

ALLERGY MANAGEMENT FOR CHRONIC EAR DISEASE A PRACTICAL APPROACH

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ABSTRACT

Chronic otitis media with effusion (OME) is increasing in frequency. The causes of OME are multiple, and the importance of allergy has been underestimated.

The role of non-IgE mediated sensitivity is often overlooked. Such sensitivity makes a crucial contribution during the early years of childhood. When a reasonably thorough work-up is performed, 94% of OME patients and 96% of chronic otitis media (COM) patients were found to have allergies. Discussion of basic concepts will facilitate correct diagnosis.

Many cases of OME may be resolved using simple allergy methods. Studies by Shambaugh and Hurst have shown excellent response among compliant patients. Nsouli has demonstrated the vital importance of food allergy. Allergy work-up and treatment as an alternative to surgery will be discussed.

Children requiring prompt surgery may have appropriate testing performed intraoperatively. Discussion includes testing methods, results, and economies of time and expense.

Patients with COM suffer from end stage disease which frequently requires operation. Removal of contributory causes of the COM would appear sensible to minimize recurrence.

Clinical evidence appears to justify the hypothesis that the middle ear is a target organ for allergy. Appropriate treatment may significantly improve both medical and surgical management of OME and COM.

INTRODUCTION

Acute purulent otitis media (APOM) may be the most common cause for sick child visits to a pediatrician's office. APOM is diagnosed at 23% of visits during the child's first year and during the second and third years of life in 34 and 35% of office visits.¹ Chronic otitis media with effusion (OME) is most commonly defined as fluid which has been present for two months or longer. The incidence of OME among children at a doctor's office varies between 11-20% during the first five years of life and is as high as 6-9% at age 7.² A Canadian study has recently demonstrated that otitis media with effusion is occurring with increasing frequency in North America.³ The insertion of pressure equalizing tubes is one of the most common operations in the United States. We need to understand the causes of this common problem.

Causes of chronic OME. Everyone agrees that anatomic problems may cause chronic otitis media with effusion. There is no doubt that such problems as cleft palate and "named" syndromes like Treacher-Collins or Goldenhar's syndrome may predispose to otitis media with effusion. The assertion that perfectly normal looking children have been cursed with anatomical problems and "poor protoplasm" should be questioned. There is certainly no question that infections may predispose to chronic otitis media, whether upper respiratory infections or actual purulent otitis media. It is estimated that 20% of episodes of acute purulent otitis media. It is estimated that 20% of episodes of acute purulent otitis media become chronic OME.⁵

After years of controversy, it appears that Dr. Bluestone has established the fact that adenoial hypertrophy will predispose to chronic OME.⁴ The mechanisms of this remain unproven. Environmental irritants such as cigarette smoke have been demonstrated to very significantly increase the risk of otitis media with effusion. Kraemer has shown a four-fold increase of chronic OME in children living with a smoker.⁶ It is possible that wood stoves may cause similar problems.

The role of allergy in chronic otitis media remains controversial. Before investigating this factor, we need to review the history of allergy.

A brief history of allergy. Before 1925, "allergy" was defined as "an altered reaction occurring over time". This very loose definition was not entirely satisfactory. In 1921, Prausnitz and Kustner published revolutionary work demonstrating that a transferable agent in the serum is responsible for positive allergic response on skin testing. Kustner was quite allergic to fish and his skin test was dramatically positive. Prausnitz had no such allergy and his skin test for fish was negative. A sample of Kustner's serum was infiltrated subcutaneously into Prausnitz's arm and they discovered that in that area skin testing for fish became positive. This clearly demonstrated that the substance responsible for skin reaction and presumably the allergic response itself was present in the serum fraction. This substance was coined "Reagin" (in 1968, Reagin was identified as IgE). Allergists worldwide became excited that a scientific basis for allergy had been established and they made efforts to modernize the study of allergy. Following an American conclave in 1925, the definition of "allergy" was restricted to the mechanism of reaction of antigen and antibody which we now know as a Gell and Coombs Type I or IgE-mediated reaction.

