Can CAM Therapies Help Reduce Antibiotic Resistance?

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Abstract

The Centers for Disease Control and Prevention (CDC) reported the consumption of 235 million doses of antibiotics in 2001. It is estimated that 20-50 percent of these were unnecessarily prescribed for viral infections. Bacteria that antibiotics have controlled in the past are increasingly developing resistance to these drugs. Today, virtually all important bacterial infections in the United States and throughout the world are becoming resistant. For this reason, antibiotic resistance is among the CDC's top concerns. A large portion of antibiotics are dispensed by pediatricians treating common outpatient infectious diseases. The overuse of antimicrobials is beginning to be discouraged as scientific evidence is emerging to support the use of other therapies. In pediatric practice an emphasis on accurate diagnoses, control of environmental risk factors, and utilization of complementary and alternative medicine (CAM) therapies could reduce antibiotic prescribing. Antibiotic resistance poses a growing threat to health. CAM therapies may provide a safer, more effective treatment for many acute infections of childhood.

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Introduction

An increasing number of strains of antibiotic-resistant bacteria are now emerging, in large part due to the overuse and misuse of antimicrobial drugs by health care providers. The Centers for Disease Control and Prevention (CDC) reported the consumption of 235 million doses of antibiotics in 2001 and estimated that 20-50 percent of these were unnecessarily prescribed for viral infections.[1] Overuse of antimicrobial drugs exerts a selective pressure among bacteria, encouraging the emergence of antibiotic-resistant strains by eliminating antibiotic-sensitive strains, promoting establishment of bacteria with rare mutations of resistance, and permitting the spread of resistant strains from infected individuals.[2,3] The proliferation of drug-resistant *Streptococcus pneumoniae* (*S. pneumoniae*) is documented worldwide. In some regions of the United States less than 50 percent of the *S. pneumoniae* strains are susceptible to penicillin.[4] While the appropriate use of antimicrobial drugs can be lifesaving, the unnecessary use of antimicrobials is creating a worldwide health threat.

Widespread use of antibiotics for viral infections, including the common cold, most sore throats, and the flu, and for self-limiting bacterial infections is prevalent in pediatric practice. Prescriptions for acute otitis media (AOM) in children are responsible for approximately one-fifth of all antimicrobials prescribed in the United States.[5] Additionally, as many as two-thirds of all infants may be exposed to antimicrobials within the first 200 days of life.[6,7] Antibiotics are commonly prescribed for children to treat AOM, bronchitis, pharyngitis, sinusitis, and acne.[8] In an effort to reduce inappropriate use of antimicrobials,

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medical policy makers have scrutinized physicians' prescribing practices in this field.

In 1995 the CDC launched a national campaign to reduce antibiotic resistance, developing strategies and materials encouraging changes in antibiotic prescribing. Treatment recommendations for uncomplicated pediatric infections have shifted from universal use of antimicrobial drugs toward symptomatic relief, watchful waiting, and other alternatives to antibiotics. Complementary and alternative medical (CAM) therapies such as homeopathy, botanical medicine, vitamins, minerals, and hydrotherapy can be effective non-drug treatments for common pediatric infectious diseases. The use of CAM therapies when antibiotics are not indicated may play a role in slowing the proliferation of antibiotic overuse in pediatric infections.

The tenets of judicious antibiotic prescribing are taught to medical students and residents in primary care specialties, but may not be adhered to in actual clinical practice. Multiple analyses of prescribing patterns consistently reveal inappropriate prescribing of antibiotics, notwithstanding the clinician's awareness of appropriate antibiotic use.[9-11] Additional investigations report that prescribing antibiotics at the first office visit tends to increase, rather than decrease, costs to patients, hospitals, and insurance companies, and has marginal impact on patient outcomes.[12] In addition to over-prescribing antibiotics, providers often address therapy failures by switching to same-class antibiotic agents.

It is noteworthy the second most common diagnosis prompting antibiotics, upper respiratory tract infection, often has a viral etiology.[5] Numerous studies have shown the administration of oral antibiotics to children with uncomplicated upper respiratory tract infections (URTI) has no beneficial impact on the course of the disease or on the risk of subsequent complications.[13-18] Additionally, medical students and residents are taught that children with symptoms of URTI, such as acute purulent rhinitis, should not be treated with antibiotics unless drainage persists for 10-14 days.[19] However, there is a striking dichotomy between what is taught and what is practiced in the primary care field. A survey of 346 family practitioners (FP) and pediatricians (PD) revealed the reasons for hasty antibiotic therapy in purulent rhinitis include: (1) the belief that many untreated patients would develop persistent purulent nasal drainage; (2) concern that AOM would develop; (3) pressure from mothers to prescribe antibiotics; and (4) the desire to allow employed parents to return to work earlier. Nevertheless, most FP (89%) and PD (97%) were concerned about the increase in bacterial resistance rates arising from unnecessary antibiotic prescribing.[9] Additionally, office visit time limitations, legal liability concerns, and drug promotion by pharmaceutical companies contribute to overuse.[20]

Alternatives to Antibiotics

The rise in bacterial resistance has prompted recommendations that allopathic doctors prescribe fewer antibiotics, which, in turn, has led to a search for alternatives. A review of the therapeutic approaches to common outpatient pediatric infectious diseases cites potential alternatives and adjuncts to antimicrobial treatment – vaccination, surgical intervention, control of environmental risk factors, and alternative medical therapies.[8] Prophylactic surgery or vaccinations are indicated in some cases, but these modalities may pose unacceptable risks for treatment and prevention of uncomplicated pediatric infections.

