

# Oral food challenges

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## ABSTRACT

Oral food challenge (OFC) is a procedure that is conducted most commonly by allergist/immunologists in their office or in food allergy centers to confirm a food allergy or to confirm tolerance to the food. The procedure as conducted in clinical practice is mostly open food challenge and, in research, a double-blind, placebo controlled food challenge. OFC has associated risks that can be minimized by having the challenges conducted by trained personnel who are prepared to treat allergic reactions and who have rescue medications available. However, OFCs have tremendous benefits to the patients and their families, including the potential to determine that a food is no longer an allergen and can be introduced into the diet. Even OFCs that result in clinical reactions have the benefit of confirming the food allergy and demonstrating the therapeutic effect of the rescue medications. The study of the outcomes of OFC has shed light on food allergy reactions and characteristics of the patients with food allergy as well as on the value of other diagnostic tests compared with OFC. OFCs have helped establish food allergy thresholds, confirm that subjects enrolled in research studies have the allergy, and demonstrate the response to the therapies tested in terms of ameliorating the allergic response or raising the reaction threshold. OFCs have also been used to promote the recent guidelines for the prevention of peanut allergy by identifying the infants at risk for peanut allergy but who are not allergic yet.

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This review is focused on a general description of the oral food challenge (OFC) procedure, its indications, conduct, and interpretation as well as its benefits and potential adverse effects. For details of the conduct of OFC, the reader is referred to publications that have described and standardized the procedure of OFC in the general population and in infants.<sup>1–3</sup> Given that physicians are indoctrinated in the principle of first do no harm, bringing a patient of any age to one's office and feeding that patient a food that the patient or the family have already told the physician has caused an untoward symptom seems counterintuitive. So, why has a double-blind, placebo controlled food challenge been consistently called the gold standard for the diagnosis of food allergy?<sup>3</sup> It is because OFC provides answers to many questions:

"How much food will I be able to consume before I have a reaction?" This is called the eliciting dose.

"If I do have a reaction, how severe will it be?" Among all tests for food allergy, OFC is the only test that answers the severity question.

"Am I allergic to foods that are in the same family or related botanical or animal families?" This answers the question of cross-reactivity.

"How long will it be until the allergy resolves, or will my allergy get worse?" This answers the question of natural history.

Although the measurement of serum immunoglobulin E specific to a food has been refined and cutoffs predict with up to 95% confidence interval whether the patient will or will not have a clinical reaction to a food when consumed, OFC is the way to predict whether the patient in the allergist's office is one of the 95% or of the 5%. Please refer to section 6 of this primer by Sanders et al for more detailed discussion of other testing modalities for food allergy.

## REASONS TO PERFORM OFC

### Clinical OFC

- 1) Diagnose or resolve a food allergy:
  - a. Confirming or refuting a food allergy as the cause of reported symptoms.<sup>4</sup>
  - b. Determining if a child is allergic or just sensitized, with no clinical allergy in cases in which infants and toddlers are tested for a food allergen before ingesting the food, and a positive test result (>0.1 kU/L) labels the child as food allergic.
- 2) Update the status of a food allergy:

Patients commonly present with a remote history of a reaction to a food and persistent evidence of

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Table 1 Types of oral food challenges, definitions, and comments

Type of Oral Food Challenge	Definition	Comment
Open	The patient and the physician know the food that is given	Easy to prepare and administer
Single-blinded	The physician but not the patient knows the food given	Suitable for older children and young adults who have heightened anxiety
Double-blind challenge or double-blind placebo controlled	Neither the physician (or any observer) nor the patient knows what food is given	Relies on objective symptoms
Graded Single feeding	Food is given in incremental amounts The whole serving is given	Most commonly used Used when food allergy reaction is not expected
Plain	The food is given in its plain form	Example: a challenge with a cup of cow's milk
Baked	The food is baked in with other ingredients	Example: challenge with a cookie or a cake baked with cow's milk
Single Multiple	One food is given Multiple foods are challenged simultaneously	Example: peanut Example: challenge done with a number of tree nuts mixed together
Threshold determining	Challenge is stopped at a preset amount and not carried out to a full serving amount	Used for research

immunoglobulin E to the food. An OFC may confirm the clinical resolution of the allergy. Even for foods such as cow's milk and eggs that are associated with resolution of the allergy, there are patients in whom the allergy lasts until the teenage and adult years. Food challenge in the office is the best way to identify those patients.