Shortly afterwards, an iconoclast named Herbert Rinkel challenged this concord. His story is worthy of our attention.

In the 1920's, Dr. Rinkel was a married medical student with several children and chronic financial problems. His parents owned a poultry farm and weekly donated one gross of eggs (144!) to feed the family. By his third year of medical school, Rinkel had developed severe rhinitis which was refractory to immunotherapy despite aggressive work up and appropriate treatment. Rinkel thought that he might be allergic to eggs and challenged himself by drinking six raw eggs. He had no reaction.

Several years later, Rinkel considered that he might be reacting to a number of foods. Rather than challenging, he eliminated several foods from his diet, including eggs, and following a few days of feeling rather ill he felt

significantly improved. He attended a medical party near the hospital and in a jovial mood he ate a piece of angel food cake. He collapsed shortly afterwards and was unconscious for about 5 minutes. His medical friends checked his vital signs which were all normal. When he woke up, he asked what in the world he had eaten and was informed that angel food cake is made with 12 egg whites.

Upon consideration, Rinkel believed that during his five days abstinence from eggs, he may have developed five days worth of potential reaction to the eggs. He believed that when he ate the angel food cake, he then suffered the cumulative reaction all at once. He tested this hypothesis by again eliminating eggs for 5 days and then deliberately eating another egg. Following this first deliberate "elimination and challenge test", he again lapsed into unconsciousness. Upon reflection, Rinkel used this experience to develop a new clinical approach to food sensitivity.

In 1936, Rinkel presented his theory of "masked" (or hidden) food allergy. This did not conform to the guidelines for Reagin mediated allergies which had been established in 1925. Rinkel speculated that there are two forms of food allergy.

First is the immediate or "nonmasked" food allergy, exemplified by the patient who is allergic to shrimp. Foods involved in such reactions usually are eaten only occasionally and provoke a prompt and obvious reaction. This type of allergy does indeed conform to the Reagin guidelines (IgE). There has never been serious disagreement over the existence of this type of food allergy.

Rinkel proposed, however, that a second form of food sensitivity exists. Foods provoking such sensitivities are usually eaten daily. Patients feel a little sick every day and never make the connection between the food and their symptom. Delayed reactions are common and reactions tend to be dose dependent. Wheat, eggs, cow's milk, corn and chocolate are commonly involved. Paradoxically, people often crave the foods to which they are sensitive, and they may feel better after eating it. This improvement in symptoms after eating a "fix" was termed "masking" by Rinkel.

The hypothesis of masked food allergy created a deep rift among physicians then practicing allergy in this country. Two groups were formed based on their political alignment. Rinkel, who was trained by the great ENT allergist, French Hansel, led the otolaryngic allergists away from the internists and pediatricians. In 1941, the American Academy of Otolaryngic Allergy was formed. The American Academy of Allergy and Immunology was formed in 1942. Unfortunately, the cold war between these two rival camps has yet to be resolved. There exists general agreement about IgE mediated disease such as allergy to pollen, epidermals, dust mites, and molds. The massive disagreement over non-IgE sensitivity is not really over its existence, but rather over the true frequency and severity of the problem.⁷

How do you get allergic to food? There are a number of mechanisms of food sensitization. Prenatally, maternal IgG crosses the placenta. One commonly sees a baby who is allergic virtually at birth to certain foods. Frequently investigation will demonstrate that the mother herself is allergic to the same food and that the baby is born with passive immunity to the food.⁸ The fact that food antigens can cross the placenta has been demonstrated but the significance of this fact is questionable.⁹

Neonatal exposure may be the most important. A newborn baby has a "leaky" mucosa which lets antigenically intact macro-molecules enter the circulation at a substantial rate.¹⁰ By age 3-6 months, an event called "closure" occurs following which the uptake of macro-molecules into the systemic circulation decreases but does not cease.¹¹ During this vulnerable neonatal period, the child is exposed to antigens both in bottle feeding and in mother's milk. The presence of antigenically intact cow's milk protein was demonstrated in mother's milk as early as 1921.¹² In clinical confirmation, Hamburger recently demonstrated that while mother's milk afforded substantial protection against atopy compared to bottle feeding with standard formula, bottle feeding with elemental formula (Nutramigen) offered further protection over breast feeding.