Children in the United States receive an average of 33 doses of 10 different vaccinations by the age of five.[21] There are potential long-term health risks associated with vaccinations, a topic beyond the scope of this paper. Varicella (chicken pox) vaccination, mandated by many states, is an example of a vaccination emerging as a prevention strategy for a common pediatric infectious disease. One author optimistically states, "In the future, new vaccine combinations with as many as six components and new methods of administration (e.g., single injection of a slow release microsphere vaccine, simple ingestion of transgenic (genetically manipulated) plants, mucosal surface intranasal spray) will reduce the susceptibility of children to common bacterial and viral pathogens."[8]

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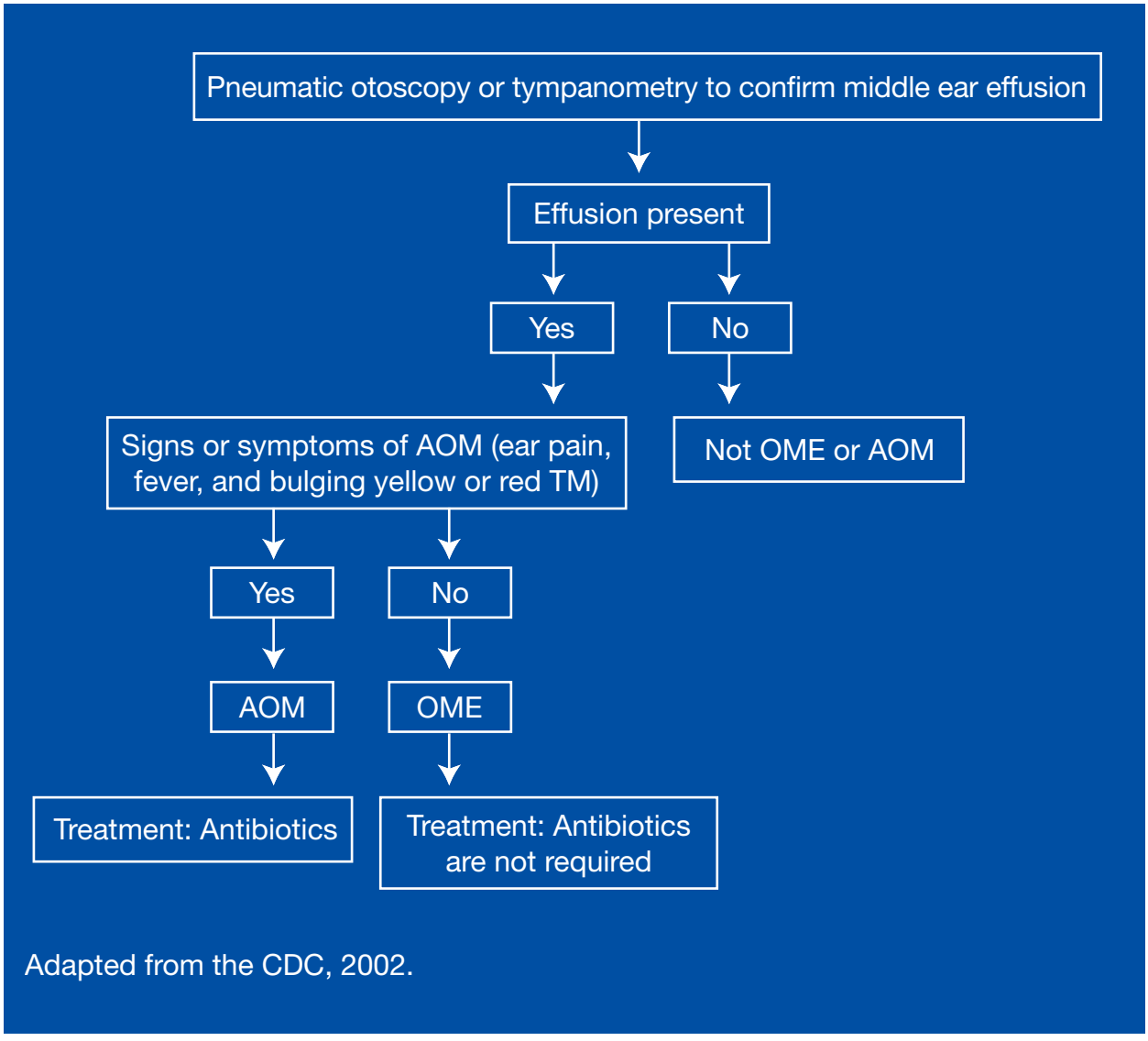
Figure 1. *The CDC's Recommendations for the Treatment of Acute Otitis Media*



