

We describe 2 cases of male infants with IgE-mediated CMA that turned into non-IgE-mediated CMA. Three cases (a previous report⁷ and our 2 cases) had similar characteristics: male sex, very precocious allergic reaction to CM, and very rapid negativization to CM proteins, and in one of these cases, we report an initial very high s-IgE level. It is known that the development of tolerance to CM, in IgE-mediated allergy, is easier to reach, greater is the decrease in s-IgE levels during a short period of time,¹⁰ but in our cases, the rapid negativization of s-IgE was surprising associated with the shift from IgE-mediated CMA to FPIES.

In conclusion, we suggest considering the possibility of a shift to FPIES in managing infants with IgE-mediated CMA and a rapid negativization of SPT and s-IgE to CM in order to implement a proper protocol of milk reintroduction.

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A quality improvement initiative to increase access to food challenges

To the Editor,

Food challenges are critical to determine whether an individual has food allergy when history and testing are inconclusive or the allergy may have been outgrown.¹ Passing a challenge may have nutritional, psychological, and financial benefits.¹⁻³ We and others have shown that challenges can be safely carried out in a clinic setting.⁴⁻⁹

Challenges are underutilized, however, which can lead to unnecessary food avoidance, increased stress, and increased costs.³ One recent study estimated that delay in a food challenge resulted in an

annual increased cost to the patient/family of more than \$4000 and an overall cost of more than \$12 000.³

Due to high demand and limited access, patients in our clinic faced a delay of 6 months between a food challenge being scheduled and carried out. The primary limiting factor in offering challenges was availability of rooms for challenges which precluded us from meeting demand with weekday challenges. We therefore undertook a quality improvement initiative to improve access and decrease wait times. We focused both on increasing utilization (the fraction

of available slots that were used) and access (the total number of challenges performed). This initiative was exempt from IRB review as it represented a quality improvement initiative.

To increase utilization, we initially analyzed the proportion of available slots in which challenges were actually conducted. We queried a subset of patients on why they canceled or did not attend scheduled challenges. Common reasons included intercurrent illness, inability to stop antihistamines, and anxiety. We also identified instances in which patients were coming to clinic without the correct food and/or an unexpired epinephrine injector.

We then used several strategies to try and increase the utilization rate of challenges. These included improved education of families on what challenges involved (eg, to bring challenge food and self-injectable epinephrine) and a process to fill slots when cancellations occurred. Patients/families were given a handout about what to expect during the food challenge and specifically instructing them to bring the challenge food and self-injectable epinephrine. In addition, each family was called 2-3 days before the challenge to review this information. Finally, whenever a cancellation occurred, a designated staff member began calling patients on a waiting list for challenges to try and schedule them. These steps led to a 6.6% absolute increase in utilization from 68.6% to 75.2%. While modest, this improvement decreased the number of unused slots by 21%.

To improve access, we also added Saturday morning challenge sessions to increase the number of available slots. A variety of providers, including allergy nurses, nurse practitioners, as well as allergy/immunology and rheumatology fellows (who were already trained in conducting food challenges), conducted the challenges, with each typically performing 3-4 challenges per day. Oversight was provided by allergy and rheumatology attending physicians, with no more than 10 challenges overseen by one attending physician. The same protocols were used as during weekday challenges.

We were able to schedule up to 20 challenges per Saturday and eventually expanded from 1 to 2 Saturday sessions per month. This was very effective in increasing the number of challenges performed as shown in Figure S1. The total number of challenges performed rose from 250 in 2014 and 255 in 2015 to 428 in 2016, a 68% increase.

Our electronic medical record did not allow us to track wait times in a systematic manner, but we observed a decrease in the time to the first available slot from 6+ months at the start of the initiative to one month at the end. This decreased wait has been sustained.

In general, patients and families were enthusiastic about increased access in general and the option for Saturday challenges in particular. Several commented that coming for the challenge was easier due to decreased issues with traffic and parking and one noted the overall feeling was more relaxed than during the week.

There were some issues noted related to challenges being performed by inexperienced personnel (typically allergy/immunology fellows instead of experienced allergy nurses). For example, in one instance, the food was left in the patient's room and the patient consumed more than the target amount of food. However, these issues

typically were minor and did not lead to any significant adverse outcomes. We insured challenges could be conducted safely by having self-injectable epinephrine along with other medicines (diphenhydramine and albuterol) readily available, along with a stretcher to coordinate transport to the emergency department as necessary. The code team at our institution was also aware and ready to respond in case of a severe reaction, but this was not necessary.