Finally, a patient's bronchial mucosa may provide an avenue for sensitization. This may be important during infancy since small babies tend to regurgitate and may aspirate.

The gut has a rather elaborate multi-layered defense against the development of food allergies. These may be breached by factors which significantly contribute to the systemic absorption of antigenically intact macro-molecules. One of these is congenital immune deficiency, approximately 90% of patients may be found to have food sensitivities. This is caused by a failure of tolerance.¹⁴

Allergic reactions make the gastrointestinal tract leaky through the release of chemical mediators.¹⁵ Gastrointestinal disease, particularly gluten sensitive enteropathy and perhaps inflammatory bowel disease¹⁶ will cause such problems and there are a number of miscellaneous factors including alcohol,¹⁷ some drugs, surgical stress, and radiation therapy. Several illnesses are associated with "leaky gut" including rheumatoid arthritis and eczema.¹⁸

Can orally ingested food allergens really stimulate Gell and Coombs Type II, III, and IV reactions? The answer is yes. This has been ably demonstrated by Trevino¹⁹ and Breneman.²⁰

In summary then, there are two major types of food allergy. The first is mediated by IgG, universally termed allergy. The second is not an IgE phenomenon and should best be termed "sensitivity". Different rules apply for testing and treatment of these very different entities.

THE ASSOCIATION OF ALLERGY AND CHRONIC EAR DISEASE

As we investigate the association of allergy and chronic ear disease, I propose this rationale: The middle ear is a sinus. Embryologically, the middle ear is formed as are the sinuses, by an outpouching from the oropharynx. Histologically, it is lined with the same type of mucosa and bacteriologically it becomes infected with the same organisms as the sinuses. I consider the middle ear to be "a high class sinus with a job". If this is true, then the same things which cause sinus trouble should cause ear trouble.

Consider further the following rationalization: The Eustachian tube is vulnerable in small children, not because of length or angle, but because of caliber. This is a situation perfectly analogous to the pediatric airway. A

small amount of swelling will completely close down a small tube where the same amount of swelling will have virtually no effect on a larger tube.

A number of studies have demonstrated the coincidence of allergy and chronic otitis media with effusion. In 1981, Mc Mahon studied 111 patients undergoing surgery for chronic OME. Ninety-three percent of these patients had at least one positive test on RAST.²¹ In 1990, David Hurst reported a series of 20 patients with rather severe chronic otitis media with effusion, each having previously had at least three sets of tubes. One-hundred percent of these 20 patients were allergic.²²

In 1990, I reported to the AAOA a series of 105 patients who were tested while undergoing pressure equalizing tube insertion. Seventy-two percent of these were found to be allergic. Only 35 children had what I consider a good work up and of these children, 54% were positive. My criteria for a "good work up" included RAST or SET testing for at least four pollens, two molds, and one dust mite. A good work up also required elimination and challenge testing or intradermal definitive provocative food testing for at least half of the foods which were abnormal on an intradermal survey test using #2 dilution (1:500 W/V).²³

More recently, Nsouli presented 104 children to the ACAI in 1991. Seventy-eight percent of these children with severe recurrent otitis media had food allergy.²⁴

To what are these children allergic? In my study, children with proven allergy had significant reactions to all classes of antigens, particularly foods. Based on elimination challenge testing, 83% of children had at least one positive food and with provocative testing the number rose to 97%. Fifty-one percent of children were allergic to molds, 56% to pollens, and a surprisingly low 16% to dust.

