Introduction of Allergenic Foods to Infants, especially Peanuts:

Interim Guidance for Canadian Dietitians

January 2017

This interim communication is from Dietitians of Canada (DC), PEN®-approved. It is intended to provide a timely summary for DC members, and Canadian dietitians in general, as they provide practice advice to caregivers of pediatric clients.

CONTEXT:

The NIAID Addendum Guidelines for the Prevention of Peanut Allergy in the United States (1) were published on January 5, 2017. This guideline gives advice regarding infant introduction of peanut stratified by infant's risk of peanut allergy (severity of eczema or the presence of an egg allergy). For recommendations where evidence is lacking, the guideline incorporates expert opinion. The NIAID guideline is officially endorsed by the Canadian Society of Allergy and Clinical Immunology (CSACI), the Academy of Nutrition and Dietetics as well as several international professional organizations. Health Canada, Dietitians of Canada and the Canadian Pediatric Society (CPS) have not officially endorsed these new guidelines at this time.

Since dietitians are one of the key professions advising parents on the introduction of solid foods, especially commonly allergenic foods, Dietitians of Canada offers the following details to inform how the scientific evidence regarding peanut introduction and current dietetic practice recommendations agree and differ from these NIAID (1) recommendations.

SUMMARY:

In brief, the key differences between the 2017 NIAID guidelines (1) and the current Nutrition for Healthy Term Infant (NHTI) recommendations in Canada (2,3) are in the different definitions of "at risk" infants, the strength of wording for introducing peanut containing food early, and the recommendation to undergo physician supervised testing/feeding before introduction for a small subset of very high-risk infants. The vast majority of infants can have peanut protein introduced safely at home (2,3). The following is a comparison of the new NIAID guidelines (1) followed by a brief summary of the evidence and a comparison with current Canadian NHTI guidelines (2,3). The NIAID 2017 guidelines are divided by infants' risk of peanut allergy.

NIAID 2017 Guideline 1:

"The Expert Panel recommends that infants with severe eczema, egg allergy, or both have introduction of age-appropriate peanut-containing food as early as 4 – 6 months of age to reduce the risk of peanut allergy. Other solid foods should be introduced before peanut-containing foods to show that the infant is developmentally ready.

The EP recommends that evaluation with a peanut-specific IgE (peanut sIgE) blood test measurement, skin prick tests (SPTs), or both be strongly considered before introduction of peanut to determine if peanut should be introduced and, if so, the preferred method of introduction.

Infants who have a positive (≥ 3 mm wheal diameter) peanut skin prick test are recommended to receive a physician supervised feeding/oral peanut challenge. Those with a positive peanut-specific IgE (≥ 0.35 kU/L) should be referred to a specialist for further evaluation including the physician supervised feeding/oral peanut challenge.

To minimize a delay in peanut introduction for children who may test negative, testing for peanut sIgE may be the preferred initial approach in certain health care settings, such as family medicine, paediatrics, or dermatology practices, in which skin prick testing is not routine. Alternatively, referral for assessment by a specialist may be an option if desired by the health care provider and when available in a timely manner."
(Please refer to the NIAID guideline for definitions of eczema and egg allergy.)

The evidence
This 2017 NIAID guideline (1) is based on the large relative risk reductions in peanut allergy among high-risk infants given regular exposure to peanut beginning between 4 - 11 months of age in the LEAP (Learning Early About Peanut) trial (4) compared to children who were not given peanut until 5 years of age. Infants at high risk of peanut allergy were defined as having severe eczema and/or egg allergy in LEAP. There was a relative risk reduction of up to 86.1% with early (4 - 11 months) compared to delayed (5 years) peanut introduction. The overall rates of peanut allergy among those children not sensitized were 2% in the exposed group and 14% in the avoidance group ($p<0.001$). For background about the LEAP trial, read this DC Evidence Clip (5).