To insure Saturday challenges were safe, we examined the proportion of challenges failed and requiring epinephrine for the first 6 months of 2016. Rates of failure were slightly higher on Saturdays (14 vs 10%), but need for epinephrine was lower (1.3% vs 2.5%). However, neither difference was statistically significant.

While a formal cost-effective analysis is beyond the scope of this article, the net financial impact was modestly positive (payments exceeded costs).

In summary, we describe a quality improvement initiative to improve access to food challenges in our large, academic allergy-immunology practice. We were able to modestly increase the utilization of challenge slots but more dramatically increase the total number of challenges performed, in the process substantially reducing the wait time.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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Serum sickness-like reaction in a pediatric patient using omalizumab for chronic spontaneous urticaria

To the Editor,

Omalizumab has been approved for chronic idiopathic urticaria (CIU)/chronic spontaneous urticaria (CSU) in children 12 years and older. Two treatment doses of omalizumab are available: 150 mg or 300 mg every 4 weeks. While 150 mg has been shown to be effective, most patients with CIU/CSU require 300 mg every 4 weeks to achieve symptom improvement.^{1,2} Although the cost of anti-IgE treatment can be high, there are reports of successful remission in CIU/CSU for difficult-to-treat cases, with 70.4% of patients treated with omalizumab reporting resolution of symptoms (vs 4.5% of placebo-treated patients).^{2,3}

Although quite effective, there are possible adverse effects of omalizumab. In 2007, a joint task force (members of the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology) reported a 0.09% occurrence of anaphylaxis after omalizumab administration for the treatment of asthma.⁴ In addition, a serum sickness-like reaction to omalizumab has been reported in an adult with asthma.⁵ We present a case of serum sickness-like reaction to omalizumab in a pediatric patient with chronic urticaria and angioedema. To our knowledge, there are no case reports of serum sickness-like reactions to omalizumab when used for chronic urticaria, or when used in the pediatric population.

An almost 12-year-old female presented to an allergy specialist with a 6-month history of rapid onset of shortness of breath, abdominal pain, and hives. Her hives were transient, did not burn, and did not leave bruising as they resolved. Shortly thereafter, in addition to the above symptoms, she began to have recurrent episodes of lip swelling that resulted in emergency room visits where epinephrine was administered with improvement in symptoms. Lip swelling improved within 30 minutes of administration of epinephrine, while her shortness of breath resolved within minutes. Thorough investigation revealed negative workup for mast cell

disorders, hereditary angioedema, autoimmune diseases (lupus, thyroid disease, and rheumatoid arthritis), *Helicobacter pylori* infection, food allergy, inhalant allergy, alpha-gal allergy, and carcinoid syndrome. Diagnosis of CIU/CSU with angioedema was made. Initial treatment consisted of high-dose H1 and H2 blockers and montelukast, with the addition of doxepin when her pruritus and angioedema persisted. While her hives improved with this treatment, daily pruritus and almost daily angioedema continued, so she was started on monthly omalizumab (300 mg) injections. Within the first month, she noticed significant improvement in her pruritus and angioedema. However, 1 week after her second injection, she developed a morbilliform rash, malaise, joint pain, and headache. She had no local reactions at the injection site. Despite these symptoms, her pruritus and angioedema remained controlled, so she elected to continue monthly injections for the next 6 months. During that time with each injection, she experienced worsening malaise, joint pain, significant cervical and axillary lymphadenopathy, and mild thrombocytopenia. Omalizumab was discontinued. Sulfasalazine was added to her daily medication regimen of H1 and H2 blockers, montelukast, and doxepin, and she was referred to a tertiary care clinic for further evaluation.

She was evaluated in our clinic 3 months after discontinuing omalizumab. She reported that her malaise, joint pain, and lymphadenopathy resolved but her pruritus and angioedema had returned. She also reported that she would have a significant worsening of her pruritus and angioedema for a few days every month as well as angioedema of her feet a few hours after cheer-leading practice. Because her persistent pruritus and angioedema were causing anxiety, she had been taking sertraline for several months. In addition, she reported missing 60 days of school due to her symptoms, and it was limiting her participation in after-school activities.