Surgical intervention is invasive and most parents and physicians consider it to be a last resort. A 1994 evaluation of the use of tympanostomy tubes for chronic otitis media found that 42 percent had been prescribed appropriately, 31 percent were equivocal, and 27 percent had been inappropriately prescribed.[22] The outcome for appropriately placed tubes is good; with less ENT-related clinic visits for those children, but little change for those placed inappropriately.[23] The insertion of tympanostomy tubes might be helpful in chronic otitis media with effusion (OME) that is unresponsive to medical management and recurrent AOM, but carries the risk of anesthetic complication, persistent perforation (in about four percent of patients), tympanosclerosis, and cholesteatoma.[24]

Controlling environmental risk factors and employing alternative medical therapies are non-invasive considerations for the treatment of common pediatric infectious diseases such as otitis media, bronchitis, rhinitis, sinusitis, and

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pharyngitis. Excessive and unnecessary use of antimicrobial drugs has created a conundrum for allopathic family practitioners and pediatricians. The responsible therapeutic choice for many pediatric patients may involve the use of CAM therapies. Emerging scientific evidence validating the efficacy of CAM modalities for common pediatric infectious diseases might facilitate increased use by all types of physicians.

Otitis Media

In the United States, otitis media is the most common reason for outpatient antimicrobial use, accounting for over 50 percent of the antibiotic prescriptions dispensed to children.[8,25] On average, children suffer one episode of AOM in each of the first three years of life.[26] It has been estimated that each year these children spend the equivalent of one month on antibiotics.[27] Increasing resistance to antimicrobial agents has been reported for the three most common bacterial causes of otitis media (*Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*).[28] A more judicious prescribing approach to AOM would significantly reduce antibiotic dispensing. In addition, avoiding unnecessary treatment of otitis media with effusion, for which antibiotics are not indicated, would eliminate 6-8 million courses of antibiotics each year.[29]

Prescribing Recommendations for Acute Otitis Media

The CDC recommends narrow-spectrum antibiotics for patients who present with the following signs and symptoms of AOM: effusion, ear pain, fever, and bulging yellow or red tympanic membrane confirmed by pneumatic otoscopy or tympanometry. Antibiotics are not recommended when there is no effusion present or effusion is present without signs and symptoms of acute infection (Figure 1). Some experts believe these guidelines result in overuse of antibiotics. A group of eight international experts evaluated data from seven randomized, placebo-controlled trials and concluded the benefit of routine antimicrobial use for AOM, judged by either short- or long-term outcomes, was unproven.[30] Additionally, the risk of a dire complication among untreated children in developed countries is minimal. In The Netherlands, among 4,860 patients with AOM who were not given antimicrobials, only two experienced mastoiditis, and both responded to treatment with oral antimicrobials as outpatients; no patient developed meningitits.[31]

Dutch guidelines do not recommend universal antibiotic treatment for children with AOM (Figure 2). AOM patients two years and older receive symptomatic treatment for the first three days and are re-evaluated if symptoms of pain or fever continue for three days. At that time the doctor may continue additional observation or give amoxicillin or erythromycin for seven days. Special treatment for tympanic membrane perforation is not suggested unless it persists for 14 days, at which time a course of antimicrobials is suggested. In children between the ages of six months and two years, management is the same as for those two years and older, except it is mandatory for the doctor to make contact by either telephone or office visit after 24 hours. If a patient exhibits no improvement in 24 hours, the doctor may either start antibiotics or wait an additional 24 hours. Referral to an otolaryngologist is suggested if patients in this age group appear to be seriously ill or do not improve after 24 hours of treatment with antimicrobials.[32]

Despite the fact that a diagnosis of AOM is a major reason for antibiotic prescription, there is no compelling evidence that children with otitis media given antibiotics have shorter duration of symptoms, fewer recurrences, or better long-term outcomes than those who do not receive antibiotics.[30] It has been estimated that at least 80 percent of children with AOM will get better without the use of antibiotics as the eustachian tube opens and the middle ear clears of infection.[33] Klein summarizes a comprehensive strategy for otitis media, including limited or no use of antimicrobials for mild disease; educating consumers about appropriate use of antibacterial drugs; implementing techniques for increasing accuracy of diagnosis of AOM versus OME; and investigating homeopathic and herbal remedies and other alternative techniques.[34]

