		283 (79.3%)	
Public	37 (14.9%)	83 (17.9%)		70 (19.6%)	
Self-pay	6 (2.4%)	11 (2.4%)		4 (1.1%)	
Other allergic conditions					
Atopic dermatitis	137 (55.2%)	292 (62.8%)	.05	267 (74.8%)	<.001
Asthma	128 (51.6%)	168 (36.1%)	<.001	143 (40.1%)	<.001
Sibling with peanut allergy	32 (12.9%)	54 (11.6%)	.85	68 (19.0%)	.02
Other food allergy	156 (62.9%)	255 (54.8%)	.04	324 (90.8%)	<.001
Milk	22 (8.9%)	46 (9.9%)	.36	145 (40.6%)	<.001
Egg	75 (30.2%)	120 (25.8%)	.17	235 (65.8%)	<.001
Milk and egg	16 (6.5%)	31 (6.7%)	.92	113 (31.7%)	<.001
OFC	16	59		51	
Passed	6 (37.5%)	35 (59.3%)	.05	41 (80.4%)	.005

*Other includes unknown, refused, Pacific Islander, and Native American.
†χ^2 comparisons between the anaphylaxis group and those children with other reactions to peanut.
‡χ^2 comparisons with all 3 groups.

(Leicky et al., 2018, p. 225)

Treatments

Now that these guidelines have been posted to prevent raising the risk of peanut allergy formation, what should be done if a child does develop a potentially life-threatening reaction to peanuts? As a parent, it is frightening knowing their children are being exposed to peanuts regularly in products that might not knowingly contain peanuts. So, it is important to identify ways to deescalate a severe allergic reaction.

There are a couple treatment options that are available depending on the severity of the allergy. One of the treatments that is currently being studied is desensitization therapy. There was a study done by Anagnostou, Islam, King, Foley, Pasea, Bond, Palmer, Deighton, Ewan, and Clark (2014) that looked at exposing children with an allergy to peanuts to peanut flour. People that had an immediate hypersensitivity reaction to peanuts and/or tested positive to a skin prick tests were eligible for this treatment. There were three phases, each phase consisted of a certain amount of peanuts ingested. The first phase consisted of 800 mg of peanut ingestion per day, and the second phase was about 1400 mg peanuts per day, etc. After only the first phase, 62% of the control group was desensitized to peanuts. This research is relatively newer and is a step in the positive direction of treatment home for those with severe peanut allergies.

Another treatment option that is available if your child develops a severe reaction suddenly is an epinephrine subcutaneous injection, aka “The Epi Pen”. The idea behind this treatment is that when a child has a severe allergic reaction, they are able to inject a subcutaneous dose of epinephrine that will suppress the inflammatory response and reduce the severity of the reaction. “Guidelines uniformly agree that its prompt administration is vital to prevent progression,

improve patient outcomes, and reduce hospitalizations and fatalities" (Fromer, 2016, p. 1244). Epinephrine was not always readily accessible to these children, but in recent years they have been available in a "pen" form that children are able to carry around with them if their allergy is severe. A lot of times the injection is kept in the school nurse's office so it is available to the child while they are at school. It also requires a lot of teaching for the child and their family, such as how to safely inject and store the medication. This provides a better peace of mind to both the parent and child for when they come into contact with the allergen, it also hopes to reduce the incidence of fatal allergic outcomes.

DISCUSSION

The theory about peanuts has changed greatly over the last 20 years. In 1999 the AAP released guidelines recommending that parents delay the introduction of peanuts to their infant children, hoping to reduce the prevalence of peanut allergies. Shortly after this, there was a slight rise in the incidence of peanut allergies, sparking concern. The most recent guidelines that were released by the National Institute of Allergy and Infectious Disease (NIAID) included specific recommendations that incorporate the high-risk status of the infant towards a peanut allergy and when to introduce peanuts (Table II) based on their study, the LEAP trial.

One thing to keep in mind when looking at these changing guidelines is that every child is different. These guidelines keep adjusting, so it is important to research the studies that support these new regulations. Peanut allergies are life-threatening and due to their severity have a tendency to produce anaphylactic reactions. Therefore, it is important to know the signs and symptoms of an allergic reaction such as, "laryngeal edema, wheezing, nausea, vomiting, diarrhea, urticaria, angioedema, and hypotension" (Patel & Volcheck, 2015, p. 1).

RECOMMENDATIONS FOR PRACTICE

The National Institute of Allergy and Infectious Diseases (NIAID) has come up with specific guidelines for providers introducing peanut products to high-risk infants with rationale supporting each claim. The NIAID released guidelines in 2010 but did not offer definitive strategies to prevent peanut allergies due to the lack of studies done on the topic. In 2017 they released a new set of guidelines with specific recommendations and rationales. This is intended for providers to use in their practice. With only a few guidelines to follow, it creates a standard of care across the board (Togias et al., 2017).

The New England Journal of Medicine conducted their own study in 2015 called the Learning Early About Peanut Allergy (LEAP) trial when they noticed a significantly higher peanut allergy rate in children from United Kingdom verses Israel (Togias et al., 2017). They looked into this further and concluded that it might have something to do with Israel introducing peanuts early into the diets of infant children, while the United Kingdom typically waits to introduce peanuts. The LEAP trial was conducted based on these observations.

"The LEAP trial randomized 640 children between 4 and 11 months of age with severe eczema, egg allergy, or both to consume or avoid peanut-containing foods until 6 months of age, at which time a peanut oral food challenge (OFC) was conducted to determine the prevalence of peanut allergy" (Togias et al., 2017, p. 2). They performed a skin prick test on these infants to determine their allergy status. The infants that tested negative were tested separately from the infants that tested positive. Of the 530 participants that originally had a negative reaction to the baseline skin test, the amount of participants that developed an allergy at 6 months of age in the

group that avoided peanuts was 13.7%, while the amount of participants that consumed peanuts only 1.9% developed an allergy. Among the infants that tested positive to the baseline skin test in response to peanuts, the prevalence of peanut allergies was about 35% in the infants that delayed introduction to peanuts, and about 11% in the infants that were exposed to peanuts early.

The NAID formulated committees to conduct a literature review on this topic from 2010 to 2016. With the research, they were able to formulate new guidelines for 2017 (Table I).

Figure 2

TABLE I. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices

(Togias et al., 2017)

The guidelines define the infant criteria as: "Severe eczema is defined as persistent or frequently recurring eczema with typical morphology and distribution assessed as severe by a health care provider and requiring frequent need for prescription-strength topical corticosteroids, calcineurin

inhibitors, or other anti-inflammatory agents despite appropriate use of emollients" (p. 4) They also defined an egg allergy as having a skin reaction of a wheal diameter of at least 3 mm or larger in response to an egg skin prick test (SPT) or an allergy to an oral dose of egg (Togias et al., 2017).

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