Task Force or Committee Report

Conducting an Oral Food Challenge to Peanut in an Infant

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Results from the Learning Early About Peanut trial and its follow-up study suggest that early peanut introduction in the diets of high-risk infants may prevent the development of peanut allergy. Allergy organizations around the world released a unified statement, the Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High Risk Infants, in response to results from the Learning Early About Peanut trial, which recommends early introduction of peanut into the diet of those children at greatest risk of development of peanut allergy. As a result, it is expected that practicing allergists will experience an increased demand to perform an oral food challenge (OFC) in infants. Allergists often perform OFCs; however, conducting an OFC in an infant creates unique circumstances that have not been considered in previously published OFC guideline documents. The purpose of this workgroup report is to provide guidance to practitioners regarding the proper approach for conducting a peanut challenge in an infant. © 2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;■:■-■)

Key words: *Food allergy; Infant; Oral food challenge; Peanut allergy; LEAP; Early introduction*

The recently released Consensus Communication on Early Peanut Introduction and the Prevention of Peanut Allergy in High-Risk Infants strongly recommends introducing peanut products into the diets of high-risk infants.[1] These recommendations are based on results of the Learning Early About Peanut (LEAP) trial, a large single-center clinical trial performed by food allergy experts in an academic children's hospital setting in which

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Abbreviations used
IV- Intravenous
LEAP- Learning Early About Peanut
OFC- Oral food challenge
SPT- Skin prick test

early introduction of peanut in high-risk infants (defined as having early onset eczema and/or egg allergy) between 4 and 11 months of age was associated with a decreased risk of peanut allergy up to 5 years of age.[2] Although an oral food challenge (OFC) is considered the gold standard for diagnosis of food allergy regardless of age, diagnostic peanut OFCs have not been typically used in infants aged 4-11 months. It is expected that the recent consensus statement will result in an increased demand to perform diagnostic OFCs in infants, and conducting an OFC in an infant includes considerations that differ from OFCs in older children, adolescents, and adults. A workgroup from the Adverse Reactions to Foods Committee of the American Academy of Allergy, Asthma, and Immunology was formed to address this need and provide guidance in conducting OFCs in infants. The purpose of this report is to expand prior advice on conducting OFCs,[3] focusing on peanut introduction in infants. Recommendations are based on available evidence and expert consensus.

INDICATIONS FOR CONDUCTING AN OFC

According to the Consensus Communication, it may be advantageous for infants with early onset (<4-6 months) atopic disease, such as severe eczema or IgE-mediated egg allergy, to introduce peanut into their diet early in life (between 4 and 11 months of age) in countries where peanut allergy is prevalent.[1] Based on the LEAP criteria, infants with severe eczema or egg allergy may benefit from consultation with an allergist or other physician experienced in the evaluation of food allergy in children if they feel support is required for introduction of peanut into the diet.[2] Such an evaluation "might consist of performing peanut skin testing [and/or] an in-office observed peanut ingestion [office-supervised feed], as deemed appropriate after a discussion with the family. The clinician can perform an observed peanut challenge for those with evidence of a positive peanut skin test response to determine whether they are clinically reactive before initiating at-home peanut introduction."[1]

The Consensus Statement does not provide guidance as to which children should be considered for an office-supervised feed versus observed peanut challenge versus recommending continued avoidance. Further advice will be forthcoming from the National Institute of Allergy and Infectious Diseases (NIAID) and falls outside of the scope of this workgroup report.

SAFETY CONSIDERATIONS BEFORE STARTING THE CHALLENGE

An observed challenge, whether to food, drug, or venom, is a practice typically reserved for the practicing allergist, and is considered a safe procedure when performed in the appropriate patient and setting. There have been no reported deaths from OFCs in the literature indexed since 1976 in PubMed; however, anaphylaxis is potentially life threatening and precautions should be taken to minimize risks. Physicians undertaking OFCs in infants should be comfortable recognizing and treating allergic reactions and anaphylaxis in this age group. To reduce the likelihood of a severe adverse outcome, it is important to consider the following precautions especially for infants with a positive skin prick test (SPT) who may be at an increased risk of reacting during the OFC.

1. Perform the challenge in a monitored setting. A physician or a nurse under a physician's supervision should monitor the patient throughout the OFC. Providers should be experienced in the evaluation and management of anaphylaxis in children.
2. Medications that may interfere with interpretation of the OFC should be discontinued, as outlined in Table I.