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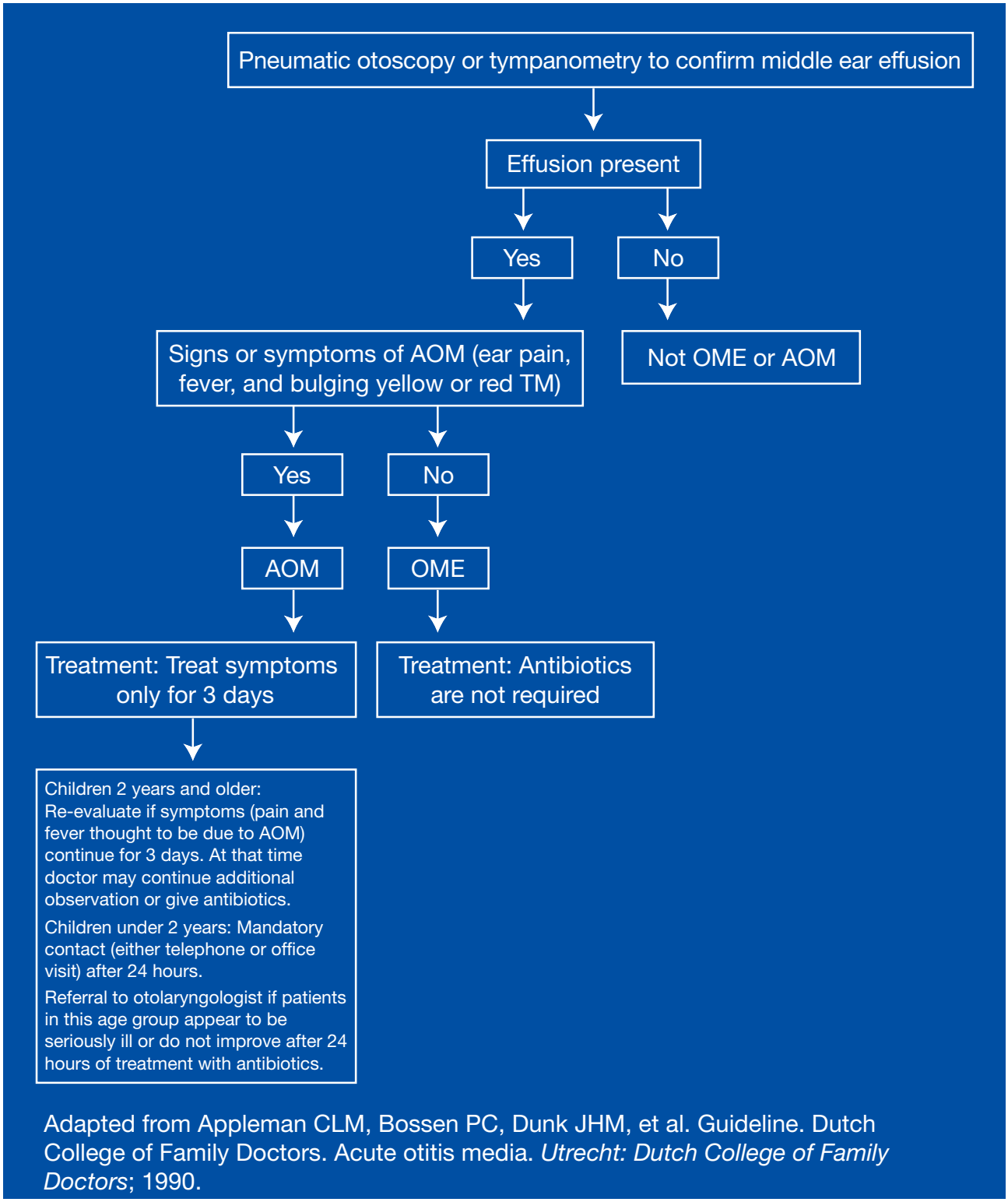
Figure 2. *Dutch Guidelines for Treatment of Otitis Media*



Adapted from Appleman CLM, Bossen PC, Dunk JHM, et al. Guideline. Dutch College of Family Doctors. Acute otitis media. *Utrecht: Dutch College of Family Doctors*; 1990.

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When antimicrobial therapy is not indicated for otitis media, as in OME, health care providers typically utilize oral analgesics (e.g., acetaminophen or ibuprofen) for pain, antihistamines and decongestants for symptom relief, and a period of watchful waiting. Rosenfeld elegantly quotes Voltaire in reference to this approach: "The art of medicine consists in amusing the patient while nature cures the disease." He concludes that while nature cures OME physicians often "amuse" parents with antibiotics, antihistamines, decongestants, or steroids even though a long-term benefit has never been shown for any of these drugs.[35] Thirty percent of OME resolves in several weeks without treatment, increasing to 90-percent spontaneous resolution in several months.[36-38]

Nutrients and Botanicals in the Treatment of Otitis Media

Antibiotic resistance and the potential that antibiotics do not change the course of AOM, as well as the recommendation not to give antibiotics for most cases of OME, could lead to a paradigm shift in the treatment of otitis media; i.e., that physicians might look to CAM therapies as the responsible first-line of therapies for most cases of otitis media, while antibiotics and surgeries become the "alternative." The new paradigm would focus on stimulating a child's immune system to combat pathogens, physical interventions that could facilitate the clearance of fluid from the middle ear, reducing known risk factors that predispose to otitis media, and investigating food and environmental allergens in children with recurrent OME.

Several nutrients and botanicals are effective in stimulating an immune response and fighting infection. Echinacea is one of the most widely used botanical supplements in North America. There are hundreds of Echinacea studies in the medical literature worldwide. One review of 34 studies using Echinacea for the prevention of upper respiratory tract infections, a common etiology of eustachian tube inflammation, showed 22 had positive outcomes that were reasonably demonstrated .[39] Another review of nine randomized trials showed eight reported some benefit of Echinacea in the early treatment of upper respiratory infections.[40] More recently, the NIH granted funding to the University of Arizona Departments of Pediatrics and Integrative Medicine to support a controlled study of Echinacea for prevention of AOM in children with a history of recurrence.[41] The study is rigorously designed and uses randomized control groups with placebos to meet the expectations of the NIH. Depending on the outcome, further rigorous studies of Echinacea and other potential alternatives may be encouraged.