Volume of Food Challenges Performed January 2014- December 2016

c-chart

Set 1: UCL = 52.30, Mean = 34.64, LCL = 16.99, from: 11/1/2015 to: 12/1/2016
Set 2: UCL = 34.05, Mean = 20.48, LCL = 6.90, from: 1/1/2014 to: 9/1/2015

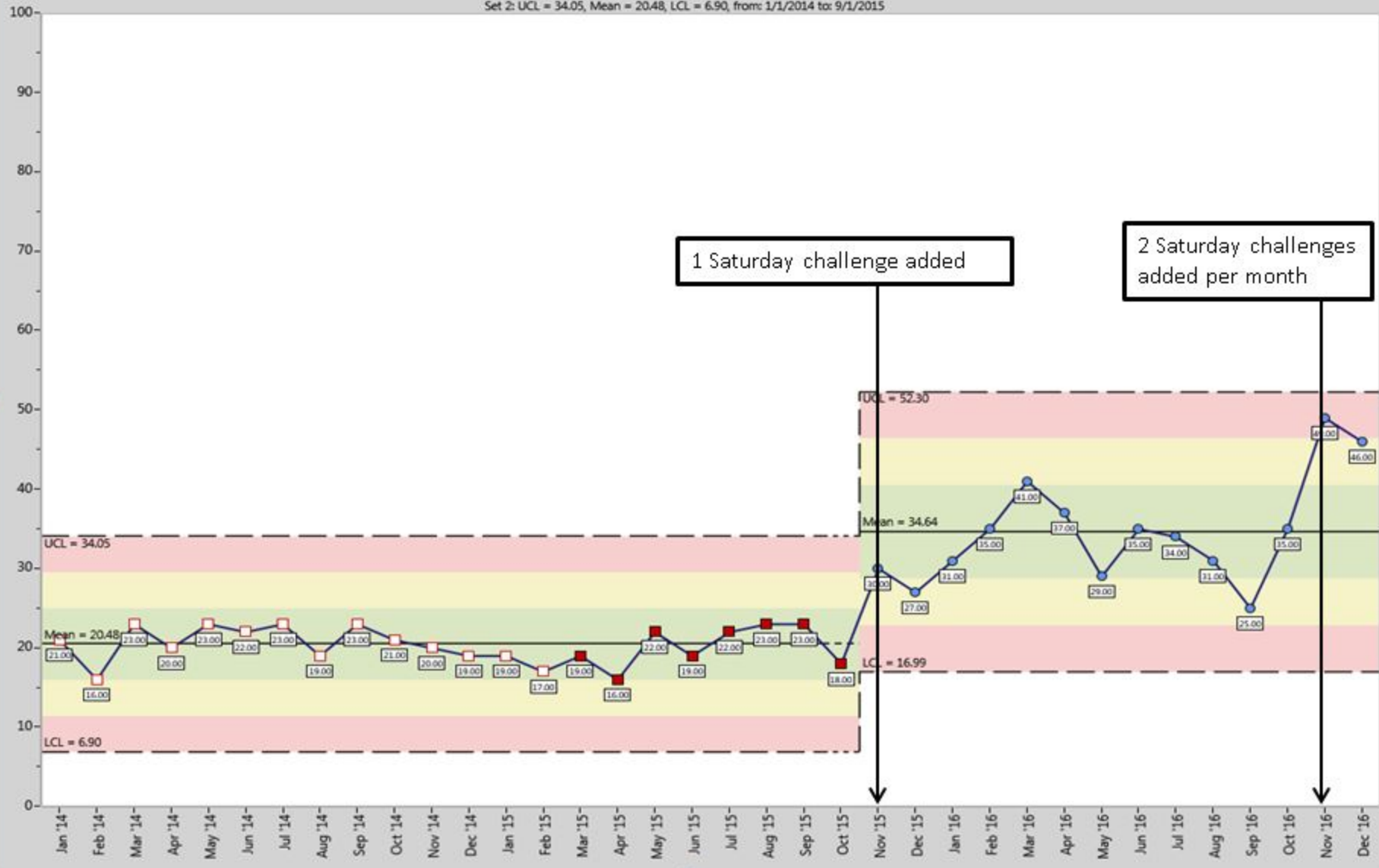


FIGURE S1

Control chart showing number of food challenges performed by month. Mean number and upper and lower control limits are noted. Arrows denote introduction of one and then two Saturday food challenges monthly.