Occasionally, in working up unusual symptom patterns or lack of response to conventional psychiatric and medical treatment, I order various laboratory tests classified under the broad rubric of "functional medicine testing." These tests basically examine the body for things, which cannot be determined by conventional testing. One of the most intriguing lines of investigation is for hidden food allergies, technically referred to as "IgG food allergies." This is the diagnostic avenue I pursue in evaluating complex cases of ADHD, autism, and pervasive developmental disorders, as well as more perplexing cases in adults where I either can't explain - or can't treat - the condition I am encountering with more conventional approaches.

The concept of "food allergy testing" is misunderstood by all but the most absolutely up-to-date physicians. Ask most physicians and they'll mutter something like "well you've got to get skin testing, and there's no real correlation between skin testing symptoms and ADHD." Actually, this is wrong on both counts. You don't have to get skin testing - in fact, this is most commonly counterproductive. There indeed may be a correlation between a skin reaction (technically referred to as an "IgE" response) and psychiatric symptoms, and when the offending agent is removed, the psychiatric symptoms, -or at least, their absolute refractoriness to being treated with commonly available agents, improves. I typically order food allergy testing when things are simply not making sense in my work with a child and his/her family, or with my adult patients. This can include ongoing, unexplained "medical" issues - like chronic constipation, hard stools, indigestion, "brain fog" despite my best efforts, mood swings, exacerbation of PMS, and so forth. I also become very suspicious of food allergy symptoms when I see children who are what I call "autistically disengaged" in the context of a severe syndrome like picture of inattentiveness or in pervasive developmental disorders. When I see cases of clear autism, or clear autistic symptoms coupled with a pervasive developmental disorder picture, I always consider getting food allergy testing. Children who I describe as having "autistic features" are disengaged from their environment like kids with full-blown autism, although typically not nearly as severely. This disengagement can be manifested as a sort of dreamy indifference, lack of emotional responsiveness or a quality of simply "not getting it," up to and including becoming angry, aggressive, and combative when provoked.

As a conventionally trained Western practitioner of medicine, trained in the classic allopathic style at Mayo Clinic in Rochester, Minnesota, I aim for the conventional workup and assessment first. The obvious reason is what I call diagnostic parsimoniousness - which means, trying to get the diagnosis right with the least fuss and most direct route possible. In medical school, we were trained that "if you hear hoof beats, don't think zebras." In other words - and to clearly emphasize this point - most ADHD is not because "the little munchkins are allergic to something that they're eating." However - and this is a big "however" - sometimes they are. My philosophy is that if what I'm doing isn't working and I'm pushing it to the limit in terms of conventional medical/psychiatric practice, or if there is abundant clinical history to document the high probability of a food allergy before we get to the point that the child is failing treatment, then at that point I will order the testing.

The origin and cause of autism is hotly debated - both in the public as well as in the peer-reviewed medical literature. Although there are more citations about food allergies and ADHD, there is growing evidence that food allergies may play a significant role in autism, as well. As of June 6, 2004, there
were 41 citations regarding the correlation of "food allergy with attention deficit disorder" in what is generally described as the "peer reviewed medical literature." This literature, and doing this search, is accessible to anyone with a computer, an Internet connection, and an open mind.

[A convenient link is: http://www.drcady.com/search_pub_med.html]

The newest citation - that of Schnoll, and colleagues, entitled "Nutrition in the treatment of attention deficit hyperactivity disorder: a neglected but important aspect" specifically notes that, "There is increasing evidence that many children with behavioral problems are sensitive to one or more food components that can negatively impact their behavior. In general, diet modification plays a major role in the management of ADHD and should be considered as part of the treatment protocol." The problem with "diet modification", of course, is obvious: you have to know what to "modify." The only way this can be done is through a long, trial-and-error process where first, one thing and then another is removed from the diet. This is like trying to drive from Boston to New York City without a map and without knowing the route. You’ll eventually get there if you keep driving in the generally correct direction, but you'll have to take lots of different routes and do a whole lot of backtracking along the way. It should be noted in the context of the prevailing medical literature that the previous position of the medical community at large has been that of an outdated view of "food allergies" as only relevant if they are the type of "allergic reaction" which is manifested by immediate, classic, obvious, and sometimes, catastrophic reactions. Children eating peanuts, for example, and then having their airways close down, are an obvious and potentially widely known phenomenon to the educated layperson. This type of allergy is technically referred to as an "IgE" allergy, and it is absolutely correct that this type of allergy can be determined with skin pricks with the potentially offending substance placed under the skin. It was this type of food allergy testing which was originally used in some of the groundbreaking work on learning disabilities and allergy in children. Millman and colleagues published a groundbreaking paper on this topic entitled Allergy and Learning Disabilities in Children in Annals of Allergy in March 1976 [vol 36, number 3, pp 149-160.] They took note of the "allergic tension-fatigue syndrome observed by Speer" and noted that it was a "symptom complex accepted by many allergists." They then went on, using both scratch test and intradermal techniques (which means "injecting allergy-provoking substances beneath the skin to see if there is an allergic reaction") and were able to positively correlate food allergies associated with IgE allergic reactions with actual changes in IQ scores. In other words; the more the food allergies, the lower the IQ scores in the children tested. The lower the food allergies, the higher the IQ scores in the children tested. This was truly a groundbreaking piece of work.

