

Editorials

Rethinking doctrine: Bronchitis, eosinophils, and bronchoscopy in pediatric asthma

The article by Just and coworkers¹ in this issue of the Journal challenges 3 doctrines regarding pediatric asthma management that are strongly held, particularly in the United States. These are that (1) bacterial bronchitis is not a clinically significant entity in pediatric asthma, (2) asthma in pediatrics is exclusively an eosinophilic/allergic disease, and (3) there is not a role for bronchoscopy in the evaluation of pediatric asthma. The article does not overturn these doctrines. However, in the context of other recent publications, it suggests the possibility that they need to be reevaluated.

The authors followed 6513 children who had been admitted to the hospital for asthma. Children less than 30 months of age were required to meet the criteria of Tabachnick and Levison² and to have had parameters identified by Martinez³ as being associated with the development of asthma, in retrospective analysis, by the age of 4 years; in older children the diagnosis of asthma required recurrent wheezing and dyspnea with β -2 reversible flow limitation. Of these admitted children, 88 underwent flexible bronchoscopy for the indications of (1) persistent episodes of wheezing resistant to conventional treatment, (2) wheezing associated with daily cough and expectoration, and/or (3) persistent radiographic parenchymal abnormality (in the absence of fever). Surprisingly, 10% of these children who met the criteria for asthma also had abnormalities not identified by routine testing (such as airway malacia, vascular ring, and viral pneumonitis) that one might expect to see in nonasthmatic, refractory wheezing.⁴ The bronchoalveolar lavage (BAL) results of these children were excluded from subsequent analysis of cellular composition.

Consistent with what was found in previous studies,^{5,6} a predominance of neutrophils in the BAL was observed in children with persistent—as opposed to episodic—wheezing; indeed, the number of neutrophils was proportional to the duration of symptoms. However, the presence of neutrophils was not associated with lower airway bacterial infection. Also consistent with previous reports in

Abbreviation used

BAL: Bronchoalveolar lavage

adults, the presence of high numbers of eosinophils in the BAL fluid was associated with the presence of allergy⁷ but did not predict the presence of persistent symptoms and was not associated with duration of symptoms. Indeed, taken together with the lack of effect of anti-IL5 antibody in adult asthma⁸ and with evidence that airway eosinophilia is not always associated with asthma,⁹ the data of Just et al suggest that allergy-associated airway eosinophilia might not always be of central importance to the pathophysiology or definition of pediatric asthma.

Remarkably, approximately 15% of the children undergoing flexible bronchoscopy who did not have anatomic lesions or viral infections had convincing evidence for bacterial bronchitis: a culture of $>10^5$ colony-forming units per milliliter of one organism—often β -lactamase-positive—in the presence of $>10^4$ neutrophils per milliliter. Unfortunately, none of the variables studied (such as age, allergy status, and symptom duration) predicted which children would have positive cultures. This information might make many of us in the pediatric community reconsider our convictions regarding bacterial “bronchitis”—from general practitioners, who might be inclined to treat cough and wheeze in children empirically with amoxicillin, to academic pediatricians, who assert that bacterial bronchitis is never a cause of cough and wheeze in children in the absence of cystic fibrosis, immotile cilia syndrome, or immunodeficiency.

Fewer than 2% of the children in this population underwent bronchoscopy, and the data of Just et al raise the possibility that pathology might have been missed in the other 98%. Thus it is fair to say that *at least* 3 to 4 of every 1000 children admitted to the hospital for relatively stringently defined asthma also had either an airway abnormality or a bacterial lower airways infection. As previously reported,⁴ flexible bronchoscopy, performed in a carefully controlled setting by an experienced physician, was remarkably safe and well tolerated by these children with asthma, though 12% experienced a transient increase in wheezing. Therefore, it might be that a subset of asthmatic children—those meeting the criteria outlined by Just et al—should be considered more liberally for flexible bronchoscopy.

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Received for publication March 22, 2002; accepted for publication March 25, 2002.

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0091-6749/2002 \$35.00 + 0 1/39/125002

doi:10.1067/mai.2002.125002

Perhaps fortunately, doctrine changes slowly. For now, it will continue to be taught that bacterial bronchitis is not relevant to pediatric asthma, that infiltration of the allergic airway with eosinophils is central to the definition of the pathophysiology of asthma, and that there is little role for bronchoscopy in pediatric asthma. Indeed, there are several issues regarding the design of the study by Just et al that can be criticized. Here are some examples: (1) the study was done, in part, retrospectively; (2) defining pediatric asthma is difficult, particularly when younger and older children are grouped together^{10,11}; and (3) previously published pediatric BAL reference values were used in place of matched control studies on healthy children.

On the other hand, the results do suggest that (1) a carefully designed, prospective study of the lower airways in a subset of pediatric patients with asthma might be important and (2) we might need to have a lower clinical threshold for thorough pulmonary evaluation—including bronchoscopy in some cases—in certain children who carry the diagnosis of asthma. At the very least, it underscores that state-of-the-art subspecialty care for pediatric asthma needs to be carried out in a multidisciplinary setting, with close collaboration between pediatric allergists and pulmonologists.

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Correction

In the article entitled "T-cell activation through the antigen receptor. Part 1: Signaling components, signaling pathways, and signal integration at the T-cell antigen receptor synapse," in the May 2002 issue of *The JACI* (Nel. 2002;109:758-70), the citing of some of the illustrations was incorrect. The citations should have read as follows:

On page 759:

- Column 1, paragraph 2, line 15: See Fig 1, *B*
- Column 2, line 6: See Fig 1, *B*
- Column 2, paragraph 1, line 3: See Fig 1, *B*
- Column 2, paragraph 2, line 10: See Fig 1, *B*
- Column 2, paragraph 3, line 5: See Fig 5

On page 762:

- Column 2, paragraph 1, line 4: See Fig 4, *A*
- Column 2, paragraph 1, line 6: See Fig 7

On page 763:

- Column 1, line 5: See Fig 7
- Column 1, line 10: See Fig 7
- Column 1, line 13: See Fig 7
- Column 1, line 16: See Fig 7
- Column 1, line 18: See Fig 7
- Column 2, paragraph 1, line 11: See Fig 8

On page 764:

- Column 1, line 2: See Fig 7
- Column 1, paragraph 1, line 6: See Fig 6
- Column 1, paragraph 1, line 13: See Fig 7
- Column 1, paragraph 2, line 2: See Fig 6
- Column 1, paragraph 2, line 7: See Fig 6
- Column 1, paragraph 2, line 9: See Fig 7
- Column 2, paragraph 1, line 14: See Fig 7

On page 766:

- Column 2, line 1: See Fig 5

On page 768:

- Column 1, paragraph 2, line 22: See Fig 8
- Column 2, line 7: See Figs 3 and 8
- Column 2, paragraph 2, line 15: See Fig 7