Food Reintroductions Application Guide

Clinical Context

When the patient improves enough to establish a better functioning baseline, they often want to know if they can reintroduce foods and reduce the number of supplements they're taking. You want to give them guidance about how to figure out which foods are OK to reintroduce, and which supplements are ok to reduce. This all needs to be done systematically, to avoid loss of the progress the patient has made.

Supplement reductions should be done before food reintroductions

This gives the clearest opportunity to understand what it looks like when the patient is functioning at their best, with the smallest set of supports, but also without the extra burdens presented by problematic foods. This is a better approach than re-burdening a patient with inflammatory foods, while also keeping the doses of anti-inflammatory supplements high enough to mask reactions to those foods. See the *Supplement Reductions Application Guide* for information on supplement reductions.

So, this Application Guide assumes that you and the patient have already gone through the cycles of work necessary to figure out the subset of supplements that the patient needs to continue using, to maintain the improved baseline that you and the patient worked to establish. Now they're steady at that improved baseline, using that subset of supplements. They have also spent at least six months completely avoiding the problematic foods. Not partial avoidance. Not "mostly" avoidance. Full avoidance. Now you're ready to work on food reintroductions.

Order of Importance of Avoidance

Foods do not have an equal likelihood of being problematic for a given patient. The following order of importance is general. Individual patient responses may be quite different. The point, however, is that being systematic about reintroductions puts the patient and you in a better position to have a chance to discover what turns out to be true about each food. Here are foods in the order of importance of avoidance.

1. Gluten-containing foods. This includes wheat, rye, barley, spelt, farro, kamut (also called Polish wheat). If the patient is reactive, these never get reintroduced.
2. Gluten cross-reactive foods to which the patient has antibodies. No antibodies? Then it doesn't matter that the food is, generically a gluten cross-reactor. If the patient is reactive, reintroductions are attempted last.
3. Other foods to which the patient has antibody elevation. These get reintroduced first, one at a time, starting with the ones that had the lowest antibody levels when originally tested.

Keep in mind also that we're mainly talking here about IgG mediated food sensitivities. The patient could also have an IgE mediated food allergy, or a histamine-promotion or lectin-mediated, or other response to a food to which they nonetheless do not have an antibody response.

The Steps

It's important for the patient to follow the steps in sequence, to have the best chance at making meaningful observations about the impact of a re-introduced food.

Step 1

Test IgG antibodies, for every food that showed an abnormal result on the original test. You're looking to see if the antibody levels for each food have come down because the patient has been avoiding the food. For a given food…

1. The antibody level didn't come down…
    a. The patient has had exposures to the food.
    b. The patient has had an exposure to a cross-reactor for that food (like mango and cashew). Yes, this sure complicates things, but I wouldn't worry about it. There are too many variables and ignoring that complexity doesn't seem to prevent making progress with the patient.
    c. The patient's immune system has made a batch of long-lived plasma cells that have been established in the bone marrow and are producing antibodies over the long term, the same as the immune system does for long term immunity to a pathogen.

    In any of these cases, the foods for which antibodies stay high can't be reintroduced. You can test these again in a few months.

2. The antibody levels came down…
    a. This either means the patient isn't reactive to this food anymore, or
    b. It means the antibodies are down because the patient has been avoiding the food. But they still have a batch of T and B memory cells in lymph nodes, waiting for reintroduction of the food.

    Here's where you're going to do careful reintroductions, one at a time, to see if the patient notices symptoms. Whether they notice symptoms or not, you will then retest antibodies, to see if antibody levels start to go up again for the foods that the patient has started eating again.

So, Step 1 is to find out about antibodies, so you know what foods you can try to reintroduce.

Step 2

Step 2 is to do the reintroductions, in the following way, one food at a time. It's laborious, but it's the best way to have a shot at getting clear data.

1. Eat the food in question (egg, for example)… eat it once. Wait three days. Remember that IgG antibody activation can occur in a 72-hour window, so if you eat egg Monday at lunch, you could wake up feeling bad Thursday morning. If Step 1 is "I didn't notice anything," then…

2. Eat eggs three days in a row, then stop. Wait 72 hours. If 1 and 2 are ok, the patient can eat that food for now, at the level they ate the food during Step 2.

3. Repeat these steps for the other foods that are not gluten cross-reactors. You're only doing this for foods that were negative on the repeat IgG antibody testing. This might take the patient eight or more weeks, depending upon the number of foods. Watch for the patient starting to do poorly, if the aggregate effect of the reintroductions turns out to be problematic. You won't always get a clear symptom spike when you introduce one food.