Nevertheless, this view of IgE "immediate sensitivity" reactions associated with changes in IQ or ADHD symptoms is now old news. It should also be noted that not all of the 41 peer-reviewed references on "attention deficit disorder with food allergy with attention deficit disorder" cited above specify these IgE positive findings as a prerequisite to having a "food allergy" related to psychiatric or mental symptoms. The subsequent literature is rich and varied. In 1985, in an article in the British medical journal, The Lancet, Egger, Carter, and colleagues, found that of 76 selected overactive children treated with an oligoantigenic diet (a diet in which symptom provoking foods were removed), "62 improved and a normal range of behavior was achieved in 21 of these." [Egger, Carter, et al. Controlled Trial of Oligoantigenic Treatment in the Hyperkinetic Syndrome. Lancet, March 9, 1985, 540-545]. No IgE skin testing was performed; rather, the children were empirically placed on an oligoantigenic diet modified from that of Egger and Carter, consisting of two meats, two carbohydrates sources, two fruits, one vegetable, and water, calcium, and vitamins. The bad news: it wasn't exactly a gourmet menu. The good news: it did not provoke food allergic reactions. In 1993, Carter et al published in Archives of Disease in Childhood that placing hyperactive children on a "few foods" elimination diet resulted in improved behavior in 59 out of 78 children. [Carter, Urbanowicz, et al. Effects of a few food diet in attention deficit disorder. Archives of Diseases in Childhood 1993;69:564-568]. The authors conclude, in their discussion: "This trial indicates that diet can contribute to behavior disorders in children and that this effect can be shown in a double blind, placebo controlled trial." Interestingly, they did not attempt to correlate the change in behavior on any sort of
presumptive IgE immediate sensitivity reaction and noted that, "The ways in which [this] diet worked remain unclear. Toxic, pharmacological, or allergic mechanisms could be involved, and the physiological effects of different foods may vary." To their credit, they also note the limitation of food restriction based on this radically restrictive dietary protocol (as they did in their previous paper, in the Lancet, 1985) "The treatment, as applied in this study, has disadvantages. It is a difficult and exacting regimen, which puts a considerable strain on the whole family. It is not yet clear whether modified diets can also be effective.....It may therefore be possible to devise a less restricted diet with similar levels of success.

In other words, they conclude that "shooting in the dark" with a radically restrictive diet and then adding challenge foods one at a time is just that: radical. In their previous paper (Lancet, 1985) they also note that it is potentially dangerous. In another article, published in Annals of Allergy in 1994, entitled Foods and additives are common causes of attention deficit hyperactive disorder in children [Boris, Mandel. Annals of Allergy, vol. 72, May 1994, 462-468], the authors found that four out of nineteen children who showed food sensitivity and improvement with the removal of the offending foods were non-atopic. That is, they would have manifested no classic "allergic reaction" to the placing of these foods under their skin in the author's elegant "double-blind placebo controlled food challenge (DBPCFC) test." To make sure this point is made adequately: if these children had been tested by the best board-certified allergist that could be found the four food sensitive children in this study - representing a statistically impressive 25% of all the children in the study and who had documented improvement when their food allergies were dealt with - still would not have tested positive to the foods to which they reacted based on conventional "skin prick" testing; nevertheless, they still would have had behavioral and concentration difficulties based on food sensitivities. To make sure that this point is understood, let me emphasize this: these kids would not have been "skin-test positive." They were therefore not manifesting Ig-E "immediate effect" allergic responses. But they were manifesting an allergic response. The most recent and thought provoking article in the literature is from June 2003. In their paper, Sabra, Bellanti and their colleagues review "IgE and non-IgE food allergy" [Sabra, Ellanti, et al. Annals of Allergy, Asthma, and Immunology 2003;90(Suppl 3):71-76]. They observed that non Ig-E mediated mechanisms may be at work. They note: "The gastro-intestinal tract serves not only a nutritive function but also is a major immunologic organ. Although previously thought to be triggered primarily by an IgE-mediated mechanism of injury, considerable evidence now suggests that non-IgE mechanisms may also be involved in the pathogeneses of FA ("food allergy"). The authors reviewed data collected from MEDLINE searches analyzing multiple syndromes, which could be caused or exacerbated by food allergies. Among the syndromes analyzed was "attention-deficit-hyperactivity disorder and behavioral disorders [sic]." Their conclusions were as striking as the original work by Millman, over 29 years previously. They concluded: "The results of this review allow the construction of a central, unifying hypothesis for a new classification of FA as follows: the clinical manifestations of FA, expressed in affected target organs, may be the result of immunologic injury mediated by interaction of food antigens with contiguous elements of mucosal associated lymphoid tissue. These appear to be modulated by relative imbalances of the Th1/Th2 paradigm, which may be the ultimate determinant governing the expression of FA as IgE-mediated, non-IgE-mediated, or mixed forms of IgE/non-IgE mechanisms of FA." In plain English, that means that you can have allergic reactions to foods causing ADHD symptoms (and other ones, as well) that cannot be found out by doing scratch testing or injecting antigens underneath the skin to see if one has an immediate reaction. Indeed, IgG allergic reactions are delayed ones!