Naturally occurring arabinogalactans found in *Larix occidentalis* are used to enhance the immune response in pediatric patients. Arabinogalactans are a class of long, densely branched, high-molecular weight polysaccharides shown to have antiviral effects and enhance natural killer cell cytotoxicity and macrophage activation.[42,43] Several immune-stimulating herbs, such as *Echinacea purpurea*, *Baptisia tinctoria*, *Thuja occidentalis*, *Angelica acutiloba*, and *Curcuma longa*, contain significant amounts of arabinogalactans.[43] Larch arabinogalactans are unique because they are FDA-approved for use as dietary fiber and in food application. Acute and long-term studies in rats and mice reveal no evidence of toxicity.[44] Larch arabinogalactans have a mild taste and high solubility in water, properties that facilitate patient compliance in the pediatric population. D'Adamo reports a decrease in frequency and severity of otitis media in pediatric patients supplemented prophylactically with larch arabinogalactans.[43]

Nutritional deficiencies contribute to low immunity and impaired resistance to infection. A selenium deficiency, for example, has been shown to inhibit resistance to infection, while selenium supplementation enhances immune function by stimulating white blood cell and thymus activity.[45-47] Essential fatty acid deficiency in combination with sub-optimal levels of vitamins and minerals may contribute to susceptibility to otitis media. Eight children with recurrent otitis media undergoing ambulatory surgery were identified as having reduced blood levels of fatty acids, vitamin A, and trace minerals including selenium. Supplementation with one teaspoon cod liver oil

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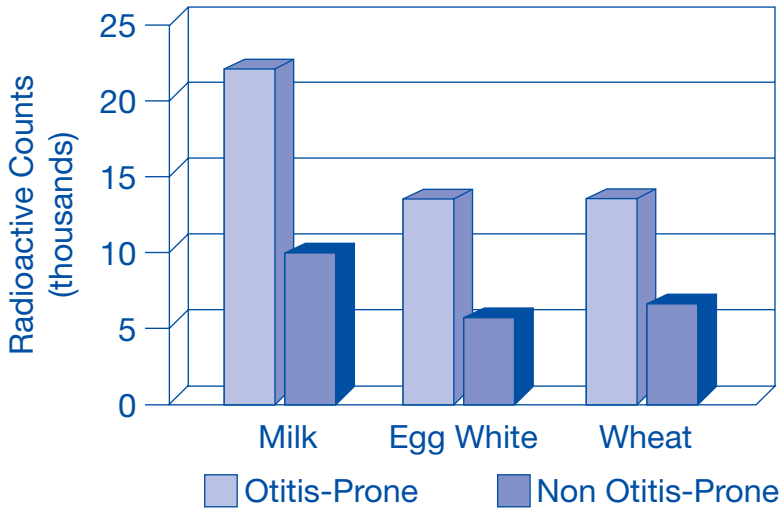
(containing both EPA and vitamin A) and one-half tablet of a selenium-containing children's multivitamin-mineral tablet per day reduced antibiotic use for AOM by 13-percent fewer days than before supplementation.[48] Larger, controlled trials are necessary to evaluate the usefulness of fish oil and children's multivitamin-mineral preparations for the prevention of otitis media and the reduction of antibiotic use.

Homeopathy in Otitis Media

Homeopathic physicians were effectively treating otitis media long before the advent of anti-microbial drugs. In fact, some references referring to homeopathy to treat otitis media are over 100 years old.[49,50] Studies investigating homeopathy versus placebo or conventional therapy have identified a positive effect using homeopathic medicines, but lack a large enough sample size to reach statistical significance.[51-53] Homeopathy might provide an attractive treatment option for practitioners and parents during the "watch and wait" period, before prescribing antibiotics.

A randomized, double-blind, placebo-controlled pilot study suggested a positive treatment effect of homeopathy when compared with placebo in AOM.[53] Seventy-five children (36 in the homeopathic group and 33 in the placebo group) from a private practice in Seattle, Washington, were included in the study. The author concluded that, although results were positive, 243 subjects would have been needed in each group to reach statistical significance. Lack of statistical significance, as well as the fact that 70-90 percent of AOM episodes resolve spontaneously without treatment,[36-38] leaves the positive treatment effect of this study inconclusive.

Figure 3. *IgG Radioallergosorbent Test Against Foods in Otitis-prone and Non-otitis-prone Children*



From: Bernstein JM. *Otolaryngol Head Neck Surg* 1993; 109:619.

A nonrandomized, open trial in Germany found a faster resolution of pain and fewer recurrences in children treated with homeopathy compared to those receiving conventional treatment.[51] The progress of AOM in children treated in a homeopathic ear, nose, and throat (ENT) practice was prospectively compared with that observed in the practices of four other ENT practitioners applying conventional methods. In this study fewer subjects participated in the conventionally treated group (103 attended the homeopathic practice compared with 28 seeking conventional treatment). Since patients were not randomized but were allowed the practice of their choice and parents who choose homeopathy as a preferred treatment choice for their children may make other healthy lifestyle choices (avoiding food allergies, breast feeding, good diet, etc.), the outcome of this study could have been significantly influenced by its nonrandom design.