TABLE I. Medication discontinuation considerations before OFC[3,23]

Medication	Last dose before OFC
Cetirizine	5 d
Cyproheptadine	10 d
Diphenhydramine	3 d
Fexofenadine	3 d
Loratadine	7 d
Short-acting bronchodilator (eg, albuterol)	8 h
Oral/intramuscular/intravenous steroids*	3 d to 2 wk
Medications that may be continued	
Inhaled/intranasal corticosteroids	
Topical steroids	
Topical pimecrolimus, tacrolimus	

OFC, Oral food challenge.
*This suggested guideline is based on the concern regarding the potential for suppression of the late-phase response. In addition, the patient who receives a short course of systemic corticosteroid may have a concomitant illness that could either interfere with interpretation of the OFC or potentially worsen the severity of a reaction. If a patient receives chronic therapy with systemic steroids for any reason, the risk vs benefit for stopping steroid therapy and substituting an alternative therapeutic agent or performing the OFC while the patient remains on steroid therapy should be evaluated on an individual basis.[3]

TABLE II. Emergency medications for infants

Medication	Dose
Epinephrine (1:1000 concentration)	0.01 mg/kg IM in the mid-outer thigh in health care settings OR 0.15 mg autoinjector IM in the mid-outer thigh in community settings[4]
Albuterol nebulization	0.15 mg/kg every 20 min × 3 doses (minimum of 2.5 mg per dose) over 5-15 min
Albuterol MDI inhalation	2 puffs, 90 mcg/puff, with face mask
Oxygen	8-10 L/min via face mask
Diphenhydramine	1.25 mg/kg/dose PO/IM/IV
Cetirizine	2.5 mg PO
Normal saline (0.9% isotonic solution) or lactated ringers	20 mL/kg/dose administered over 5 min
Steroids	Prednisolone 1 mg/kg PO OR Solu-Medrol 1 mg/kg IV

IM, Intramuscular; *IV*, intravenous; *MDI*, metered-dose inhaler; *PO*, by mouth.

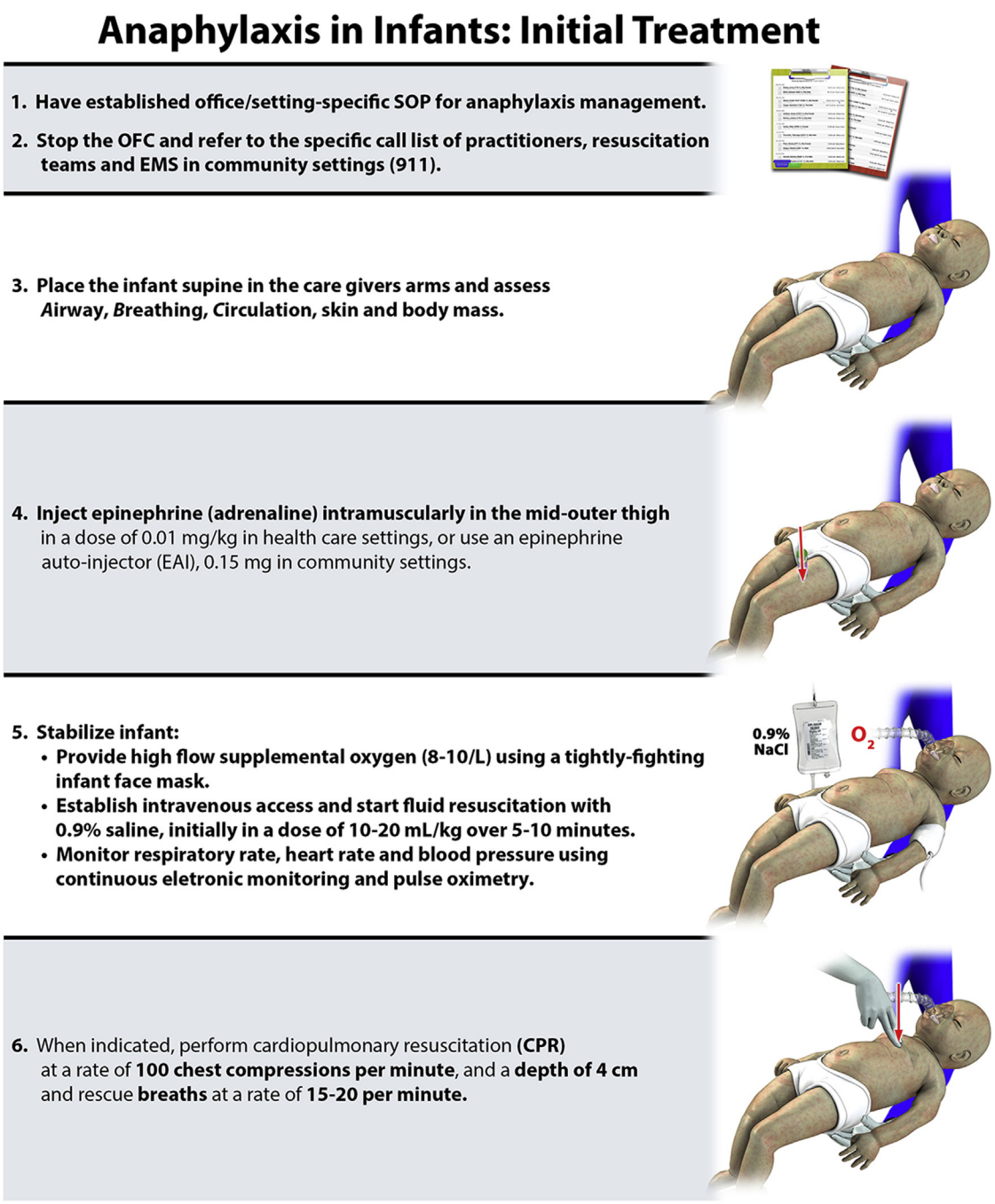

FIGURE 1. Initial treatment of anaphylaxis in infants.