And here is the vexing part about IgG food allergies -it's like experiencing a hit and run driver. By the time the victim is found, the driver of the car that struck him has already fled the scene. Unless there is a direct witnessing of the accident, the driver's car cannot be correlated with the hapless victim. IgG food allergies, in fact, manifest as much as one to two days after being encountered. Thus, the "driver" has already fled the scene by the time the "victims" (cognitive symptoms, vague gastrointestinal complaints, etc.) were found. Unless the two can be closely tied together, there is absolutely no way that one can be related to the other. This is why in the past, and before there were
good IgG food allergy testing panels, the only way you could remove the most likely offending agents was to simply chop them all out of the diet, see if the child got better, and then reintroduce them one by one. This was basically a "brute force" technique, and certainly would not endear the hapless practitioner to the child if that were the advice the parents were getting.

Another interesting article appeared more recently, in March of:2003: "Nutrition in the Treatment of Attention-Deficit Hyperactivity Disorder: A Neglected but Important Aspect" [Schnool, Burshteyn, et al. Applied Psychophysiology and Biofeedback Vol 28, No. 1, 63-75]. The authors noted that, "ADHD is multi-determined and complex, requiring a multifaceted treatment approach. Nutritional management is one aspect that has been relatively neglected to date. Nutritional factors such as food additives, refined sugars, food sensitivities/allergies, and fatty acid deficiencies have all been linked to ADHD. There is increasing evidence that many children with behavioral problems are sensitive to one or more food components that can negatively impact their behavior. ....In general, diet modification plays a major role in the management of ADHD and should be considered as part of the treatment protocol." The bottom line here is that the peer-reviewed medical literature is witnessing an unprecedented shift in our current understanding of food allergies. Before 1976, the notion of a food allergy (immediate reaction IgE or anything else, for that matter) causing mental or psychiatric symptoms was not widely regarded. Following that, the theme of the literature was, for a decade or two, at least, that "if it didn't cause a skin rash or a positive skin test, it wasn't a real food allergy." The evolving notion at this point, supported by multiple studies is that IgG foodallergy testing can provide valuable assistance in elucidating the possible causal or exacerbating role of foods which can provoke allergic reactions in children (and adults), and which would never be able to be identified previously with the exception of a Draconian, exceptionally limited diet with subsequent food challenges [as per Carter, et al, 1993]

The corollary is that, frequently, IgE food testing, absent any obvious clinical history of catastrophic "food reactions" is not only pointless, but a needlessly painful, as well as thoroughly useless, diagnostic model. It is for these reasons that I order IgG "food allergy testing" on patients in whom I feel the symptoms and/or lack of response to treatment justify it.