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Allergy in Otitis Media

An allergic etiology has long been suspected in children with recurrent OME. There is considerable lack of uniformity of opinion on the relationship between allergy and OME, however. The reported incidence of allergy in children with this disease varies from near zero in some studies to more than 80 percent in others.[54] Bernstein, an accomplished ear, nose, and throat research specialist, suggests recurrent OME is related to allergy in 35-45 percent of cases.[54-56] Researchers in 1965 suggested an allergic mechanism, not only as the major cause of OME, but also as a predisposing factor in as many as 85 percent of AOM cases.[57] Some researchers and clinicians have emphasized the role of food allergy in producing the disease; others have stressed inhalant allergies.

In the case of inhalant allergies, OME develops as a result of immunoglobulin E (IgE) mediated hypersensitivity to inhaled antigens. Release of biological mediators of inflammation from basophils and mast cells occurs in the nasal and nasopharyngeal mucosa. These mediators likely produce eustachian tube edema and inflammation, predisposing to middle ear effusion and viral or bacterial infections.[58-60] Researchers at the Children's Hospital of Buffalo demonstrated how viral upper respiratory tract infections may initiate IgE antibodies on the surface of viral-infected cells, leading to the development of OME in a similar manner to inhaled allergens.[61]

Other clinicians and researchers believe OME is a result of blood-born antigen-antibody complexes, formed as a reaction to certain foods, traveling to the dermal target cells through circulation.[62] The middle ear cleft, nasal or nasopharyngeal mucosa, and cheeks (as seen in infantile cheek eczema) are considered target locations for the antigen-antibody complexes. It appears that in the otitis-prone child food immune complexes are more likely to exist than in children who are not otitis prone (Figure 3). Manifestations of food allergy are not limited to otitis media and may include chronic rhinitis, eczema, chronic cough, enlarged tonsil or adenoid tissue, and wheezing.[63]

The onset of allergic symptoms generally follows the withdrawal of breast milk with its high levels of protective secretory IgA, suggesting the development of hypersensitivities to specific foods during this period.[62] Several authors implicate the lack of or short duration of breastfeeding as a risk factor for otitis media.[64-67] The loss of protection from gut hyperpermeability otherwise furnished by secretory IgA allows undigested, highly antigenic foreign protein to penetrate the mucosa, yielding contact with plasma cells in the lamina propria and production of antibodies to the foods.[62] Infants experiencing recurrent OME while on human breast milk have been shown to have acquired immune complexes *in utero* and via breastfeeding through the mother's allergic diathesis. In one small trial, cessation of episodes of AOM and OME were noted when offending foods were eliminated from the mother's and child's diets.[68]

Other Infectious Diseases and Antibiotic Alternatives: Rhinitis, Bronchitis, Sinusitis, Pharyngitis

In the case of viral rhinosinusitis, children frequently present with copious thick, clear or yellow nasal discharge. Antibiotics are not indicated unless discharge persists for 10-14 days.[19] An estimated 50-percent reduction in antimicrobial use for mucopurulent rhinitis would result if treatment was initiated only after day 10 of discharge; 6.5 million unnecessary prescriptions for antibiotics would be avoided.[1]

The vast majority (90+ percent) of uncomplicated acute bronchitis cases are caused by viral infection,[69] for which antibiotics are not recommended treatment in immunocompetent children without comorbid conditions.[70,71] Practitioners often prescribe antibiotics based on the common misconception that purulent secretions indicate bacterial infection; however, randomized, placebo-controlled trials have failed to support a role for antibiotic treatment of uncomplicated acute bronchitis.[72-81]

Mild or moderate acute bacterial sinusitis does not require antibiotic therapy.[20,70] Severe or persistent symptoms, including fever (> 102° F), unilateral facial or maxillary pain, and periorbital swelling lasting longer than seven days are considered indications for antibiotics.[82] Initial

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antimicrobial treatment should be with a narrow-spectrum agent after culture and sensitivity testing. The usual etiological pathogens acquired from the environment include *S. pneumoniae* and *H. influenza*. Oral amoxicillin with clavulanate is considered first-line treatment for community-acquired sinusitis.[70,82] Establishing an accurate diagnosis of bacterial sinusitis is challenging but critical, because viral rhinosinusitis is 20-200 times more common than bacterial sinusitis.[83]

Antibiotics are appropriate for the treatment of group A streptococcal pharyngitis to prevent sequela such as rheumatic fever or glomerular nephritis. However, only 10-15 percent of pharyngitis cases are caused by group A streptococci; the remaining cases have a viral etiology.[20,70] Clinical findings cannot reliably differentiate streptococcal from viral pharyngitis. Diagnosis of group A streptococcal pharyngitis should be based on results of an antigen test (rapid strep kits) or throat culture. Negative results on antigen tests should be confirmed with a culture. A brief delay in initiating antibiotic therapy to process a throat culture does not increase the risk of latent sequela[84] and presumptively starting antibiotic therapy pending results of a culture is discouraged.[85] By following these guidelines, antibiotic dispensing could be reduced by seven million prescriptions per year, a 50-percent reduction in antibiotics dispensed for pharyngitis.[1] The time between a negative rapid strep test and results of a throat culture provides an opportunity for practitioners to utilize immune-stimulating vitamins and botanicals, homeopathy, hydrotherapy, and other CAM therapies.