3. Documentation of verbal or written informed consent should be considered.[3]
4. Before starting the feeding obtain baseline vital signs, such as weight, temperature, respiratory rate, heart rate, oxygen saturation level, and a baseline blood pressure, and perform an appropriate physical examination, including skin, oropharynx, heart, and lungs. Vital signs should also be checked at any point during the OFC if there is a perceived change in clinical status and at discharge. Obtaining a reliable blood pressure in an infant may be challenging, and in cases when it is not possible to obtain a reliable reading, particular attention should be paid to the infant's physical examination and clinical appearance. Symptoms of hypotension may include delayed capillary refill time (>2 seconds), altered mental status (ie, more difficult to arouse or awaken), pale or mottled skin, cool extremities, and tachycardia.
5. Emergency medications should be readily available and it is helpful to have appropriate doses calculated based on the infant's size before starting the challenge (Table II). Medications to have on hand include epinephrine, H1 antihistamine,

TABLE III. Special considerations for anaphylaxis in infants[5]

Age	Vitals
When is it hypotension?	Systolic blood pressure (mm Hg)
Infants (1-12 mo)	<70
1-10 y	(Age × 2) + 70
When is it tachypnea?	Respiratory rate
2-12 mo	≥50 breaths/min
1-4 y	≥40 breaths/min
When is it tachycardia?	Heart rate
<2 y	>160 beats/min

albuterol, supplemental oxygen and supplies, and intravenous (IV) fluids. Epinephrine should be given intramuscularly in the mid-outer thigh at 0.01 mg/kg of a 1:1000 concentration. Use of an epinephrine autoinjector (0.15 mg) as an alternative option has been recommended in community settings.[4] It is important to note that antihistamines and glucocorticoids should not be used as initial treatment or monotherapy for anaphylaxis and should not delay administration of epinephrine when indicated.[4] Figure 1 and the recent review by Simons and Sampson[4] provide suggestions for addressing treatment of anaphylaxis in infants.

Regarding necessary equipment, anaphylaxis practice parameters recommend having an oxygen source, pulse oximeter to monitor oxygen saturation, stethoscope, sphygmomanometer, appropriate size nasal cannulas, masks, bag-mask ventilation kits, and oropharyngeal airways present or readily available for treatment of anaphylaxis.[5] It is critical to select the appropriately sized equipment (eg, blood pressure cuffs, IV cannulas, masks) for the successful evaluation and treatment of infants. A range of equipment sizes should be available. Refer to Table III for blood pressure, respiratory rate, and heart rate values considered hypotensive, tachypneic, and tachycardic in infants.

6. IV access may be obtained at the discretion of the provider. The LEAP study protocol stated that infants with suspected peanut allergy defined as SPT wheal >1 mm, peanut specific IgE >0.1 kU/L, or a previous reaction to peanut, and one of the following: (1) a history of anaphylaxis or (2) a history of a food reaction involving severe emesis should have IV access obtained before commencing the OFC; however, no children in the study required the use of the IV. The authors reported that they have performed 2325 OFCs in children at their hospital with 200 positive challenges and all were effectively managed without the requirement for IV access.[2] Previous trials evaluating safety of OFCs have reported infrequent use of IV fluids with use ranging from 10 of 1273 OFCs (0.008%) in a low-risk population[6] to 7 of 74 OFCs (10%) in a high-risk population.[7] Urticaria was the most common presenting symptom of a positive OFC in young children described in the HealthNuts population[8]; however, some infants did have symptoms of anaphylaxis. No markers (eg, SPT or serum-specific IgE) have been identified that predict reaction severity. IV lines were not placed before commencing challenges in any of the infants in the HealthNuts population. Although IV lines are rarely used in OFCs, it is recommended by this workgroup that physicians assess the capability of their office staff for starting an IV in an infant and consider this limitation before commencing an OFC in an infant. If it is not possible to start an IV line in an infant, an emergency plan should be in place that may include starting an intraosseous line and allowing expedient access to emergency care if needed.

PREPARATION FOR THE OFC

It is important that the infant is in good health at the time of the challenge. This includes optimal control of atopic dermatitis and asthma, in addition to the absence of symptoms of any concomitant illness to allow for correct interpretation of the challenge outcome and minimize the risk of a severe reaction.[3] Before beginning the challenge, verify that medications that may interfere with test interpretation have been discontinued (Table I). A light meal may be given 2 hours before the challenge (ie, half of the infant's usual amount).[3]

Timing of the challenge is particularly important. Considerations include timing the challenge with a normal feeding time for the infant, and avoid scheduling the challenge during a typical naptime. Inform the family that if the infant reacts he may need to be observed for several hours after resolution of symptoms. Parents may want to bring things to entertain the infant such as books, toys, and so on. A checklist of considerations and steps for challenge preparation are included in Table IV.