We have to ask how allergic these children actually were. Are we overstating our case and reporting a series of children allergic to just one little dinky allergy? A positive reaction was defined as RAST Class I or #2 endpoint on SET. The results indicate that these children are significantly allergic. The percentage of tested antigens which were positive may provide a useful measure. Among children from 6 to 24 months of age, 17% of the mold antigens tested were found to be positive. Among children 2 years and older, the percent of positive antigens was 30-35%

Pollens showed a slightly different picture with children under 4 having relatively little reactivity. From 5 year old, however, 50% of the antigens tested were positive.

SUCCESSFUL TREATMENT OF CHRONIC OME BY ALLERGY MANAGEMENT ALONE

The proceeding studies have demonstrated that children with OME have a higher incidence of allergic problems than would be expected in the general population. Is this only coincidence? Several studies prove an etiologic link.

In 1983, Shambaugh published a series of 101 children with chronic OME treated by allergy management alone. Of these children, 13 were unable to comply and were treated surgically. Ten were lost to follow up. With 78 patients cured by allergy management alone, Shambaugh claimed a success rate of 77%. Looking more critically at the data, however, we see that 78 of 78 compliant patients with known follow up were successful, giving a true success rate of 100%. Interestingly, 19 of these children cleared with only inhalant allergy treatment while the others required some degree of food allergy management.²⁵

In 1990, Hurst published the response of 20 patients with refractory chronic OME to allergy treatment alone. Eleven patients were fully compliant and their problem was resolved. Three patients totally refused allergy management and required further operations. Six patients had variable noncompliance doing well while they were receiving allergy treatment and relapsing when they were off treatment. Hurst's total success rate was 55% (11/20), but success rate among compliant patients with a 3-year follow up was 100% (11/11).²²

Recently, T.M. Nsouli reported a fascinating series of 104 children with chronic OME. He found that 78% (81) were food allergic. Eighty-six percent of these children (70/81) cleared after a 16-week elimination diet. Ninety-four percent (66/70) recurred after introduction of the offending foods.²⁴ This series certainly provides excellent evidence for the association of food allergy and otitis media with effusion.

AN ALTERNATIVE TO SURGERY?

Allergy management is not always practical as an alternative to surgery. There are certain limitations which need to be considered. First, the anatomical problem of a huge adenoid or congenital deformity must certainly be treated in the appropriate surgical fashion. Consider also that an allergy work up can be lengthy and that tube placement may be urgent, particularly in a child with substantial hearing loss, recurring infection, or damage to the tympanic membrane. Furthermore, it may be quite difficult to test small children and babies. One does not wish to prolong the work up in patients who need prompt resolution of their symptoms.

INTRAOPERATIVE TESTING FOR ALLERGY

Why would we want to both place pressure equalizing tubes and perform allergy testing at the same time? This may be explained by the following rationale. Our patient needs prompt intubation but PE tubes are only a temporary solution. Estimates of reinsertion rates vary in the range of 20-30%, but good data are lacking.²⁶⁻²⁷ PE tubes then do not solve the problem, only buy time. Furthermore, allergy work up is very easy while a child is asleep. The child's anesthetic is only very rarely prolonged by allergy testing. Moreover, symptoms other than OME are often corrected.

Who then should be tested? All chronic OME patients requiring operation are candidates for an allergy work up. Particularly, test those with a strong history of allergy, those whose physical examination is consistent with allergy, without other risk factors such as cigarette smoking and giant adenoids, and finally and especially, those with recurring

disease who have previously had PE tubes. Children may be tested at any age, particularly for foods and molds. I prefer intraoperative testing for small children and “needle-phobics”.

For what should we test? The selection of antigens is important. Any food that is tested must be in the diet at least every third day. Most small children end up getting tested for about 20 foods, many of them hidden, such as malt, soy, and egg. One must be very careful not to test any food which is known to cause severe reaction.

