

# Early Asthma Tied to Bacteria in Neonatal Airways

BY ROBERT FINN  
San Francisco Bureau

Infants whose airways are colonized by one or more of three bacterial species are significantly more likely to develop asthma by 5 years of age than are other children.

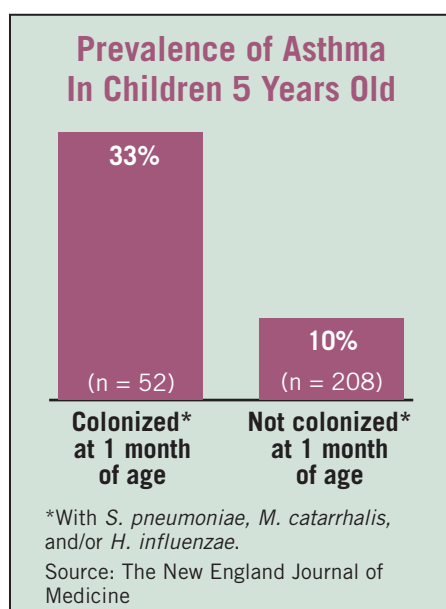
Dr. Hans Bisgaard and his colleagues from the Copenhagen University Hospital found colonization with *Streptococcus pneumoniae*, *Haemophilus influenzae*, and/or *Moraxella catarrhalis* in 1-month-old infants also was associated with significant increases in the risk of the later development of certain asthma precursors, including persistent wheeze (hazard ratio 2.01), acute severe exacerbation of wheeze (HR 3.14), and hospitalization for wheeze (HR 3.57). Colonization by *Staphylococcus aureus* at 1 month of age, on the other hand, was not associated with an increased risk of asthma or its precursors, nor was colonization with any of the organisms at 12 months of age (N. Engl. J. Med. 2007;357:1487-95).

It's unlikely that this association is causal, Dr. Erika von Mutius wrote in an accompanying editorial (N. Engl. J. Med.

2007;357:1545). Instead, early colonization with those three organisms may signal a defective innate immune response, and it is that defective immune response that promotes the development of asthma.

The investigators followed 321 infants as part of the Copenhagen Prospective Study on Asthma in Childhood (COPSAC). All infants were born to mothers with current or previous asthma. Physicians aspirated samples from the asymptomatic infants' hypopharyngeal region at 1 and 12 months of age, and these samples were cultured for the presence of the four bacterial species. At 1 month, 21% of the infants were found to be colonized with *S. pneumoniae*, *H. influenzae*, and/or *M. catarrhalis*, and 61% were colonized with *S. aureus*. At 12 months, 71% were colonized with the first three organisms and only 13% were colonized with *S. aureus*.

Children colonized at 1 month of age who were available for testing at 5 years had a 33% (17 of 52) prevalence of asthma at that age, compared with 10% (20 of 208) in those not colonized. Total IgE was increased by 47% in colonized children; there was no significant increase in specific IgE.



Investigators adjusted the results for a number of possible confounders.

While Dr. Bisgaard and his colleagues proposed that bacterial colonization may induce neutrophilic inflammation of the airways and thereby cause asthma, Dr. von Mutius, professor of pediatrics at Munich

University Children's Hospital and head of the outpatient clinic for asthma and allergy, disagreed. Colonization may indicate a defective clearance of those flora. The impaired innate immune response also might be expected to decrease a child's resistance to viruses, and studies have recognized that people with asthma are unable to limit viral infections to the upper respiratory tract.

It's possible, Dr. von Mutius wrote, that exposure to certain bacterial strains may contribute to the development of asthma by inducing inflammatory responses in a child's airway. But, if that were the case, treatment with antibiotics during the first weeks of life should protect children from developing asthma. While no clinical trial has examined this question, several population-based cohort studies have failed to find an association between early antibiotic therapies and the risk of asthma.

The study was supported by unrestricted educational grants from Pharmacia/Pfizer Inc. and AstraZeneca. Dr. Bisgaard has received lecture and advisory board fees from Aerocrine Inc., Altana Inc., AstraZeneca, GlaxoSmithKline, MedImmune Inc., Merck & Co., and Pfizer.

## Inner-City Preschoolers With Asthma Should Be Evaluated Every 3 Months

BY ELIZABETH MECHCATIE  
Senior Writer

A study of preschool-age, inner-city children with asthma found marked fluctuations in the degree of asthma control within 3 months, suggesting that frequent evaluations of asthma control in this population may be warranted, investigators reported.

"We know asthma is an unstable disease, but we underestimated just how unpredictably it could behave over time, especially in inner-city kids," the study's lead author, Dr. Hemant P. Sharma, noted in a statement issued by Johns Hopkins University, Baltimore, where he is a pediatric allergist.