CHALLENGE METHODS

Food options, portion sizes, and approach to the OFC

LEAP investigators used open (unblinded) OFCs to 3.9 cumulative grams of peanut protein at baseline or a 2 gram open feeding if skin testing was negative.[2] Similar graded challenge protocols for peanut are provided (Figure 2). Options 1 and 2 are recipes using smooth peanut butter diluted with either a fruit or vegetable puree (Option 1) or hot water (Option 2). Option 2 will provide a smaller total volume than Option 1. Option 3 provides an alternative with either peanut butter powder or peanut flour, and Option 4 is a challenge protocol using Bamba snacks. As outlined in previous OFC guidelines, the OFC should be conducted in an area where the peanut challenge product can be safely prepared and measured.[3] Using clean disposable plates, cups, and utensils during the OFC lowers the risk of cross-contact with other allergens between OFCs. Waiting 15-20 minutes between dose servings is typical, although longer times may be used if there is a suspicion that a reaction may be occurring but objective symptoms are not yet present.

Be particularly mindful of the infant's development and ability to ingest various textures. In general, liquids and soft purees are tolerated by 4-6 months of age. An infant may progress to thicker purees and foods that dissolve easily (eg, teething foods such as crackers or toast) between 7 and 9 months of age. Before the challenge, verify with the parent that the food texture offered in the challenge and/or fruit puree if the peanut product is being mixed has already been tolerated at home. It is also prudent to have the parent provide different food options in case the infant refuses the offered food. Interpretation of oral aversion suggested by personal preference versus a sign of allergy during a challenge may be difficult in an infant. Consider allowing more time for a challenge in an infant than might be allotted for an older child due to the unpredictable nature of aversions and behavior. Dosing volumes outlined in Figure 2 may

TABLE IV. Considerations and preparation for infant OFC

Before the challenge

1. Have an open discussion with the family with particular emphasis on plans after the challenge. For instance, if the family states that they will not be able to feed the infant peanut products on a regular basis after the challenge, then reconsider the necessity of performing the challenge.
2. Optimize control of atopic dermatitis (AD) and asthma. Do not perform the challenge in an infant with poorly controlled AD, wheezing, coughing, URI symptoms, or febrile illness within the previous 1-2 wk due to the fact that viral illnesses may decrease reaction threshold and interfere with assessment of symptoms during a challenge.
3. Remind parents that the infant may have a light meal (eg, half of the usual serving) 2 h before the challenge.
4. Verify that the food texture to be offered in the challenge and/or fruit or vegetable puree if the peanut product is to be mixed has already been previously tolerated.
5. Remind the family to bring entertainment, toys, music, etc. during the challenge.

Day of the challenge

1. Confirm with family that medications that may interfere with OFC interpretation have been discontinued, as outlined in Table I.
2. Documentation of verbal or written informed consent should be considered.
3. Obtain the infant's weight, temperature, heart rate, blood pressure, respiratory rate, and oxygen saturation level.
4. Perform a thorough physical examination including examination of ears (do not perform the challenge if the infant has evidence of an ear infection), oropharynx and nose (getting baseline visualization of uvula and tongue, rhinorrhea, congestion, etc.), lungs (listen for wheezing, crackles, or coarse breath sounds), and skin (looking for any rashes, urticaria, birth marks, etc.).
5. Calculate doses of emergency medications (Table II).
6. Prepare the food challenge product (Figure 2).
7. Administer doses as outlined in Figure 2. Give each dose 15-20 min apart. Perform a brief physical examination including visualization of the oropharynx, auscultation of the lungs, and visualization of the skin between each dose.
8. Repeat vital signs with any noted change in the physical examination.
9. The ingestion challenge should ideally be performed over 1-2 h. If the challenge takes longer than 2-3 h, interpretation may be difficult because of the full dose being dispersed, and repeating the challenge at another time may be considered.

Postchallenge instructions

Infant ingests full amount and does not have a reaction

- Instruct family to provide an age-appropriate, safe peanut product totaling 6 g of protein per week, divided over 3 servings (eg, 2 tsp of peanut butter puree per serving at least 3 times per week).

Infant ingests more than half of the challenge (completes dose 3) but refuses the remainder (doses 4 and 5)

- Instruct the family to give an equivalent amount at home and if tolerated, increase serving to an age-appropriate, safe peanut product totaling 6 g of peanut protein per week divided over 3 servings (eg, 2 tsp of peanut butter puree per serving at least 3 times per week).

Infant does not complete dose 3 but tolerates doses 1 and 2

- Results are inconclusive. Continue peanut avoidance and return for challenge at another time (eg, in 1-2 wk or longer depending on family preference).

Infant has a reaction during the challenge and is considered allergic

- Instruct family on peanut avoidance.
- Provide food allergy action plan and discuss the signs and symptoms of a food-induced allergic reaction.
- Provide a prescription for 2 autoinjectable epinephrine devices and demonstrate appropriate use with a trainer device.

OFC, Oral food challenge; *tsp*, teaspoons; *URI*, upper respiratory infection.

be appropriate for older infants, but the volume may be especially challenging for younger infants (eg, ≤6 months). If the full feeding is not achieved, clinical judgment should be used to advise whether the infant is or is not allergic. Table IV provides recommendations that may be given in case the full challenge dose is not ingested.