Treatment of Infections with Hydrotherapy

Among the drugless methods used in the treatment of acute disease, the use of water is one of the most powerful and under-utilized therapies. Historically, medical books commonly explained hydrotherapy for use in both the hospital and home setting.[86] Since the advent of antibiotics in the 1940s, few physicians have utilized hydrotherapy techniques. Hydrotherapy utilizes hot and cold applications of water to manipulate the quantity of blood flow through a given tissue. Adequate blood flow brings oxygen, nutrients, and red and white blood cells to the target tissue. This basic physiological manipulation of blood and lymph flow can support the body in its fight against infectious disease and can be performed in conjunction with antibiotics or other CAM therapies. Practitioners can teach parents simple techniques they can use at home during the "watch-and-wait period" or when antibiotics are not indicated.

The heating throat compress is indicated for sore throats and cervical lymphadenopathy. To apply a heating throat compress, a cotton cloth (two layers thick, wide and long enough to encircle the neck, soaked in cold water and wrung out) is wrapped around the neck and covered with a wool or flannel cloth large enough to entirely cover the cotton cloth. The compress heats and dries, resulting in increased circulation to the neck and throat area.[86] When treating small children, due to the location of the compress around the neck, the compress can be applied during the daytime hours, under parental supervision. Heating throat compresses in combination with salt-water gargles[1] are two effective hydrotherapies indicated for pharyngitis and lymphadenopathy.

Nasal lavage, the use of hypertonic saline nasal irrigation, has a long history of use in sinonasal diseases, including chronic rhinosinusitis and allergic rhinitis. Hypertonic nasal irrigation has been shown to increase mucociliary clearance and ciliary beat frequency.[87] A prospective, controlled clinical trial of 211 patients with sinonasal disease showed statistically significant improvements in 23 of 30 nasal symptoms.[88] Nasal lavage has also been shown to be an efficient treatment for sinusitis in children.[87] Patient education regarding the proper technique for nasal lavage is imperative to achieve compliance. Additionally, several nasal irrigation products have been developed to simplify the technique.[89]

Another longstanding hydrotherapy treatment thought to stimulate the immune system is the warming socks treatment.[90] The patient's feet are soaked in hot water for 5-10 minutes until the skin is erythematous. Remove the feet from the water and dry with a towel. Immediately apply a pair of cold wet cotton socks (wet the socks in very cold water and wring out thoroughly) and

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then place a pair of dry wool socks over the wet cotton socks. This therapy is most effective if the patient is covered, kept warm, and goes directly to bed.

These and other hydrotherapy techniques are appropriate adjuncts for treating pediatric infectious diseases. When done correctly the treatments are safe, nurturing, and effective. Instructional patient handouts describing the techniques and indications for specific hydrotherapy treatments are useful and save time. Prescribing hydrotherapy treatments when antibiotics are not indicated may alleviate parental expectations to receive antibiotics, subsequently reducing unnecessary antibiotic prescriptions.

Botanicals and Nutrients for Other Infectious Diseases

Although CAM therapies have been used for centuries to combat pediatric infections, most currently lack scientific validation. There are literally hundreds of herbs, vitamins, hydrotherapies, and spinal manipulations that are thought to stimulate the immune response.

Astragalus membranaceus has been prescribed for centuries as a tonic to build stamina and promote immune function. Astragalus root is high in immune stimulating polysaccharides and has been shown to enhance phagocytic activity of monocytes and macrophages *in vitro*[91,92] as well as display antiviral and antibacterial activity in mice.[93,94]

Orally administered calf thymus extract is thought to provide broad-spectrum immune enhancement by improving thymus gland activity. Clinical trials have shown that thymus gland extracts shortened the course and reduced the number of respiratory infections per year in children with a history of recurrent URTI. In one study, 40 children ages 3-9 years who had suffered from recurrent respiratory infections during the previous winter were randomly divided in two groups. Twenty-one children were given calf thymus extract and 19 given placebo. The trial was carried out according to double-blind schedule from October through January. There was a statistically significant reduction in the number of catharral bouts, assessed by the family doctor, and improvements in overall wellness, evaluated by parents, only in the treated children.[95]

A similar study attempted to elucidate the mechanism of calf thymus extract in children with recurrent respiratory infections. Forty-six children suffering recurrent respiratory infections were enrolled on the basis of number of respiratory infections in the previous year. Twenty-three children were treated with calf thymus extract and 23 served as a control group. Interleukin-2 production was assayed in all children before and after the trial. A significant reduction in the frequency of respiratory infections was noted only in the treatment group, but no significant modification of interleukin-2 was observed in either group.[96] These studies confirm the effectiveness of treatment with calf thymus extract in children suffering from recurrent respiratory infections, but the mechanism of clinical improvement remains to be explained.