Moving from the better-characterized correlation with food allergies and ADHD to autism, several articles are instructive. As of August, 2004, there are only ten papers in the peer reviewed medical literature available on Medline which deal with "food allergies with autism." One of the most interesting, "Food allergy and infantile autism," was authored by some Italian physicians [Lucarelli S, Frediani T, et al. Panminerva Med. 995 Sep;37(3):137-41] of the Department of Paediatrics, University f Rome, in LaSapienza, Italy. They verified that a cow's milk free diet, or removal of other foods which gave a positive result after skin testing in 36 autistic patients resulted in a "marked improvement of behavioral symptoms" after a period of 8 weeks on a diet of elimination of the offending foods. On laboratory analysis, these physicians found high levels of a specific antibody, IgA, for casein, lactalbumin, and beta-lacto globulin; they also found elevated IgG and IgM for casein, a protein in milk. These levels were found to be significantly higher than antibodies obtained in a control group. Because of the clear symptomatic improvement after skin-test positive foods were removed from the diet, as well as the differential in antibody levels between the autistic children and the control group, the authors were led to hypothesize "a relationship between foodallergy and infantile autism as has already been suggested for other disturbances of the central nervous system." The most recent citation available is by P.M. Kidd: "Autism, an extreme challenge to integrative medicine; Part 2: Medical Management" [in Alternative Medicine Review. 2002 Dec;7(6):472-99]. He notes, among other things: "Dietary restrictions, including removal of milk and other casein dairy products, wheat and other gluten sources, sugar, chocolate, preservatives, and food coloring are beneficial and prerequisite to benefit from other interventions." In addition to identifying and removing foods to which autistic children are allergic, a holistic and balanced approach is reviewed in this article, including attention paid to the gastrointestinal tract, detoxification of heavy metals, and appropriate vitamin and mineral supplementation. The correlation between an elevated inflammatory response and autism was
characterized in the paper, "Innate immunity associated with inflammatory responses and cytokine production against common dietary proteins in patients with autism spectrum disorder" published by Jyonouchi and Itokazu of the University of Minnesota [Neuropsychobiology. 2002;46(2):76-84]. They began their research with the clinical observation that found: "Children with autism spectrum disorder (ASD) frequently reveal various gastrointestinal (GI) symptoms that may resolve with an elimination diet along with apparent improvement of some of the behavioral symptoms." In their study, they basically measured the inflammatory response with several biomarkers against common allergens associated with autism: gliadin, cow's milk protein, and soy, using the response of peripheral blood mononuclear cells as their "signal" of immune reactivity. They found pro-inflammatory responses related to all three of the dietary proteins noted above in children with autism as opposed to the control children in the study, and hypothesized that this apparent association may be partly associated with an inflammatory response in the gastrointestinal tract associated with exposure to allergic dietary proteins. There are, to be fair, "negative studies" in the literature disputing any possible link between gut disorders and autism.

One of the most interesting, as well as methodologically flawed, studies, is that of Black, C, et al: "Relation of childhood gastrointestinal disorders to autism: nested case-control study using data from the UK General Practice Research Database [British Medical Journal 2002 Aug 24;325(7361):419-21]. In this study the authors found essentially "no difference in the number of increased gastrointestinal symptoms recorded by the general practitioner" between autistic children and normal controls. Indeed, they noted 9% of children with autism and 9% of normal children had a history of gastrointestinal disorders by symptom review, only. No immune testing of any kind was done; no experiments with dietary restrictions were performed. This last study is probably one of the most illustrative cases of the "negative studies" which are reported in the literature. In general, one can design a study to prove whatever one's point of view truly is. This study presented in the British Medical Journal is almost guaranteed to find no correlation between gut inflammation and allergic response, because the simple fact of the matter is that one cannot diagnose subtle immune dysfunction or gut inflammation sufficient to cause psychiatric symptoms simply by plopping a child on an exam table, looking at him or her, and poking on the child's belly. Nor can one expect as the authors did in this study, to have a parent announce to the general practitioner, "I believe that my child's symptoms are due to gastrointestinal inflammation of an allergic etiology," when, in fact, the symptoms are so subtle, and often so delayed after eating an allergic reaction-provoking food, that there is simply no way that even the most attuned mother could pick up on it.

It is perhaps here that we should leave our discussion from the medical literature, with these clear lessons learned. A child can have allergic reactions to foods without a positive skin response to "food allergy testing." This means that limiting diagnostic work up to "scratch tests" and intradermal injections according to hide-bound medical tradition is simply inadequate. Inflammatory reactions in the gut can affect the brain. There is abundant evidence in the peer reviewed medical literature linking, in some case, both ADHD and autism to clearly defined food allergies. Absent any specific food allergy testing to guide one, any attempt to remove all likely foods which might be either causing or exacerbating ADHD or autism is difficult, expensive, and quite possibly, dangerous. It is like trying to drive across the United States without a map: you may get there eventually, but you could have lots of problems along the way and it would certainly take a much longer time and be much more expensive. The only rational laboratory testing is that which includes IgG ("delayed reaction") food allergy testing. One problem remains to be discussed: the enormous difference between the level of accuracy and sensitivity required in injecting an antigen underneath a child's skin to "see if an allergic reaction occurs" and that required to do similar testing in a laboratory micro titer plate from a blood sample. The accuracy and sensitivity of the testing is orders-of-magnitude different. Before commencing food allergy testing with my patients, I reviewed the options available to me and settled on Immuno Laboratories in Ft. Lauderdale, Florida. The testing there, called "ELISA" (which stands for enzyme-linked immunosorbent assay) was a direct offshoot of the use of ELISA testing for hepatitis and, later AIDS. Dr. John L. Rebello, Ph.D., the laboratory director at Immuno Laboratories, was one
of the original researchers using ELISA methodology for the testing of the AIDS virus. Dr. Rebello has been the laboratory director there since, 1986. In addition to scrupulous training of new technicians there, as well as institution of stringent quality control measures, Dr. Rebello applied his earlier ELISA research to the development of the IgG testing for in-house use at Immuno Laboratories.

