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Increasing Awareness of the Low Risk of Severe Reaction at Infant Peanut Introduction: Implications During COVID-19 and Beyond



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The novel coronavirus disease 2019 (COVID-19) has spread internationally, with more than 18.2 million individuals affected and more than 694,000 deaths internationally, including more than 155,000 deaths in the United States.¹ Multiple guidelines have emerged on the management of care during COVID-19, including a North American guideline on contingency planning for allergy/immunology clinics and a phased approach to resuming suspended allergy/immunology clinical services.^{2,3} These guidelines advocate health care resource reallocation that restricts access to all but the most essential ambulatory visits by shifting to virtual visits for most ongoing care.³ In addition, in the face of a very highly contagious pandemic, some have been hesitant about face-to-face interactions in the emergency department (ED).

As a result, COVID-19 may make some families more reluctant to introduce peanut early at home, especially among infants at a higher risk of developing peanut allergy. Little guidance exists about early food introduction during the COVID-19 pandemic. The goal of this article is to provide reassurance about the safety of early peanut food introduction, even during the current COVID-19 pandemic.

THE RISK OF A SEVERE REACTION ON FIRST INGESTION OF PEANUT IN INFANCY IS EXTREMELY LOW

Infant anaphylaxis tends to be mild, and mortality upon first ingestion during infant food introduction has not been described.⁴ First, even if anaphylaxis were to occur, evidence from the ED shows that infant anaphylaxis is milder than in older children. In a recent large retrospective cohort study of 1518 infants and children presenting with food allergy reactions to the ED in California, infants presented with respiratory symptoms less often than children age 1 year and ages 2 to 4 years (6.8%, 16.1%, and 23.9%, respectively; $P < .001$).⁵ Another retrospective review of 357 children with food-induced anaphylaxis seen in the ED in Chicago similarly noted a lower frequency of respiratory symptoms in infants, with wheezing in only 2% of infants younger than 12 months compared with 19% for those aged 12 to 23 months ($P = .008$), 31% for those aged 2 to 6 years ($P < .001$), and 22% for those older than 6 years ($P = .001$), and more frequent skin involvement ($P < .001$).⁶ Also, egg^{5,6} or cow's milk⁶ was a more common cause of food-induced reactions in infants presenting to the ED, instead of peanut.

Besides the relative mildness of infant anaphylaxis when it occurs, large observational studies and randomized controlled trials have found early introduction of peanut in infancy to be safe, with anaphylaxis being extremely low. In the Learning Early About Peanut study, only 7 of 319 (2.2%) high-risk infants randomly assigned to the peanut consumption group had a positive oral food challenge (OFC) at baseline.⁷ Symptoms were predominantly cutaneous and were treated with oral antihistamines (6 of 7) and oral steroids (1 of 6); none of the reactions required epinephrine. In the population-based HealthNuts cohort, of those infants who were introduced to peanut at home by age 12 months, reactions of any severity were rare (32 of 1320; 2.4%) and only 1 of 1320 (0.08%) had possible anaphylaxis due to wheeze (although later tolerated peanut on OFC at age 14 months).^{8,9} Using higher risk infants as the denominator, 1 of 185 (0.54%) had possible anaphylaxis due to wheeze. Using lower risk infants as the denominator, 0 of 1135 (0%) had possible anaphylaxis.

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A longstanding major concern of some allergists has been the fear of presumed severe reaction in infants with large positive screening SPT results before first ingestion (especially infants with a history of eczema), because the Learning Early About Peanut study did not do baseline OFCs in infants with SPT wheal diameter of more than 4 mm. To address this, a recent retrospective chart review of 84 infants that screened for peanut sensitization using the National Institute of Allergy and Infectious Diseases guideline approach noted that of the 7 infants with positive SPT wheal diameter of 3 to 7 mm who received an OFC, 3 of 7 (43%) reacted but all reactions were mild (cutaneous and/or upper respiratory) and responded to antihistamines.¹⁰ No anaphylaxis was noted and epinephrine was not required, and of those with negative SPT result, all infants were introduced to peanut at home with no reaction. Another retrospective chart review included a larger number of infants (70) who received OFCs after National Institute of Allergy and Infectious Diseases–based screening SPTs, which were even higher risk (>75% had eczema and ~50% had egg sensitization).¹¹ The study noted overall high tolerance to peanut on OFC (77%), and among infants with SPT wheal diameter of more than 4 mm, outcomes were very reassuring: 25 of 40 (63%) with SPT wheal diameter of more than 4 mm tolerated peanut, which included 13 of 18 (72%) with SPT wheal diameter of 5 to 7 mm and 12 of 22 (55%) with SPT wheal diameter of more than 7 mm. For the 16 of 70 (23%) who reacted at OFC, 9 infants were given epinephrine as a precaution for mild to moderate symptoms, with none having any significant respiratory, cardiovascular, or neurologic symptoms.

Based on the above evidence, the key takeaways are that the risk of severe reaction to peanut in infancy is extremely small, even among infants who experience anaphylaxis and even among infants at very high risk of developing peanut allergy. Therefore, peanut can be safely introduced at home for all infants (including higher-risk infants), during COVID-19 and once the pandemic has been controlled.

MOVING BEYOND SCREENING TO ADDRESS HESITANCY AMONG FAMILIES

Some families may not be comfortable introducing peanut in infancy without some form of preemptive evaluation, despite education of the above. However, preemptive screening would be considered very low priority when resuming in-person clinical visits.³ During COVID-19, some laboratories are closed and some allergy offices are exclusively virtual. Waiting for screening with SPT and/or specific IgE testing could result in delayed introduction and inadvertently increase the risk of peanut allergy. In addition, some of the barriers to preemptive screening including resource limitations, high rates of clinically irrelevant false-positive test results, lack of availability of infant OFCs, and poor cost-effectiveness are amplified during this time.¹²

For families with hesitancy, a shared decision-making approach that reviews benefits and risks is required, as is clear risk communication, including in the recognition and management of anaphylaxis.¹³ One novel approach for hesitancy that completely circumvents screening and has recently been shown during COVID-19 to be feasible is virtual physician-supervised home peanut introduction, especially among higher risk infants.¹⁴

This approach could be continued post-COVID-19, especially for families living in remote areas, settings where infant

OFCs are unavailable, or settings where there are no local allergists.

INCREASING AWARENESS OF THE LOW RISK OF SEVERE REACTION AT INFANT PEANUT INTRODUCTION IS NEEDED

Although food introduction during COVID-19 may be a significant concern for families, little international guidance exists on the safety of early introduction during the pandemic. The Canadian Pediatric Society has released a communication supporting early food introduction at home among infants at risk despite COVID-19.¹⁵ We now have a variety of newer data that support the extremely low risk of severe reaction upon infant first ingestion (even among higher-risk infants), which should be used to educate parents and inform statements from allergy organizations.

COVID-19 gives us an opportunity to reframe how we reassure families about the extremely low risk of severe reaction upon infant food introduction. Even among infants at a high risk of developing peanut allergy, there is evidence that early peanut ingestion at home is very safe and now is the time to start demedicalizing it.

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