Vitamin C has antiviral, antibacterial, and immune modulating effects.[97,98] The role of vitamin C in common cold treatment and prevention has been studied extensively with conflicting results. Placebo-controlled trials have shown that vitamin C supplementation decreases the duration and severity of common cold infections. However, the magnitude of the benefit is substantially varied and may be more significant in children. A review of 23 studies of vitamin C for cold treatment found that, on average, vitamin C produces greater benefit for children than for adults. In five studies of adults administered 1 g vitamin C daily, the median decrease in cold duration was only six percent, whereas in two studies with children administered 2 g vitamin C daily the median decrease was 26 percent.[99] Although the author hypothesizes that age is the main factor effecting the magnitude of benefit of vitamin C, dose effect can not be ruled out from these studies.

Double-blind studies using identical twins as controls have also supported the use of vitamin C in the treatment of the common cold. A study using 95 pairs of identical twins with one twin taking vitamin C and the other a placebo resulted in a shortening of the average duration of

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symptoms by 19 percent.[100] A second study using 44 school-aged identical twins reported shorter and less severe illness in the younger children; the effect of vitamin C was less substantial for older children.[101]

It has been shown that the stress of infection reduces plasma ascorbic acid levels in children. During infection ascorbic acid is utilized rapidly, being transferred from the plasma to leukocytes in order to keep leukocyte ascorbic acid levels within normal limits during infection.[102] Subjects under acute physical stress have also benefited from vitamin C for the prevention of upper respiratory infections. Three small studies using subjects undergoing acute physical stress reported common cold incidence decreased by an average of 50 percent in these populations.[103] In one study the subjects were school children at a skiing camp in the Swiss Alps, in another they were military troops training in northern Canada, and in the third they were participants in a 90 km running race. In each of the three studies a considerable reduction in common cold incidence in the group supplemented with vitamin C (0.6-1.0 g/day) was found.

Many viral infections are spread chiefly by aerosol, rather than by fomites or personal contact.[104] The nasopharyngeal mucosal surfaces can protect against viral transmission. Vitamin A maintains the integrity of the epithelial and mucosal surfaces and their secretions, as well as stimulating mononuclear phagocytosis, lymphocyte blastogenesis, and antibody response.[105-108] Additionally, shea butter (from the seed of the African shea butter tree, *Butyrospermum parkii*) placed intranasally was found to be effective against nasal congestion in upper respiratory infections by soothing mucous membranes and reducing inflammation of the tissue.[109]

Researchers claim garlic has antibacterial activity comparable to that of standard antibiotics, based on *in vitro* pharmacological studies.[110] In addition to potential antibacterial action, *in vitro* studies have shown antiviral activity against influenza type A and B, cytomegalovirus, rhinovirus, viral pneumonia, and rotavirus.[110] A randomized, placebo-controlled clinical trial found allicin-containing garlic supplements can prevent viruses responsible for the common cold and expedite recovery from infection. In the study, 146 volunteers were randomized to receive either a garlic supplement or placebo for three months beginning in November. The treatment group had fewer colds than the placebo group (24 versus 65), shorter duration of symptoms (1.52 versus 5.01 days), and fewer days challenged virally (111 vs 366).[111] Garlic should be used raw or added to food just before it is removed from the heat to preserve potency. Cooked garlic has not been found to maintain its antimicrobial activity.[112] Garlic capsules standardized to allicin content may be an effective alternative to fresh garlic.[113]

Discussion

Indiscriminate antibiotic use has resulted in antibiotic resistance being one of the CDC's top concerns.[1] The practice of universal antimicrobial prescribing is being strongly discouraged, while scientific evidence is emerging to support the use of non-antibiotic therapies without compromising patient care. Physicians who prescribe antibiotics have the responsibility to preserve their efficacy by withholding them when not indicated. Emphasis on patient education regarding the proper indications for antimicrobials, prognosis of an infection, and alternative treatment recommendations may curtail parental expectations for antibiotics. Studies have shown clinician education contributes more to patient and parent satisfaction than receipt of an antimicrobial prescription.[114]

Consequences of inappropriate antibiotic prescribing include unnecessary risk of adverse reaction or allergic response, additional health care expense, and promotion of bacterial resistance. The use of subtherapeutic concentrations of antibiotics as growth promoters for farm animals, the widespread use of antimicrobial cleaning agents, and the use of antibiotics in veterinary practice all bear evaluation.[115] Distinguishing between viral and bacterial infections and becoming proficient in prescribing non-drug treatments such as hydrotherapy, homeopathy, botanical agents, vitamins, and minerals should contribute to a reduction in antibiotic prescribing.

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The art of medical practice has been eroded by the concept there is a pill for every ailment. In pediatric practice the emphasis on reducing universal antibiotic prescribing through more accurate diagnosis, control of environmental risk factors, and utilization of CAM therapies potentially could result in a paradigm shift. In the new paradigm, the art of practice may be restored with an emphasis on patient education, prevention, reduction of known risk factors, accurate diagnoses, and utilization of simple therapies thought to stimulate the immune system. This approach to common childhood infections may eliminate millions of antibiotic prescriptions, while improving overall patient care and satisfaction.

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