Stopping the food challenge

In general, infant food challenges should be stopped at the first objective signs of an allergic reaction, and the reaction should be treated appropriately. Because infants are nonverbal, subjective complaints may be lacking and results may be equivocal, owing to the difficulty in judging OFCs in this population. For these reasons, it is particularly important to carefully observe for objective signs of a reaction, though consideration should be given to terminating OFCs even in the absence of clear allergic symptoms. Subtle symptoms may include ear picking, tongue rubbing, putting a hand in the mouth, or neck scratching.[3] More obvious signs of an allergic reaction include sneezing, rhinorrhea, urticaria, angioedema, coughing, wheezing, stridor, vomiting, diarrhea, flushing, scratching, tachycardia, and rarely hypotension. Potential signs of anaphylaxis can be difficult to interpret because they also occur in healthy infants and may include irritability, clinging to a caregiver, inconsolable crying, and somnolence.[4] In case of symptoms that are difficult to interpret, provider discretion may be used in determining whether to proceed with the challenge or rather to consider repeating the challenge on another day.

Du Toit et al[2] noted predominantly skin symptoms in infant peanut challenges at study entry in the LEAP trial. No subjects were reported to have wheezing or hypotension. Epinephrine was not required for any infant. Of the 7 subjects (2.2% of those challenged)

General instructions:
There are 5 incremental doses in the observed challenge. Doses may be given 15 to 20 minutes apart. Observe for symptoms of reactivity before giving the subsequent dose.
The measurement of a "level" measuring teaspoon used in this protocol is recommended over the measurement of a "rounded" teaspoon used in Du Toit et al[2] to promote consistency and ease of measurement. The peanut protein content is however similar.

OPTION 1: Smooth Peanut Butter Puree Recipe (3.96 g peanut protein)

Option 1 Instructions:

1. Measure peanut butter dose 1.
2. Add measured dose 1 previously tolerated infant puree fruit or vegetable to the measured peanut butter dose. Stir until well blended.
3. May adjust the infant puree amount to achieve desired consistency.
4. Label dose 1.
5. Repeat steps 1-3 for doses 2-5; labeling the finished dose with the appropriate dose number.
6. Feed dose 1 and observe for symptoms of reactivity for 15-20 minutes.
7. If no symptoms, repeat with doses 2-5 observing for symptoms of reactivity for 15-20 minutes between each dose.

Dose	Peanut butter (teaspoon)*	Equivalent weight (g), (Peanut protein content [g]) †	Pureed fruit or vegetable volume (teaspoon)	Total volume (teaspoons)
1	1/8	0.67 (0.15)	1/2	5/8
2	1/4	1.33 (0.29)	3/4	1
3	1/2	2.67 (0.59)	1	1 ½
4	1	5.33 (1.17)	2	3 ‡
5	1 ½	8 (1.76)	4	5 ½
		Total protein: 3.96 g		

FIGURE 2. Observed peanut challenge protocol options. *The amounts (volume in teaspoons) of peanut butter are approximate measures to keep the dosing as practical as possible. †The peanut protein content is calculated based on the average amount of protein for a range of butters using the USDA Nutrition Database.[24] ‡3 teaspoons = 1 tablespoon. §The information regarding peanut powder and flour reflects averages obtained from the producers. Most brands of peanut flour/peanut butter powder are approximately 50% peanut protein by weight. However, weight may vary based on the fat content and also the brand chosen; therefore, a weight measurement may be more accurate than household measurements. ¶The amount of Bamba sticks are approximate measures looking at a range of Bamba products i.e., Bamba snacks from different parts of the world have a varied peanut protein content. The peanut protein content of Bamba was calculated according to the publication by Du Toit et al.[2] This recipe was developed based on this protein content of Bamba; however, an alternative, similar peanut puff snack may be used as long as the peanut protein content is known and adjustments in dosing are made accordingly. #It may not be necessary to mix Bamba with water for infants who are able to eat foods of similar texture.

who reacted during the entry challenge, all 7 received antihistamine and 1 also received a corticosteroid.

Koplin et al[8] reported results from more than 1500 OFCs in 12-month-old infants who were recruited from the general population. OFCs were conducted for peanut, egg, and sesame. Peanut OFCs were performed giving a cumulative total of 1.94 teaspoons of peanut butter (2.1 g of peanut protein) divided over 6 servings each given 20 minutes apart.[9] Challenges were performed and monitored by registered nurses and supervised by a study physician. Importantly, and of relevance to these recommendations, all OFCs were undertaken with study nurses blinded to SPT and history of previous reaction. This was to ensure that all challenges were performed in a standardized way and to prevent bias in stopping challenges early in patients with large SPT wheal sizes or previous reactions. The predetermined stopping criteria consisted of observation of one or more of the following objective signs: 3 or more noncontact, concurrent urticaria lasting more than 5 minutes, facial angioedema, vomiting, or early signs of anaphylaxis (eg, wheezing, persistent cough, hoarse cry, etc.) (Figure E1). Urticaria was the predominant symptom whether due to peanut, egg, or sesame. It is important to note that urticaria may be small in size and the infant should be carefully examined before commencing the observed introduction and before administration of each challenge dose.