3) Determine the status of peanut allergy before commencing peanut allergy feeding in children at risk of peanut allergy per the guidelines on prevention of peanut allergy.<sup>5,6</sup> Please refer to section 16 by Leonard for a complete discussion of the use of OFC in this regard.

### Research OFCs

Over the past 2 decades, several large clinical trials have been conducted to test the safety and efficacy of different forms of immunotherapy for food allergy. Very meticulously dosed and documented double-blind, placebo controlled OFCs confirmed the food allergy and determined the eliciting dose of a reaction at baseline and after treatment.<sup>7-11</sup>

### WHAT ARE THE FORMS OF OFCS?

OFCs are done in different arrangements dictated by the age of the patient, the indication for the challenge, and the food being challenged (Table 1).

### HOW LONG DOES OFC TAKE AND WHAT ARE THE OUTCOMES?

At a minimum, OFC lasts 1.5 hours: time to prepare and take the food, and then a minimum 1 hour of observation. Graded OFC may last 4 hours, and a double-blind, placebo controlled food challenge usually occurs over two session on 2 different days. The outcomes of OFC vary and are documented, as shown in Table 2.

### WHO SHOULD PERFORM OFCs AND WHERE?

Because OFC always has the risk of a patient having an allergic reaction, OFC needs to be performed in a setting where the physician and staff are trained to recognize the signs and symptoms of allergic reactions, and the office is ready to treat such reactions, even if severe. OFC is part of fellowship training in allergy/immunology, and the graduates should be able to perform OFC in their offices. However, because OFC are taxing in the requirement of time and effort, not all allergist/immunologists offer them in their practices. OFC are more commonly offered in academic centers, specifically those that have an established food allergy center and in practices that specialize in the diagnosis and management of food allergy. These centers have the expertise to recognize and treat serious allergic reactions in a patient in a timely manner and have the

Table 2 Oral food challenge outcomes, interpretations, and recommendations

Outcome of Oral Food Challenge	Interpretation	Recommendation
“Passed” or “negative” challenge	The patient is not allergic to the food	The food can be introduced in diet <i>ad lib</i>
“Failed” or “positive” challenge	The patient is allergic to the food	The food is avoided
Incomplete	The patient refuses to eat the food,	Challenge to be repeated
Inconclusive	The symptoms are vague and undetermined	Challenge to be repeated

space capacity to dedicate a room for a single patient for a whole clinic session.

Practicing allergist/immunologists may be more likely to perform a very-low-risk rather than a high-risk OFC in their office; thus knowledge of the risk stratification of patients with suspected food allergy is beneficial. An example is cow’s milk allergy, which may cause severe reactions; it rarely does so in younger infants, in whom the reactions are most likely mild, cutaneous (in the form of skin rashes), and, possibly, gastrointestinal (in the form of vomiting or diarrhea). The advantage of starting with low-risk challenges is that practicing allergist/immunologists would gain experience and confidence in performing the challenge. Compared with publications about OFCs and the diagnosis of food allergy, publications that actually detail prospective protocols and outcome results are few.<sup>1,2,12</sup> Thus, gaining one’s own experience is essential.

An example is in recognizing early signs of a reaction. In toddlers, their refusal of the food during a challenge invariably precedes the onset of a symptom. Contrary to the popular belief that food allergy causes hyperactivity, children’s demonstration of a pending reaction is their curling up in their parent’s lap and stopping their active play or interaction with the clinic personnel. Most early cutaneous reactions are followed by more widespread cutaneous reactions if more doses of the food are given, so, it is best to discontinue the challenge and postpone to another time rather than insisting on proceeding. OFC in older children and teenagers are best performed in either a single-blind or a double-blind, placebo controlled fashion because most older children complain of subjective symptoms of throat itching and other symptoms consistent with anxiety over ingesting a food they have been very well trained to avoid for years.

