



Letters

Institution of clinic scheduling guidelines for early introduction of peanut in high risk infants



Over the past 2 decades, the approach to peanut introduction and preventing peanut allergy has drastically changed.¹ The Learning Early About Peanut (LEAP) study² provided evidence for the National Institute of Allergy and Infectious Diseases (NIAID) guidelines³ for early peanut introduction. The current recommendations have complexities and criticisms regarding how to implement the guidelines; specifically with the shortage of allergists and possibility of developing peanut allergy while on waitlist for appointments.^{4,5} Despite these criticisms, many parents are eager for early introduction.⁶ We retrospectively evaluated our scheduling protocol aimed at minimizing wait time in introducing peanuts in high-risk infants.

We took a retrospective evaluation of infants at high risk for peanut allergy, as identified by the LEAP study,² who were referred to our academic tertiary care pediatric allergy office from July 2016 through September 2017. Our hospital system houses a pediatric and family medicine residency. Because of the timing of the rollout, we based our scheduling on interim guidelines and LEAP study.^{2,7} This time period included the launch of our allergy clinic with 2 allergists and was stopped when a new physician started. We see a mixture of general allergy and immunologic complaints. We had 9 sessions of clinic/week, each with 3 new patients/session and an average of 7 patients/session. Each week we had 8 food challenge slots (2/day). We are located adjacent to a pediatric hospital and emergency room. Our referral guidelines prioritized appointments for any patient younger than 12 months old, regardless of risk, and held 4 new patient slots per week for these patients. If these reserved appointment or challenge slots were not filled within 7 days from appointment, any new patient was scheduled. If there were no appointments available within 2 weeks, a physician would review the referral to determine urgency and scheduling. We also reserved 2 food challenge slots every week to be able to offer in-office peanut introduction in patients who were deemed to require it. Challenges were performed with a 6-step procedure, using a cumulative dose of 4.8 g peanut powder. Because NIAID guidelines were not published, this protocol was chosen as a conservative protocol based on published data and experience of the authors. Patients were monitored for 90 minutes after last dose. Screening, interpretation of tests, and treatment decisions were left up to the discretion of the attending physician. Patients who had not yet introduced solid food were instructed to introduce infant cereal daily for more than 2 weeks before challenge. Skin prick test measurements were recorded as longest diameter measured.

Disclosures: Nicholas Hartog: Horizon pharmaceutical speaking and advisory board; Takeda Pharmaceuticals speaking; Astrazeneca advisory board. Theodore Kelbel: Astrazeneca advisory board; Regeneron/Sanofi Genzyme advisory board and speaking. Andrew Kampfschulte: none

Funding Sources: none.

We identified 65 patients that fit high-risk criteria. Of the subjects, 36.9% were female and 63.1% were male. Patients not included in the analysis were younger than 12 months old, scheduled by the same protocol, but did not have severe eczema or egg allergy. Because of electronic medical record limitations, the no-show and cancellation rate for these slots is unknown, and we were unable to track the number of referrals needing physician review. The source of referral was pediatricians in 87.5%, dermatology in 7.8%, and 4.7% from other sources. Mean age at referral was 220 days old (range, 95–358 days). Patients were first evaluated in clinic a mean of 18.9 days after referral (range, 2–62 days). In 31 patients in whom peanut in office graded oral food challenge (OFC) was offered, the challenge was completed a mean of 11.2 days after initial appointment (range, 0–51). In total, patients were evaluated and peanut OFC completed in a mean of 31.25 days (range, 7–56 days). During this time, the mean time to first appointment for other referrals was 94.3 days (Table 1). Patients were deemed to be high risk for peanut allergy because of subjectively defined severe eczema alone 48 patients (73.8%), egg allergy alone in 12 patients (18.5%), and both egg allergy and severe eczema in 5 patients (7.7%).

Of patients screened with skin testing before introduction of peanut, 18 (27.7%) were advised peanut avoidance, OFC was recommended for 31 patients (47.7%), and 16 (24.6%) were recommended to introduce peanut at home. No reactions were reported with home introduction. For patients offered graded OFC, 12 (38.7%) had a positive challenge, 18 (58.1%) had a negative challenge, and 1 (3.2%) did not show to appointment. Symptoms of positive challenge were urticaria in 12 (100%) and vomiting in an additional 2 (16.7%) patients. No angioedema, wheezing, or hypotension was observed. Ten (83.3%) were treated with diphenhydramine, and in addition 4 (33.3%) with prednisolone a single dose of epinephrine.

Adverse events were minimal: 1 patient developed food protein–induced enterocolitis syndrome after the recommended introduction of rice cereal before peanut OFC, 1 patient reacted with hives outside of the 90-minute observation period, and 1 patient reacted to peanut at home 1 month after a passed OFC in clinic.

Limitations include the retrospective nature, with no pre-set criteria for screening or recommendations for introduction of peanut. We based our scheduling guidelines on interim and anticipated guidelines.⁷ This is also a single-center tertiary care pediatric hospital, which can affect external validity, although we would argue the safety of challenges and scheduling issues surrounding the NIAID guidelines apply broadly to many allergy clinics.