Subjects also experienced vomiting, angioedema, and anaphylaxis (anaphylaxis rate 2.4% of 535 positive challenges). Anaphylaxis was more common in sesame and peanut challenges compared with egg challenges (6 of 385 positive egg challenges [1.6%], 5 of 121 positive peanut challenges [4.1%], and 2 of 29 positive sesame challenges [6.9%]), although this was not statistically significant. All subjects with anaphylaxis (n = 13) received epinephrine, and 9 of those also received albuterol. None required

OPTION 2: Smooth Thinned Peanut Butter Recipe (3.96 g peanut protein)

Option 2 Instructions:

1. Measure peanut butter dose 1.
2. Slowly add measured dose 1 hot water and stir until peanut butter is dissolved, thinned and well blended.
3. May adjust water volume (or add previously tolerated infant cereal) to achieve desired consistency.
4. Label dose 1.
5. Repeat steps 1-3 for doses 2-5, labeling the finished dose with the appropriate dose number.
6. Check the final temperature of the thinned peanut butter before serving. It should no longer be hot.
7. Feed dose 1 and observe for symptoms of reactivity for 15-20 minutes.
8. If no symptoms, repeat with doses number 2-5 observing for symptoms of reactivity for 15-20 minutes between each dose.

Dose	Peanut butter (teaspoons)*	Equivalent weight (g), (Peanut protein content [g])†	Volume of hot water (teaspoons)	Total volume (teaspoons)
1	1/8	0.67 (0.15)	1/8	1/4
2	1/4	1.33 (0.29)	1/4	1/2
3	1/2	2.67 (0.59)	1/2	1
4	1	5.33 (1.17)	1	2
5	1 ½	8 (1.76)	1 ½	3‡
		Total protein: 3.96 g		

OPTION 3: Peanut flour or peanut butter powder (3.88 g peanut protein)

Option 3 Instructions

1. Measure peanut flour or peanut butter powder dose 1.
2. Slowly add dose 1 of previously tolerated pureed fruit or vegetable to dose 1 peanut flour or peanut butter powder and stir until well-blended. You may increase or reduce volume of puree to achieve desired consistency. Note: increasing the volume may increase the difficulty of getting through the entire protocol with a young baby.
3. Label dose 1.
4. Repeat steps 1-3 for doses 2-5; labeling the finished dose with the appropriate dose number.
5. Feed dose 1 and observe for symptoms of reactivity for 15-20 minutes.
6. If no symptoms, repeat with doses number 2-5 observing for symptoms of reactivity for 15-20 minutes between each dose.

Dose	Peanut flour or peanut butter powder (teaspoon)*	Equivalent weight peanut flour or peanut butter powder§ (g) (Peanut protein content [g])	Pureed fruit or vegetable volume (teaspoon)	Total volume (teaspoon)
1	1/8	0.25 (0.13 g)	1/2	~3/4
2	1/4	0.5 (0.25 g)	1	1 ¼
3	1/2	1.0 (0.5 g)	2	2 ½
4	1	2.0 (1.0 g)	3‡	4
5	2	4.0 (2.0 g)	6	8
		Total protein: 3.88 g		

FIGURE 2. (*CONTINUED*).

OPTION 4: Bamba peanut snack (Osem) (3.9 g peanut protein)

Option 4 Instructions:

1. Measure Bamba sticks for dose 1.
2. Prepare the first dose:
   a. Slowly add hot water to measured Bamba and stir until peanut solution is dissolved, thinned, and well blended. You may increase or decrease the water volume to achieve desired consistency.
3. Label dose 1.
4. Repeat steps 1-3 for the remaining doses 2 through 5, labeling the finished dose with the appropriate dose number.
5. Check the final temperature of the thinned Bamba solution before serving. It should no longer be hot.
6. Feed dose 1 to infant and observe for symptoms of reactivity for 15-20 minutes.
7. If no symptoms appear, repeat with doses 2-5 observing for symptoms of reactivity for 15-20 minutes between each dose.

Dose	Bamba dose (sticks)	Equivalent weight (g), (Peanut protein content [g])¶	Volume of hot water# (teaspoons) (approximate – will need to be adjusted for each child)	Total volume (teaspoons)
1	1	0.81 (0.1)	½	~3/4
2	3	2.43 (0.3)	1	~1 ½
3	5	4.05 (0.5)	1 ½	~2 ¼
4	10	8.1 (1.0)	3‡	~4
5	21	17.01 (2.0)	6	~7 ½
		Total protein: 3.9 g		

FIGURE 2. (*CONTINUED*).

intensive care admission, and no biphasic reactions were observed. It should be noted that 39 of 226 infants had transient urticaria during the OFC (lasting less than 5 minutes and therefore did not constitute stopping criteria), and 5 (13%) of those 39 individuals had a reaction at home with subsequent dosing within the next 48 hours.

Although data regarding infant food challenges are limited, based on the best available evidence, urticaria is likely to be the most common symptom observed in a positive food challenge in an infant. In the algorithm of major and minor criteria developed to judge OFCs in the LEAP study, the investigators considered urticaria to be a major criterion sufficient to stop the challenge but required $\geq$3 urticarial lesions to do so (Figure E1). It is also important to note that anaphylaxis may occur in the absence of dermatologic symptoms.