Current Canadian guidelines in NHTI
NHTI 6-24 months (3) does not contain guidance specific to "high risk" infants, as defined by the NIAID guideline. Using the traditional definition of "at risk" of atopy, NHTI advises, "Common food allergens, such as peanut, fish, wheat (including iron-fortified infant cereals with wheat), milk products, soy and whole eggs, can be introduced *from about six months of age*. Several of these foods, such as iron-fortified infant cereals with wheat, fish and whole eggs, should be among the first solid foods offered because they are also a source of iron."

Comment
The 2017 NIAID recommendation is supported by high quality evidence from one randomized controlled trial (4) as well as expert opinion from 26 international professional organizations.

The LEAP trial (4) was important since it demonstrated that among infants at high risk of allergy, earlier rather than later peanut ingestion dramatically reduces the risk of peanut allergy. This finding is important since previous public health advice had been recommending delayed introduction of allergens to high-risk infants. (See "the Bottom Line" section on p. 4, for a discussion about the timing of the introduction of solids.)

The LEAP trial (4) protocol had infants in the early introduction group eating at least 6 grams of peanut protein per week, divided into three of more meals. Peanut protein introduction must be age appropriate since both whole peanuts and non-diluted peanut butter are choking hazards for infants. Please see the NIAID guideline (1) for descriptions for additional information for infants who are highly sensitized to peanut (and thus peanut introduction should be avoided) and for advice about family members in the household who may be allergic to peanut. In the appendix to this guideline, please see how age-appropriate peanut protein was introduced to young infants in the LEAP trial (e.g., recipes for non-choking forms of peanut and instructions for how to feed) (4).

NIAID 2017 Guideline 2:

"The Expert Panel suggests that infants with mild-to-moderate eczema should have introduction of age-appropriate peanut-containing food around 6 months of age, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy. Other solid foods should be introduced before peanut-containing foods to show that the infant is developmentally ready. The EP recommends that infants in this category may have dietary peanut introduced at home without an in-office evaluation. However, the Expert Panel recognizes that some caregivers and health care providers may desire an in-office supervised feeding, evaluation, or both."

The evidence

This NIAID recommendation is largely based on expert opinion. As mechanisms of sensitization are not thought to be different based on degree of eczema, there is potentially a large benefit to early introduction in this population. In addition, as described in the NIAID guideline (1), in the LEAP trial (4), some infants testing positive for egg allergy had eczema that was categorized as mild to moderate. However, the quality of evidence is low because the majority of participants in the LEAP trial had severe eczema, making it difficult to draw conclusions about infants with mild to moderate eczema.

Current Canadian guidelines in NHTI

For infants "at risk" of atopy, NHTI (3) advises "Common food allergens, such as peanut, fish, wheat (including iron-fortified infant cereals with wheat), milk products, soy and whole eggs, can be introduced from about six months of age".

Comment

This 2017 NIAID recommendation was largely based on expert opinion that infants with mild to moderate eczema would likely benefit from early peanut introduction despite the lack of clinical data for this group. There is no difference between this recommendation and what NHTI (3) currently advises.

NIAID 2017 Guideline 3:

"The Expert Panel suggests that infants without eczema or any food allergy have age-appropriate peanut-containing foods freely introduced in the diet together with other solid foods and in accordance with family preferences and cultural practices."

The evidence

This NIAID guideline was primarily informed by a lack of evidence to suggest that immune mechanisms of oral tolerance differ in infants without eczema or food allergy when compared to infants at high risk of peanut allergy. The EAT trial, which sampled infants from the general population in the UK, found there was no significant difference in the intention-to-treat analysis in proportion of children with a food allergy at age 3 when peanut, cooked egg, cow's milk, sesame, whitefish, and wheat were introduced starting between approximately 3 months compared to at 6 months, but found a significant improvement in the per-protocol analysis with a lower risk of food allergy for the early introduction group, 2.4% vs. 7.3%, p=0.01 (6). A feasibility study for the EAT trial found 97% of infants who had solid foods introduced starting at 3-4 months were still breastfeeding at 6 months. Therefore, the introduction of commonly allergenic foods to breastfed infants starting at 3-4 months did not impact overall breastfeeding duration (7). The Jewish study compared the allergy prevalence of Jewish children living in the UK and in Israel (8). The prevalence of peanut allergy was one-tenth the rate among the children raised in the Israel (where peanut was introduced early and eaten frequently) compared to those raised in the UK (where peanut introduction was delayed).