Molds are very important among my patients. We practise in a river valley and have found a large number of clinically significant mold species. We now test 20 molds.

Pollens may be quite important, but if a child is younger than 4 years old, it is not cost effective to test for pollen allergy. An exception may be made for a child with a very strong clinical history. Dust mite allergy is rather similar to pollen and does not appear to be clinically significant factor in children younger than about 3 or 4 years old.

Methods: Intraoperative testing may be performed several different ways. The simplest method is phlebotomy for RAST testing. My own experience indicates that RAST is excellent for pollen (perhaps better than skin testing !) and quite good for dust mites. RAST testing is of less value for moulds and is simply not cost –efficient for foods. Other in-vitro methods of food allergy testing have failed to demonstrate clinical utility with the exception of ALCAT.²⁸

Intradermal testing may be useful. Single dilution intradermal testing is not standard AAOA technique, but as a short-cut in a selected patient it is cost effective and safe with acceptable accuracy. For example, I test small children for molds with a #1 dilution (1:100) which has proven to be safe, quick, and inexpensive. It is mandatory that appropriate controls are used. Without a negative control, the test is invalid. I recommend using 1:10 W/V stock concentrates so that the glycerin in your testing extract is only 5%. I have found that testing with antigens in 10% glycerin is less reliable.

Older children may have stronger mold sensitivities. I perform RAST or SET for the five strongest reactors in my region before doing any other mold testing. If the SET or RAST shows mild levels of sensitivity for these molds; it appears to be safe to proceed with #1 intradermal testing for the rest of the antigens which generally are milder reactors. This offers the patient a very substantial savings in both money and number of needle sticks that he has to endure.

The intradermal technique may also be applied to foods. Dr. Frank Waickman of Akron, Ohio, teaches a technique of testing for foods commonly in the diet using a 4 mm wheal of a #2 dilution (1:500 W/V). The testing is inexpensive, quick, and inclusive. This test gives surprisingly good results. From reviewing several hundred tests, I have found that antigens which are at least 2 mm larger than the control wheals have a 70% true positive rate upon elimination challenge or provocative testing. Interestingly, antigens which grow only 1 mm larger than the controls will have a 40% true positive rate when confirmatory testing is performed.

The clear disadvantage of intradermal survey testing for foods is that the patient must do a confirmatory elimination/challenge or provocative-neutralization test. Corey and Danford in 1990 showed that a highly educated group of patients had less than 50% compliance with elimination challenge diets.²⁹ Furthermore, the popular perception is that the operation has solved the problem by inserting temporary PE tubes. Many people feel that the elimination/challenge work leaves them “nothing to eat”. Parents often express the concern that the intradermal definitive provocative food test is too painful. My own study showed a “good work up” in only 35% of patients who underwent the survey tests.

Some of the disadvantages of single dilution testing are overcome by skin titration. The most common method employed is the classical SET espoused by the AAOA. This is a very useful technique for testing pollens, molds, fungus, dust, epidermals, and even cigarette smoke. The majority of younger children can have testing started with a #3 dilution and if this is negative, the tester may then skip to a #1. Remembering that the classical progression of positive dilutions grows by 2 mm for each stronger dilution, an accurate endpoint may be extrapolated.

A newer technique may be the most useful for food sensitivity testing. King introduced the “multi-test” recently, given impetus by the AAOA Cooperative study which demonstrated the clinical utility of the skin whealing response.³⁰ This may be considered the definitive *Intraoperative* food test. The test starts with a #1 dilution. For all foods positive on a #1 dilution, a #2 dilution is placed. Titration is continued every 10 minutes until a negative wheal is reached.