Step 3

Redo the IgG antibody tests for the foods that the patient reintroduced. This should be done at least three weeks after the introduction of the last food, to give your immune system a chance to build a new batch of antibodies. If antibody levels have gone back up, it suggests that the reason the antibody levels went down was that the patient was avoiding the food. They should go back to avoiding the food.

Step 4

Repeat Steps 2 and 3 with the gluten cross-reactive foods. Note that the patient may have insight about which of these might be tried and which should not be tried, based on their experiences with the foods.

Gluten Cross-Reactors

There are eight gluten cross-reactive foods. Rice, oat, corn, millet, yeast, sesame, coffee, milk products (every animal milk except camel). What does it mean for a food to be a gluten cross-reactor?

Let's talk about oat as an example. Cross-reactivity means that, in a research setting, a structure on gluten has also been identified on another food. So, for each food that is a gluten cross-reactor, there is some sequence of amino acids (called an epitope) in common with gluten. If a patient has an antibody that binds to that structure in common between gluten and the other food, oat for example, then the patient could do a perfect job of avoiding gluten-containing foods (wheat, rye, barley, spelt, kamut, farro), but every time they eat oats, the immune system will react to the oat exactly as though the patient was eating gluten. The patient won't get better. So, when you start to consider reintroductions of gluten cross-reactive foods, you need to consider the risk that if this mechanism is taking place, the reintroduction could function as a gluten exposure.

Now let's suppose your patient had an IgG antibody reaction to oat on their original test. They've avoided oat for six months. Their repeat oat IgG test is negative.

Remember that the IgG blood test is a test to see if there is an antibody in the patient's blood that reacts to the food. But it doesn't tell you if the antibody is reacting to the epitope shared with gluten. The test only tells you that an antibody in the patient's blood reacted with oat.

So, the key question you're trying to get insight about here is whether your patient's original food antibody result was abnormal because the patient has an antibody to that food that is to the epitope (amino acid sequence) shared with gluten (which means eating the food triggers the same reaction as eating gluten) or if the patient's antibody to that food is to another part of the food (which means eating that food is just like eating any other food the patient has IgG antibodies against, and has nothing to do with gluten). If it's the latter, the stakes are lower. Eating that food might be inflammatory, or might involve other mechanisms, but it would not be as concerning as if it were functioning as a gluten cross-reactor.

The first and key thing to ask the patient about is whether eating that food gives them symptoms identical to those they get when they eat gluten. That would imply that the food is triggering the same immune response as if they ate gluten. If they say yes, the food gives them the same symptoms as when they eat gluten, don't reintroduce that food. If no, you can try to reintroduce the food, using Steps 2 and 3.

Things to Keep In Mind

If the patient has persistent but modest elevation of antibodies despite what they think of as complete avoidance, their immune system may simply have succeeded in making long lived plasma cells (LLPC's) that reside in the bone marrow and continue to generate antibodies. This is similar to the idea that a modest amount of IgG against a virus constitutes the background immunity that exists in a person who had a viral infection at some point, but doesn't have one anymore. You'd also perhaps expect some T and B memory cells that are self-renewing. All of that yields what we hope is effective immunity against a pathogen we've seen before but which isn't infecting us now. If the patient has modest antibody elevation on their repeat test, despite complete avoidance, it's likely they'll have an immune response when they try to reintroduce the food. This is why it's important to not try reintroducing foods to which the patient has antibodies when you test after six months of avoidance.

It's also possible that the persistence of antibodies despite food avoidance is because their avoidance might not be accurately executed. They may be getting a food as an ingredient they're not aware they're getting. And it's worth helping them figure out hidden sources like shampoo or skin cream, as well as food ingredients.

Also keep in mind that if a person shows antibodies to something like wheat or gluten on a lab test despite avoidance, the antibody elevation might reflect that they've been eating a cross-reactive food, so that the elevated antibody level is being driven by the cross reaction. They might have had zero wheat/rye/barley/spelt/kamut/farro, for example, but plenty of oat.

It's also necessary to consider polyreactivity. The literature suggests that polyreactivity mostly involves IgM. But clinically, I see plenty of patients for whom reducing inflammation and especially Th17-mediated inflammation, seems to quiet down their antibody responses significantly. For these patients, their first lab tests for IgG (foods, viruses, self-tissue antibodies) often show nothing normal. All tested analytes are abnormal. This raises the question of whether the patient's antibodies are more sticky, so that they bind more readily to whatever antigen is being tested. This is driven by antibody glycation. IL-21 and IL-22 are Th17 and Th22 cytokines that drive glycation. If the panel comes back with NONE of the tested items normal, think about Th17 and Th22, and think about TNFα and IL-6 mediated inflammation.