Currently there is variability among allergists in implementation and screening before peanut introduction in high-risk infants.⁸ As

Table 1

Time in Days from Referral to Our Clinic to Evaluation with Our Scheduling Algorithm

Mean Age at Referral	220.9
Mean Age at Evaluation	231.8
Mean Time from Referral to Appointment	18.9
Mean Time from Appointment to Challenge	11.2
Mean Time from Referral to Challenge	31.2
Mean Time from Referral to Appointment (General Clinic)	94.3

the demand for evaluation before introduction increases, allergists will need to respond by seeing these patients in a timely fashion. Previous studies have highlighted some challenges in implementation of guidelines at tertiary care centers.⁹ By prioritizing infants younger than 12 months of age referred to our clinic, we were able to evaluate and challenge high-risk infants within a month. This prioritized scheduling can help high-risk patients be seen in a timely matter despite a relative allergist shortage in some areas. This adds to the literature that graded OFCs to peanut in infants are safe and there is a need for more allergists to perform OFCs in infants. We would encourage the use of scheduling algorithms that prioritize scheduling of infants at high risk for peanut allergy.

Theodore Kelbel, MD*
 Andrew Kampfschulte, MS†
 Nicholas Hartog, MD*

*Helen DeVos Children's Hospital Allergy and Immunology
 Department, Michigan State University College of Human Medicine
 Grand Rapids, Michigan

†Spectrum Health Office of Research, Grand Rapids, Michigan
Nicholas.hartog@spectrumhealth.org

References

1. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol*. 2010;126:S1–S58.
2. Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372:803–813.
3. Togias A, Cooper SF, Acebal ML, et al. Addendum guidelines for the prevention of peanut allergy in the United States: report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. *Ann Allergy Asthma Immunol*. 2017;118:166–173.
4. Wood RA, Burks AW. LEAPing forward with the new guidelines. *J Allergy Clin Immunol*. 2017;139:52–53.
5. Greenhawt MJ, Fleischer DM, Atkins D, Chan ES. The complexities of early peanut introduction for the practicing allergist. *J Allergy Clin Immunol Pract*. 2016;4:221–225.
6. Lai M, Sicherer SH. Pediatricians underestimate parent receptiveness to early peanut introduction. *Ann Allergy Asthma Immunol*. 2019;122:647–649.
7. Fleischer DM, Fleischer DM, Sicherer S, et al. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. *Pediatrics*. 2015;136:600–604.
8. Abrams EM, Singer AG, Soller L, Chan ES. Knowledge gaps and barriers to early peanut introduction among allergists, pediatricians, and family physicians. *J Allergy Clin Immunol Pract*. 2019;7:681–684.
9. Stukus DR, Prince BT, Mikhail I. Implementation of guidelines for early peanut introduction at a pediatric academic center. *J Allergy Clin Immunol Pract*. 2018;6:1784–1786.

Isolated parenchymal pulmonary presentation of familial Mediterranean fever



Readily available exome sequencing is revolutionizing practitioners' ability to establish diagnoses with previously undefined disorders. Exome and genome sequencing have led to the identification of unique gene-disease associations in which clinical phenotype has been previously unknown to be associated with a specific genotype. Identification of unique gene-disease associations has led to a change in management in more than one-third of newly diagnosed patients.¹ Familial Mediterranean fever (FMF) is an autoinflammatory disorder caused by homozygous and heterozygous mutations of the *MEFV* gene encoding pyrin.² FMF manifests as acute, intermittent, 1- to 3-day fever and polyserositis, which improve with colchicine.³ This case report describes a patient with atypical parenchymal pulmonary presentation of FMF with the absence of fevers and serositis.

A 60-year-old Italian/Polish man presented with a 1-year history of dyspnea with productive cough, chest discomfort, and intermittent diaphoresis, although no fevers. History included obesity, obstructive sleep apnea, gastroesophageal reflux, selective IgA deficiency, and a 30 pack-year smoking history. He did not have recurrent infections; immunoglobulin levels were previously checked because his daughter was diagnosed with selective antibody deficiency. Pertinent physical examination revealed diffuse, bilateral crackles and hypoxia (oxygen saturation as measured by pulse oximetry in the low 80% on room air). Chest computed tomography revealed diffuse ground glass haziness in most of the pulmonary parenchyma with centrilobular nodules, peripheral nodules, and mediastinal and hilar lymphadenopathy (Fig. 1). Pulmonary function testing revealed

forced expiratory volume in 1 second (FEV₁) of 2.96 L (89% predicted), forced vital capacity (FVC) of 4.01 L (92% predicted), FEV₁/FVC ratio of 74%, and a mild reduction of diffusing capacity of the lungs for carbon monoxide of 65%, which normalized to 81% when corrected for alveolar volume. There was no change after bronchodilator administration. Complete blood cell count and quantitative immunoglobulin levels were normal except for an IgA level less than 20 mg/dL. The results of hypersensitivity pneumonitis panels and human immunodeficiency testing were negative. The antinuclear antibody test result was positive at 1:40 with a fine speckled pattern.

Bronchoscopy revealed normal mucosa and anatomy. Bronchoalveolar lavage revealed a nucleated cell count of 235/μL; 75% of cells were lymphocytes (99% T cells with a CD4/CD8 cell count of 24). Biopsies revealed mild chronic inflammation with intra-alveolar foamy macrophages, several CD117⁺ mast cells within the interstitium and airway wall, loosely formed nonnecrotizing granulomas, and absence of Langerhans and malignant cells. Cultures yielded *Citrobacter freundii* and *Escherichia coli*; no growth for acid-fast bacilli, viruses, or fungi was seen.

Multiple therapies were trialed, including azithromycin, doxycycline, trimethoprim-sulfamethoxazole, moxifloxacin, oral prednisone, azathioprine, leflunomide, and fluticasone propionate-salmeterol inhaled, with minimal improvement. The patient continued to develop progressive hypoxia with oxygen saturation to 69% requiring 6 L of oxygen and 40 mg of daily prednisone. He moved out of his house for months because of possible unknown exposures, yet his symptoms persisted.

Whole exome sequencing (WES) was performed and revealed a heterozygous genetic mutation of the *MEFV* gene (c.2084A > G;