There are several advantages to using King’s multi-test intraoperatively. First, the elimination/ challenge and provocative-neutralization compliance problems are eliminated or minimized. Secondly, the patient’s family is given a firm diagnosis on the same day as surgery. Neutralization injections or drops may be promptly formulated from the results of the test. Unfortunately, there are some disadvantages as well. Foremost among these is the time factor. It takes up to 10 minutes to place the food survey alone. Waiting 10 minutes for wheal growth and then placement of subsequent wheals means that the multi-test may take 45 minutes or more. Another fair criticism is that this technique may unduly limit the antigen selection for testing. Furthermore, the accuracy of the neutralizing dose may be sacrificed using this technique. When IDPFT tests provoke symptoms, about 1 in 4 foods neutralize on a multiple of the first negative wheal. Using the multi-test technique, these neutralizing doses will be suboptimal.

The best approach to intraoperative food testing is yet unproven. Even after a full work-up, compliance remains a problem, as demonstrated by Dr. Hurst. There appears to be one key to patient compliance: the patient must perceive their disease as worse than the treatment.

CHRONIC OTOMASTOIDITIS AND ALLERGY

It appears that COM is a continuation of the same process which causes chronic OME. If that is the case, then we should expect COM patients to have a similar allergic profiles as chronic OME patients.

In 1990, I presented a series of COM patients who had tympanoplasty or mastoidectomy and tympanoplasty and found that they indeed had the same incidence of allergy and allergic profile as my chronic OME patients. Reviewing three years’ records, 57 patients were found to have undergone surgery for COM. Forty-four of these

patients had some allergy testing. Those who were not tested included 2 with congenital cholesteatoma, 1 each with cleft palate, Down syndrome, traumatic perforation, tuberculous otitis media, and 7 patients who just refused testing.

Among the 44 patients who were tested, 91% had at least one allergy. Twenty-six of the twenty-seven patients with "good work up" (96%) were found to be allergic. Specifically, 70% were allergic to mold and 25% of the antigens tested were positive. Fifty-eight percent had pollen allergy to mold and 25% of the antigens tested reacting abnormally. Forty-five percent were dust allergic. Again, foods appear to be the most important. Seventy-eight percent of patients who did even one elimination challenge test had at least one positive food and 91% of patients who had IDPFT for at least one food were found to have a positive reaction.²³

The logical question arises that since these patients all need operations anyway, why should we bother to test and treat their allergies? I believe that the grafted tympanic membrane and ossicles are not as good as those that the patient was born with. If the underlying cause of the patient's disease is not corrected, the problem may certainly recur. I feel that correcting their allergic problem will reduce the frequency of reoperations. My general impression is that allergy testing and treatment compliance is significantly better in this group, probably because they perceive that their disease is more serious. Unfortunately, getting rid of cigarette smoke is harder. These people are actively smoking and not just passively exposed. Cantrell's important work demonstrating significantly increased risk of surgical failure among smokers is ample incentive to ask the patient to stop smoking.³¹

I routinely suggest allergy testing and attempt to get started on treatment before the operation. I go ahead with the operation if the patient is hesitant about doing the allergy work up.

SUMMARY

- Over 90% of chronic OME and COM patients have allergies when an adequate work up is performed.
- Food sensitivities, most of which are non-IgE mediated, play an important role.
- Allergic management of chronic OME may be a successful alternative to surgery.
- Allergic management of chronic OME and COM appears to be a logical adjunct to surgical treatment.
- AAOA propaganda: Why should an ENT do the allergy work?

We have the best knowledge of anatomy, physiology, and pathophysiology of the ears, nose, and throat. ENT allergists are more free of IGE dogma and have a better understanding of food sensitivity. Otolaryngic allergy techniques are modern and quantitative, achieving excellent results.

As surgeons, we are the allergic patients last recourse. Our insight may prevent unnecessary operations, both primary and revision.

Our challenge beyond treating symptoms, is to find and correct the underlying cause of the disease. Understanding the dynamics of allergy will help us meet this challenge.

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