There were several reasons I selected Immuno Laboratories. Not only do they offer IgG food allergy testing, but they also offer "IgE testing from a blood sample." That means that my patients can actually have their immediate response, potentially devastating food allergies checked from a blood sample, instead of having to lie on a table and have their skin punctured or scratched. It is frequently important to check both. Other tests, which are available, include IgE testing for environmental allergies (like mold, various grasses, cat and dog dander, etc.) as well as ELISA testing for candida infections of the gut ("intestinal dysbiosis") and gliadin - a protein from wheat, which causes celiac sprue. The antigens and micro titer plates for the Immuno One BloodPrint™ (the IgG food allergy testing which is so critical in understanding subtle food reactions) as well as the other tests are "custom built" in house. Dr. Rebello observes, "None of the immunoassay components, including the 115 food antigen micro titer plates with positive and negative controls and the conjugates, are presently available [elsewhere] in a commercial kit." This is one of the reasons why poor reproducibility of test results has been an all too common problem in the area of laboratory testing of food allergies. Immuno Laboratories has perfected a series of quality control techniques, which include positive and negative control serum samples in wells on each individual micro titer plate used to test patient serum. One quality control technique is that each of the 115 food antigens which are used for testing are optimized for concentration before being applied to the micro titer plates so that the same level of consistency is maintained week to week and month to month. In addition to positive and negative controls on each plate, for every patient, a weekly in-house split sample is also run. Basically a blood sample with known high reactivity is divided up into two samples. This split run is obtained from a sample, which Dr. Rebello personally selects that has already been run and has at least 25 or 26 food allergies of high intensity noted. Using patient serum left after a test is run, Dr. Rebello takes some of the left-over, puts it into two different samples and then sends them through the lab. These are essentially "fake labeled" in the lab so that it appears that these two samples came from two different people. (This is similar to a "mystery shopper" program - the sales clerks, or, in this case, the lab techs, never know who the "mystery shoppers" are.) Dr. Rebello expects less than a 10% variance between the results posted for these duplicates. There is some variability expected, simply because the testing is so sensitive, but with the quality control standards put into place, less than 10% variance is achievable. As far as I know, this is the best quality control and laboratory oversight in the entire "food allergy testing" industry.

There are two over-arching conclusions of this article. The first is that there is overwhelming scientific evidence for the usefulness of evaluation of food allergy testing in ADHD, autism, and other psychiatric disorders which are not yielding to conventional diagnosis or therapeutic interventions. The second is that the only reasonable way for this testing to be done is with a laboratory which has a well documented quality control process in place, both proactively - from the ground up - and manifesting in ongoing monitoring and sampling of the results. To pursue testing without validation of the test is illogical and inadvisable. With excellent testing, however, sometimes vexing and "untreatable" cases can be understood and appropriate interventions made. When I have had the experience of watching nine out of possible nine symptoms of inattentiveness vanish with removal of allergic foods and the use of nutraceutical supplements, instead of having to prescribe stimulants for children, I know that what I am using is the best science available at the time. It's also wonderful to watch children with severe pervasive developmental disorders who, for the first time, start interacting more appropriately and who have rage fits that suddenly disappear after I instruct the parents on what foods to remove from their diets. It's great that, even though they are there for me to use if I have to, in some cases I don't have to use heavy-duty psychiatric medications. In the early 21st century, the level of sophistication and knowledge, which is available in the medical literature, and is available for active diagnostic use in a commercially available form, are both astonishing. The groundwork for further
research in food allergies and their causative or exacerbating effects on attention deficit disorder and autism is laid. Through the Internet, medical information is being disseminated to parents and physicians alike at an astonishing pace. All that the open-minded physician or parent has to do is reach out, tap into the information stream, and work toward bettering the lives of children and patients whose lives we touch.

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