The practicing allergist/immunologist should take advantage of the academic and research centers that routinely perform OFC. One way is for the allergist/immunologist and his or her clinic staff to attend the academic center clinics and have a refresher course in the subtleties and the hands-on experience of performing OFC. The other way would be to consult with the academic centers about the appropriateness of a challenge in a specific patient or to send their patients to

have their more risky challenges performed at the academic center.

#### WHAT ARE THE BENEFITS OF OFC?

The most important benefit of OFC is to answer the question of whether this patient is allergic to this food. The benefits of OFC that demonstrates that the patient is not allergic are obvious in that the patient can introduce the food into the diet. However, food challenge that demonstrates that the patient is allergic also has many benefits, including confirming the concern of the patient or parent, and justifying the tedious dietary eliminations that are needed. OFC demonstrates what a clinical reaction is to the patient and often shows that the threshold of reactivity is much higher than the patient and family imagined.

For example, patients with peanut allergy always have a concern about foods that carry the label of “may contain” or “manufactured in a facility that processes” peanut. The cross-contamination, if it occurs, is thought to be in a few milligrams of the protein amount. Food challenge to peanut might demonstrate that the eliciting dose (the amount of the food that is followed by a reaction) of peanut is >300 mg of the protein dose or up to a peanut. This allays the anxiety of the patient and parents. Similarly, in foods that are consumed in various forms, *e.g.*, eggs that are consumed scrambled or boiled or baked in foods, a challenge to plain eggs and to baked eggs may demonstrate differential tolerance and allows one form of the food to be introduced into the diet.

The type of food used in a challenge can ease the patients and the families into eating the food openly. Many parents report and suspect minor contaminations of meals with the putative food allergens as a source of often vague symptoms. Food challenge with baked cow’s milk or eggs, when the amount of cow’s milk or eggs is calculated and known, reassures patients and their parents about the issues of minor contamination. It also paves the way for repeated challenges with the open food, even though starting with very small amounts.<sup>13</sup>

OFC that results in a reaction is a live demonstration of how to administer the treatment, how to make a decision on which treatment to give, *e.g.*, provide an

antihistamine or administer injectable epinephrine, and to see firsthand the immediate effect of the treatment. Epinephrine results in an immediate resolution of the food allergy reaction symptoms, which is commonly a pleasant surprise for the patient and family. OFCs that have resulted in reactions have taught us a lot about food allergy. Several publications have examined the outcome of OFC. The publications have categorized the reactions and have related the prechallenge test results and history to the outcome of challenges, which generated a proven and practical approach to food allergy.<sup>12,14</sup>

### ARE THERE OTHER CONSIDERATIONS?

It is mostly our practice to perform OFCs without inserting intravenous access. The reasons are multi-fold. First is comfort. Children are uncomfortable with an intravenous line in place. Because the purpose of the challenge is usually to get them to eat the food openly and comfortably, we do not believe that we need to send a message of too many precautions and discomfort around eating the food. But most importantly, if challenge fails and the patient develops symptoms, we like to demonstrate to the patient and his or her family a real-life treatment scenario, with epinephrine or antihistamines, and without the intravenous access, because, in real life, this would not be in place.

In our experience, in failed challenges, seeing the symptoms and the effect of the therapy in resolving them immediately has been the reason that garners the parents' gratitude for having performed the challenge and their trust of the physician. It also assists them in accepting repeated challenge when indicated. A challenge should not be performed without the complete consent and comfort of both the child who is of age to express his or her opinion and all the parents. A challenge should always be viewed as an elective procedure. Also the personnel performing the challenge should continuously assert to the parents that the challenge can be stopped at any time even if for just the reason that either the child or the parent becomes anxious and does not want to proceed.

### CLINICAL PEARLS

- OFC is the only clinical test that confirms a food allergy.
- Besides the clinical history, OFC is the only procedure that determines the severity of a food allergy.
- OFC can be performed at all ages and for all foods.

- An experienced allergist/immunologist can perform OFCs safely and comfortably for the patient and family.

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