Middle Ear Infections, Antibiotics, and Asthma

By Dan Murphy, D.C., D.A.B.C.O.

On September 13, 2006, the *Journal of the American Medical Association* published a randomized controlled trial concerning the protocol for the treatment of acute otitis media, titled:

Wait-and-See Prescription for the Treatment of Acute Otitis Media[1]

Key points from this article include:

1. "Acute otitis media is the most common reason for which an antibiotic is prescribed to children," accounting for an "estimated 15 million antibiotic prescriptions written per year in the United States."
2. "Untreated acute otitis media has a high rate of spontaneous resolution, with similar rates of complications whether antibiotics are prescribed or withheld."
3. "Resistance to antibiotics is a major public health concern worldwide and is associated with the widespread use of antibiotics."
4. The typical length of antibiotic therapy prescribed for children with acute otitis media is a 10-day course, and Amoxicillin is prescribed 92% of the time.
5. Diarrhea is the most frequently reported side effect of taking antibiotics for acute otitis media.
6. Immediate treatment of acute otitis media with antibiotics increases the rates of diarrhea by 2- to 3- times compared to the wait and see approach to treating acute otitis media.
7. These authors showed that waiting to prescribe antibiotics for acute otitis media is a "successful treatment strategy."
8. This randomized controlled trial has shown that waiting to use antibiotics for acute otitis media "significantly reduces the use of antibiotics" without compromising clinical results.
9. Most pediatricians in the U S are trained to routinely prescribe antibiotics for acute otitis media and "believe that many parents expect a prescription."
10. Only a "small minority of practitioners who care for children routinely use watchful waiting" before prescribing an antibiotic for acute otitis media.
11. "The risks of antibiotics, including gastrointestinal symptoms, allergic reactions, and accelerated resistance to bacterial pathogens must be weighed against their benefits for an illness that, for the most part, is self-limited." **[Very Important]**
12. The routine use of waiting to prescribe antibiotics for acute otitis media "will reduce both the costs and adverse effects associated with antibiotic treatment and should reduce selective pressure for organisms resistant to commonly used antimicrobials." **[Very Important]**
13. The waiting to prescribe antibiotics approach "substantially reduced unnecessary use of antibiotics in children with acute otitis media."

The bottom line from this study is that since acute otitis media is usually a self-limiting illness, and because utilization of antibiotics is associated with significant risks (including antibiotic resistance and gastrointestinal symptoms), the best approach is to "wait-and-see" rather than to immediately prescribe antibiotics. Curiously, a significant known risk from the pediatric use of antibiotics that was not mentioned in this article is the risk of atopic disorders, including allergy and asthma.

The March 2006 issue of the journal *Chest* published a systemic review and metaanalysis concerning the use of antibiotics in infancy and the development of asthma, titled:

Original Research – Asthma

Does Antibiotic Exposure During Infancy Lead to Development of Asthma?[2]

Key points from this article include:

1. Increasing antibiotic use in children coincides with "an increase in physician visits for otitis media, and a high rate of inappropriate prescribing for viral upper respiratory infections and bronchitis."
2. "This increase in antibiotic use in children has been accompanied by an increase in the prevalence of asthma and has led to the hypothesis of a causal association."
3. Asthma is the most common chronic disease of children, affecting about 12.5% of western country children.
4. In industrial countries, asthma has increased significantly over the last 30 years and is a major public health concern.

5. The "Hygiene Hypothesis" suggests that "growing up in a more hygiene environment with less microbial exposure may increase atopic (T-helper type 2) immune responses and, thus, the development of asthma." **[Important]**
6. The increased asthma risk after antibiotic exposure in the first year of life is 105% increased risk with a range between 41%-199%.
7. The increased risk for the development of asthma after exposure to antibiotics in the first year of life in the four retrospective studies reviewed was 182% with a range between 107%-285%.
8. For each additional course of antibiotics in the first year of life, the risk of developing asthma increased 16% with a range between 5%-28%.
9. "The use of antibacterials in the first year of life is associated with subsequent development of asthma."
10. "Exposure to at least one course of antibiotics in the first year of life appears to be a risk factor for the development of childhood asthma."

Over the past decade numerous other studies support the conclusions published in this issue of *Chest*. One such review article was published January 2001 in the journal *Allergy*, and titled:

EAR INFECTIONS – MURPHY

The causes of the increasing prevalence of allergy: Is atopy a microbial deprivation disorder?[3]

Key points from this article include:

1. "The atopic diseases, i.e., primarily bronchial asthma, atopic dermatitis, and allergic rhinoconjunctivitis, were rare a few decades ago, but constitute today an increasingly severe public health problem."
2. "The increase in the prevalence of the allergic diseases, especially in those born after 1960, is almost explosive, and there are now epidemics of allergic diseases in many countries."
3. "The prevalence of asthma in children and young adults has tripled and quadrupled in many industrialized countries during the last two decades."
4. "If the assumption that early viral or bacterial infections protect against the development of allergic diseases is correct, vaccination should lead to an increase of allergic disorders." **[WOW!]**
5. Antibiotics act nonspecifically and have the ability to kill not only pathogenic but also commensal bacteria.
6. Studies show a significant relationship between treatment with antibiotics during the first 2 years of life and later development of allergy.
7. "Multiple courses of antibiotic treatment are associated with higher allergy prevalence, and treatment with broad-spectrum antibiotics appears to be more likely associated with allergy development than is ordinary penicillin."
8. "Microbial agents do indeed play a protective role in the development of allergic disease," and "it is tempting to assume that the protective effect may be primarily evoked by bacterial infections."
9. Atopic sensitization begins in utero, and the first few months of life are also crucial.
10. Once atopic sensitization occurs, it tends to be persistent.
11. "A change in the 'microbial load' seems to be the most probable cause of the increase in the allergic diseases."
12. "It thus seems likely that atopy is a 'microbial deprivation disorder' "

Importantly, this article notes that atopic sensitization begins in utero. In 2002, the *American Journal Of Respiratory and Critical Care Medicine* published a cohort study titled:

The Importance of Prenatal Exposures on the Development of Allergic Disease[4]

Using a birth cohort of 24,690 children, the authors investigated a number of perinatal exposures on the incidence of asthma, eczema, and hay fever. Their findings show that exposure to antibiotics *in utero* is associated with an increased risk of asthma in a dose-related manner. Other key points from this article include:

1. "The prevalence of allergic disease has increased dramatically in the developed world during the second half of the 20th century, and it has been suggested that this increase is in part due to reductions in early microbial exposure."
2. Approximately one third of mothers are prescribed antibiotics during pregnancy, and this exposure is associated with an increased incidence of allergic diseases, especially asthma.
3. "Our results suggest that exposure to antibiotics *in utero* is associated with a dose-related increase in the child's risk of allergic disease."
4. Exposure to antibiotics *in utero* is associated with an increased risk of asthma, eczema and hay fever, in a dose-related manner.
5. The prevalence of allergic disease has increased dramatically in the developed world during the last 50 years, paralleling antibiotic use and reductions in early life microbial exposure.
6. Because the immune system develops *in utero*, factors that modify microbial exposure at this time may have a long-term impact on the risk of developing allergic disease. One such factor is *in utero* exposure to antibiotics.

Sadly, a study published earlier this year[5] indicates that globally, "with each decade, the prevalence of asthma increases 50 percent," with more than 300 million people suffering with asthma. "The World Health Organization said 255,000 people died from asthma in 2005, and that deaths are projected to rise by almost 20 percent in the next 10 years."

These studies support a prospective that would encourage the banning of antibiotics, except for life-threatening bacterial infections.

References

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