The 6-month study of 150 predominantly black children aged 2-6 years (mean age 4.4 years) with asthma living in Baltimore evaluated their long-term controller medication use and their use of asthma-related health care at baseline, and at 3 and 6 months. At baseline, the children were classified into National Asthma Education and Prevention Program control categories for asthma: mild intermittent (37%), mild persistent (17%), moderate persistent (21%), and severe persistent (25%).

Only 39% of the children reported long-term use of con-

troller medication (inhaled corticosteroids, cromolyn and nedocromil, oral leukotriene modifiers, long-acting  $\beta$ -agonists, and oral theophylline), wrote Dr. Sharma and his associates.

At 3 months, asthma control had deteriorated in 46% of the children who had mild intermittent asthma at baseline and in 33% of those with mild persistent asthma at baseline. Changes in control also were seen at 3 months in more than half of the children with moderate persistent asthma at baseline and in about half of those with severe persistent asthma at baseline.

Among children with persistent symptoms at baseline, "even greater shifts were observed between baseline and 6 months," at which time a change in the degree of asthma control was seen in more than two-thirds of the children with persistent symptoms at baseline (Pediatrics 2007;120[5]:e1174-81).

These results "underscore the labile nature of asthma," and suggest that assessments of asthma control in young, inner-city children "should be repeated at least every 3 months to take advantage of opportunities to prevent future morbidity," Dr. Sharma and his associates said.

Poor control of asthma was an independent predictor of the children's use of asthma-related health care (unscheduled doctor

visits, emergency department visits, and hospitalizations) during the preceding 3 months, with a significant association between poor asthma control and recent use of asthma-related health care, "suggesting that asthma control is related to overall recent disease activity," they said. For example, 5% of those with mild intermittent asthma had an unscheduled doctor visit related to asthma within the previous 3 months, compared with 23% of those with moderate persistent asthma, and 42% of those with severe persistent asthma.

Their reported use of long-term controller medications, however, was not an independent predictor of their use of asthma-related health care.

The ability to accurately identify children who are at the greatest risk of morbidity in the future is a "key component" of successfully preventing asthma-related health care use and targeting high-risk children, but information about which clinical factors predict the risk of future asthma-related health care use among children is lacking, the authors wrote.

These findings have "direct implications to inner-city black children, who bear much of the asthma burden in the United States." The authors indicated they have no financial relationships to disclose.

## Elective C-Section Linked To Respiratory Morbidity

BY JONATHAN GARDNER  
Contributing Writer

Elective cesarian section increases by up to fourfold the risk of respiratory morbidity in babies delivered at 37-39 weeks of gestation, compared with babies delivered vaginally or by emergency C-section at the same gestational age.

That finding—from a Danish cohort study of 34,458 singleton deliveries—suggests that elective C-section should wait until after the 39th week, the study investigators wrote.

"Carrying out elective caesarean sections at greater gestational ages may, however, result in higher rates of intrapartum caesarean sections because some women would go into spontaneous labour (in our population, 25% of spontaneous intended vaginal deliveries started before 39 weeks' gestation)," wrote Anne Kirkeby Hansen of the Aarhus (Denmark) University Hospital and associates. "Compared with elective caesarean sections, intrapartum caesarean sections may carry an increased risk of complications such as uterine rupture in women with previous caesarean section, infections, or even maternal mortality."

The risk of respiratory morbidity (transitory tachypnea of the newborn, respiratory distress syndrome, persistent pulmonary hypertension of the newborn)

was increased in babies delivered by elective C-section at 37 weeks (odds ratio 3.9), 38 weeks (OR 3.0), and 39 weeks (OR 1.9), compared with newborns intended for vaginal delivery. Risk was not increased at 40 weeks (OR 0.9).

The data were adjusted for factors such as smoking and parity, the study authors wrote. (BMJ 2008;336:85-7).

The analysis included all live-born singletons born without malformation between 37 and 41 weeks' gestation at one institution between 1998 and 2006.

In all, 2,687 liveborn babies were delivered by elective C-section and 2,877 were delivered by emergency C-section. The remaining were born vaginally.

A total of 1.8% of all babies had a respiratory problem, with 0.2% of them having serious respiratory morbidity (a condition requiring treatment for at least 3 days with continuous oxygen supplementation, nasal continuous positive airway pressure, or any period of mechanical ventilation). The relative risk for serious respiratory morbidity was increased in those delivered by elective C-section at 37 weeks (OR 5.0) and 38 weeks (OR 4.2), compared with vaginal delivery. At 39 weeks, the odds ratio was 2.4, but this increase in risk was not significant.

The authors said hormones released during normal vaginal delivery may help prevent respiratory problems.