Recommended stopping criteria from this workgroup are included in Figure 3.

It is important to note that the physician is encouraged to use discretion and clinical judgment when assessing the challenge outcome. For example, symptoms such as a change in affect may be noted that make interpretability especially challenging with this age group. In such cases, it may be appropriate for the clinician performing the challenge to decide if a challenge dose should be repeated, the next dose should be delayed, or if the challenge should be stopped and repeated on another day. If clinically indicated dosing is stopped. Objective symptoms that recur on 3 doses or persist (eg, 40 minutes) are more likely indicative of a reaction than when such symptoms are transient and not reproducible.[10] Stopping criteria for the LEAP trial and HealthNuts trials may also be used as a reference for stopping a challenge and are included in Figure E1.

Treating reactions

Vital signs should be obtained and the infant should be examined at the first signs of a reaction. The infant may be placed in a supine or semireclining position and intramuscular epinephrine should be given in the mid-outer thigh at the first signs of anaphylaxis (Figure 1).[4] Absolute indications for epinephrine use include coughing, difficulty swallowing, dyspnea, wheezing, cyanosis, dysrhythmia, repetitive vomiting, hypotension, respiratory arrest, bradycardia, and/or loss of consciousness.[11] IV fluids may be additionally necessary in case of hypotension, repetitive emesis, and/or severe diarrhea, and albuterol and oxygen may be considered adjunctive treatments for lower respiratory symptoms. H1 antihistamines may be given for mild symptoms of an allergic reaction (eg, localized dermatologic symptoms, pruritus, rhinoconjunctivitis)[3] and as adjunctive therapy for more severe reactions. Multisystem reactions including mild symptoms involving 2 or more organ systems are also considered anaphylaxis[12] and should be treated with epinephrine. It is usually recommended to observe a child after a positive challenge for at least 2-4 hours.[3,10] An observation period of at least 1-2 hours is usually recommended for a child who does not show symptoms during the challenge (ie, passes the challenge).

Adverse Reactions to Foods Committee Stopping Criteria*
The OFC should be stopped if any one of the following symptoms are present during the OFC:
Skin • ≥3 urticarial lesions • Angioedema • Confluent erythematous, pruritic rash Respiratory • Wheezing • Repetitive cough • Difficulty breathing/increased work of breathing • Stridor • Dysphonia • Aphonia Gastrointestinal • Vomiting alone not associated with gag reflex • Severe abdominal pain (such as abnormal stillness, inconsolable crying or drawing legs up to abdomen) that persists for ≥ 3 minutes Cardiovascular • Hypotension for age not associated with vasovagal episode
If 2 or more of the following are present the OFC should be stopped:
Skin • Persistent scratching for ≥ 3 minutes Respiratory • Persistent rubbing of the nose or eyes for ≥ 3 minutes • Persistent rhinorrhea for ≥ 3 minutes Gastrointestinal • Diarrhea

FIGURE 3. Suggested food challenge stopping criteria from the Adverse Reactions to Foods Committee of the American Academy of Allergy, Asthma, and Immunology. *It is important to note that the physician is encouraged to use discretion and clinical judgment when assessing the challenge outcome. Whenever observed signs or symptoms are inconclusive it may be appropriate for the clinician performing the challenge to decide if a challenge dose should be repeated, the next dose should be delayed, or if the challenge should be stopped and repeated on another day. If clinically indicated, dosing is stopped. Objective symptoms that recur on 3 doses or persist (e.g. 40 minutes) are more likely indicative of a reaction than when such symptoms are transient and not reproducible.

RECOMMENDATIONS AT DISCHARGE

Recommendations for the infant who passes office introduction

There are limited data regarding the appropriate amount of the allergenic food to be ingested for an infant who is not allergic (ie, passes the food challenge or has no evidence of sensitization). Du Toit et al[2] recommended ingestion of at least 6 g of peanut (ie, 2 bags of Bamba [1 oz per bag] or 5 teaspoons of peanut butter) divided over at least 3 meals per week for the first 5 years of life. The LEAP trial did not address use of alternative forms of peanut protein, the minimal length of treatment necessary to maintain tolerance, or potential risks of premature discontinuation or sporadic feeding of peanut. We recommend a discussion with the family before the challenge about their intent and plan to regularly serve peanut products. Based on the available evidence and opinion, regular and ongoing consumption (ie, at least 3 days a week) of a moderate amount of peanut products may be considered appropriate.