Current Canadian guidelines in NHTI

Recommend exclusive breastfeeding for the first six months. Recommend meat, meat alternatives, and iron-fortified cereal as an infant's first complementary foods (2).

Comment

Because healthy term infants are without identified risk (2), compared to the definition used in the NIAID guidelines (1), there is no evidence to suggest deviation from Canada's current infant feeding guidelines (2).

Other Canadian policy documents:

The Canadian Pediatric Society has a position paper, re-affirmed in 2016, entitled *Dietary Exposures and Allergy Prevention in High Risk Infants* (13), endorsed by Dietitians of Canada (see www.dietitians.ca/infant).

Currently, in 2017, the CPS is developing a new Practice Point about the optimal age for the introduction of solid foods. DC's representative to the CPS, Becky Blair, is contributing to this initiative. DC members will be advised as and when new information is made available.

The Bottom Line:

The key advice from the 2017 NIAID guidelines is that parents should introduce peanut-containing food early, at around 6 months, and give regularly thereafter. Infants at high risk of developing peanut allergy (NIAID-defined, different than in any other guideline) are recommended to receive testing as well as a physician supervised feeding (if testing is positive) the first time peanut is introduced, whereas the vast majority of infants can be introduced to peanut safely at home. The 2017 NIAID guideline also provides practical instructions for preparing and feeding non-choking forms of peanut.

There is still good reason to continue to follow the advice in NHTI's 6-24 month's *In Practice* section regarding the introduction of commonly allergenic foods at about six months (3).

In addition, NHTI also advises:

- When first offered, avoid offering more than one of the common food allergens per day,
- Wait 2 days before another common food allergen is introduced,
- As new foods are introduced, encourage parents to watch for signs of allergy,
- Ensure size and texture of the food is age appropriate, and
- Continue to offer the commonly allergenic food regularly to maintain tolerance.

Current practice guidance offered in NHTI (3) does not contradict current available evidence from the LEAP (4) and EAT (6) trials. It is important to introduce solid foods to infants at about six months for reasons of allergen exposure, the need for iron-containing foods (2), and supporting food texture acceptance and less picky eating (9,10).

However valuable the LEAP trial was, it did not answer questions about if there is an ideal time within the 4 - 11 months window that is most beneficial to prevent peanut allergy. Therefore, we do not know the ideal time of introduction within the age range of 4 -11 months. There is currently no evidence of harm of introducing peanut protein between 4 - 6 months for food allergy risk (4,6), breastfeeding duration (7), or growth in infants (11).

Overall, families concerned about food allergy prevention in infants, especially high-risk infants, should consult with a physician.

Compelling research continues to emerge demonstrating a possible food allergy risk reduction. For example, a recent systematic review reported moderate level evidence of a reduced risk of egg allergy amongst infants introduced to egg protein between 4 - 6 months (12). As this area of research continues to evolve, and as our understanding of the biology of allergy increases, national policy changes for all Canadian infants related to the ideal age for the introduction of solids may be warranted.

Resources:

Introducing peanut-containing foods to prevent peanut allergy (*Video, 2 minutes* - American College of Allergy, Asthma and Immunology)

Evidence Clip: Food Allergy Prevention in Infants (Dietitians of Canada, 2016)

Eczema in babies and young children (BC Health Link, 2011)

For subscribers to Practice-based Evidence in Nutrition (PEN®): see additional content

Food Allergies – Low Risk Infant

Food Allergies – High Risk Infant

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