

## Bacteria in the respiratory tract and wheeze in children

Colonisation is more common in symptomatic children, but causation is not established



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In the linked cohort study Bisgaard and colleagues assess the association between wheezy symptoms in young children and the presence of bacteria in the airway.<sup>1</sup> Lower respiratory tract illnesses presenting with cough, shortness of breath, or wheeze are common in preschool years.<sup>2</sup> It has been proposed that, for the management of preschool wheeze, a distinction is made between episodic and multiple trigger wheeze.<sup>3</sup> Episodic wheeze is defined as wheeze in discrete episodes of up to two to four weeks' duration, usually triggered by a viral infection, and with the child being well in between. In multi-trigger wheeze, the child has distinct episodes of wheeze but also has intermittent symptoms, such as cough and wheeze at night or in response to exercise, crying, laughter, mist, and cold air, between these episodes. Viral infections are again the most common triggers, but multi-trigger wheeze is often associated with allergic features, and many children with preschool multi-trigger wheeze progress to chronic asthma. Current guidelines recommend the use of bronchodilators for wheezing episodes.<sup>3</sup> Children with multi-trigger wheeze may also benefit from

inhaled corticosteroids and leukotriene receptor agonists. Antibiotics have not been recommended for the treatment of preschool episodic wheeze or multi-trigger wheeze.

This approach is contested by Bisgaard and colleagues' study.<sup>1</sup> The authors included 361 infants born to asthmatic mothers who were followed until the age of 3 years. They confirmed a positive association between viruses and preschool wheeze (odds ratio 2.8, 95% confidence interval 1.7 to 4.4) and also found a significant association between bacteria and preschool wheeze (2.9, 1.9 to 4.3), which was independent of viral detection. For all episodes of lower respiratory tract illness the children were seen in the study centre and the condition was classified as wheeze or "clinical pneumonia," which was defined as tachypnoea, fever, and crepitations over the lungs without wheeze. In addition, children were scheduled to be seen once a year. At each visit hypopharyngeal aspirates were taken for bacterial culture and rhinopharyngeal aspirates were taken for polymerase chain reaction analysis of viruses and atypical bacteria.

Viruses were detected in 40% of asymptomatic children,

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in 65% of wheezy episodes, and in 70% of episodes with clinical pneumonia. Bacteria were detected in 62% of asymptomatic children, 86% of wheezy children, and 93% of children with clinical pneumonia. Most commonly *Streptococcus pneumoniae* was identified, followed by *Haemophilus influenzae* and *Moraxella catarrhalis*. Atypical bacteria were detected in fewer than 2% of the children. Thus in both conditions—wheezing and non-wheezing lower respiratory tract illnesses—viruses and bacteria were detected significantly more in affected children than in asymptomatic children. The positive association with the detection of bacteria remained significant after adjusting for the detection of viruses. The authors suggest that this might have important effects on the treatment of preschool wheeze if the role of bacteria can be confirmed.

The high bacterial detection rate reported in asymptomatic children in this study casts some doubt over a causative role for bacteria. The findings confirm a previous study investigating bacterial colonisation of newborns by conventional culture methods.<sup>4</sup> All nose and throat smears from 3 day old babies produced positive cultures. Another study using culture independent molecular methods for the detection of bacteria has shown that the lower respiratory tract—which was thought to be sterile—is highly colonised by bacteria. Bronchoscopy was performed on 24 adults and 20 children and found that every cm<sup>2</sup> contained a mean of 2000 bacterial genomes, including *H influenzae* and *S pneumoniae*.<sup>5</sup> Thus, positive bacterial cultures may merely reflect colonisation of the upper and lower respiratory tract rather than indicating that bacteria are the cause of the infection. Viral infections may indirectly facilitate bacterial growth, thereby increasing detection rates in acute episodes.

Ultimately, only controlled clinical trials with antibiotic treatment can resolve this debate, as the authors rightly acknowledge. Besides the studies discussed by Bisgaard and colleagues,<sup>6, 7</sup> the findings of two other randomised controlled trials might be more informative. These trials investigated the effect of adding an aminopenicillin to standard care of acute exacerbations of asthma in chil-

dren<sup>8</sup> and adults,<sup>9</sup> and they found that antibiotics had no benefit. These findings are particularly interesting because aminopenicillins are generally effective against *H influenzae* and *S pneumoniae*—the most commonly detected bacteria in this study. However, these trials are limited by the small number of people included (44 and 71). Unless well designed and high powered clinical trials unambiguously show a benefit of antibiotic treatment there is no need to revise the management guidelines for preschool wheeze.

The findings are nonetheless interesting because they emphasise the need for a better understanding of the role of bacteria in the development of asthma and acute exacerbations of the disease. The advent of culture independent molecular methods that can detect much higher numbers of known and unknown bacteria will allow a better understanding of the role of bacteria in the colonisation of mucosal surfaces in the airways, their interaction with local host immune responses, and eventually their contribution to disease onset and progression.

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