It is important to note that a risk of allergy development exists for children who pass the challenge; therefore, follow-up after 3-6 months is recommended to enforce the importance of regular ingestion of peanut. Du Toit et al[2] reported subsequent reactions in 2.8% (9/319) of the children in their study who initially tolerated peanut. Reasons for discontinuation in the LEAP trial included parental caution to feed peanut, development of urticaria during feedings, eczema flares deemed secondary to peanut, anaphylaxis to peanut in one child, and food protein induced enterocolitis syndrome (FPIES) to peanut in one child.[2] Other investigators have reported subsequent development of peanut allergy despite frequent ingestion or having passed an observed challenge.[13-15] Relapse has been reported with cessation of exposure among previously peanut-allergic children who pass a challenge but fail to stably incorporate peanut into the diet.[14] Reasons for the development of subsequent allergy are unknown; however, particular attention should be given to families with a high-risk infant who are either hesitant to feed the allergen frequently at home or the child refuses to ingest the food at home. Caregivers should be instructed to contact the office in case of any acute adverse symptoms associated with peanut feeding at home and/or worsening of chronic conditions such as atopic dermatitis or gastrointestinal complaints.

- Use utensils, cutting boards and pans that have been thoroughly washed with soap and water. Consider using separate utensils and dishes for making and serving safe foods. Some families choose a different color to identify the safe kitchen tools.
- If you are making several foods, cook the allergy-safe foods first.
- Keep the safe foods covered and away from other foods that may splatter.
- If you make a mistake, you cannot remove the allergen from the meal. Even a small amount of cross contact makes a food unsafe.
- Wash your hands with soap and water before touching anything else if you have handled a food allergen. Sanitizing gels or water alone will not remove an allergen.
- Wash counters and table with soap and water after making meals.
- Do not share food, drinks or utensils. Teach children not to share these items when they are at school or with friends.

FIGURE 4. Tips to avoid cross-contact.

Food allergy management and minimization of cross-contact

For an infant who is determined to be allergic to peanut, the family should be provided a prescription for autoinjectable epinephrine, and its use should be demonstrated. It is recommended that food-allergic individuals receive a prescription for 2 autoinjectable epinephrine devices and they should carry both at all times.[16,17] In addition, a food allergy action plan should be reviewed, detailing symptoms of an allergic reaction and the appropriate treatment to be administered.[18]

Many infants commencing early introduction of peanut products may have an older sibling with a peanut allergy. If an infant with a peanut allergic sibling is able to introduce peanut into their diet, then cross-contact within the home will become a concern. Cross-contact refers to inadvertent transfer from a food containing an allergen to a food that does not contain the allergen.[19] Tips for avoiding cross-contact at home are outlined in Figure 4.

The reader is encouraged to read a recent review for additional information regarding food allergy management,[20] which is outside of the scope of this workgroup report. The review addresses numerous topics including label reading, recognition of a food-induced allergic reaction, use of a food allergy action plan, treatment of a reaction, precautions to take when traveling, and communicating with restaurant staff when eating outside of the home.

CONCLUSIONS

The LEAP and LEAP-On trials provide high-quality, Level 1 evidence that peanut allergy can be prevented through early introduction in high-risk infants, an approach recently supported by global allergy societies.[1,2,21] Specific recommendations about how to operationalize the findings into daily practice are lacking. In response to this need, a workgroup from the Adverse Reactions to Foods Committee of the American Academy of Allergy, Asthma, and Immunology was formed. Here we issue some suggested guidelines to prepare allergy offices for OFCs and management of anaphylaxis in infants at high risk for developing peanut allergy. These guidelines were developed based on consensus expert opinion and relied heavily on published experience from the LEAP and HealthNuts trials.[2,8,9,22] Although we are encouraged from the LEAP and LEAP-On results that early feeding may begin to stem the recent increase in peanut allergy prevalence, implementation into real-world settings remains an important challenge. Allergists will play a key role in ensuring the safety and long-term health of this vulnerable population. We await more formal recommendations on early-life, complementary feeding practices from the NIAID-sponsored Working Group and European Academy of Allergy and Clinical Immunology.

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LEAP OFC Stopping Criteria
A positive food challenge will be defined by the presence of either of the following: • One or more major criteria. • Two or more minor criteria. An indeterminate food challenge will be defined by the presence of one minor criterion. A negative food challenge will be defined by the absence of major or minor criteria. All symptoms should be of new onset and not due to ongoing disease. Symptoms must occur no later than 2 hours after the last dose.
MAJOR CRITERIA
• Confluent erythematous pruritic rash • Respiratory signs (at least one of the following): wheezing inability to speak stridor dysphonia aphonia • ≥ 3 urticarial lesions • ≥ 1 site of angioedema • Hypotension for age not associated with vasovagal episode • Evidence of severe abdominal pain (such as abnormal stillness or doubling over) that persists for ≥3 minutes
MINOR CRITERIA
• Vomiting • Diarrhea • Persistent rubbing of nose or eyes that lasts for ≥3 minutes • Persistent rhinorrhea that lasts for ≥3 minutes • Persistent scratching that lasts for ≥3 minutes

HealthNuts OFC Stopping Criteria
• ≥3 concurrent non-contact hives lasting for 5 or more minutes • perioral or periorbital angioedema • vomiting (not including gag reflex-induced vomiting occurring during feeding), or • evidence of circulatory or respiratory involvement (defined as anaphylaxis). The oral food challenge is declared positive when any one of these criteria appear within 2 hours of ingestion.

FIGURE E1. Learning Early About Peanut (LEAP) and HealthNuts Oral Food Challenge stopping criteria.[2,8]