

NEWS & VIEWS

Algorithms in Allergy and Clinical Immunology

Medical algorithm: Diagnosis and treatment of preschool asthma

Preschool children frequently present with respiratory symptoms. Parents use wheeze to describe many different noises, and it is important to determine what is actually being heard; indeed, until a physician has heard wheeze, diagnostic caution is wise. A thorough history and physical examination should focus on whether the child has normal airways, but recurrent viral colds; whether an airway or other disease is present; and the nature of any airway disease (Box 1). Assessment of atopy will guide the likelihood of symptoms persisting.

No therapies, including early use of inhaled corticosteroids (ICS), prevent susceptible children progressing from early preschool wheeze to eosinophilic atopic asthma. Treatment is based on current symptoms rather than trying to modify future prognosis. Secondly, nonpharmacological interventions, such as encouraging smoking cessation and minimizing other adverse environmental exposures, are essential.

If the child has an airway disease, the next parental question is almost inevitably, is it asthma, Dr? The *Lancet* Commission has defined asthma as a clinical syndrome characterized by wheeze, breathlessness, chest tightness and sometimes excess cough. It is an umbrella term, and the next question is, what sort of asthma does the patient have? Specifically, in preschool children, two treatable traits should be considered:

1. Does the child have bronchodilator responsive variable airflow obstruction?
2. Does the child have eosinophilic airway inflammation which is therefore likely to respond to ICS?

The difficulty of making measurements in routine clinical practice makes objective determination of treatable traits challenging. Lung function measurements are usually impractical, with the exception of impulse oscillometry. Response to acute use of bronchodilators can be assessed by auscultation and oxygen saturation measurements. If available, measurement of exhaled nitric oxide should be considered. We know that some but not all preschool children have ICS-responsive eosinophilic airway inflammation. Different groups have argued that ICS should be reserved for children who have symptoms between viral colds, or really severe attacks. However, a

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Box 1 Categorizing the preschool child with respiratory symptoms

1. Normal child (the hardest diagnosis of all), often complicated by parental anxiety
2. Important underlying diagnosis (there is a wide differential diagnosis, eg foreign body, tuberculosis)—rare but essential to get right
3. Minor conditions such as gastro-oesophageal reflux, rhinitis which may exacerbate or mimic lower airway symptoms
4. A preschool wheeze/asthma syndrome

recent study suggested that ICS should be reserved for preschoolers with a peripheral blood eosinophil count $\geq 300/\mu\text{L}$ and aeroallergen sensitization. This needs to be confirmed prospectively, but in the absence of either of these findings, we are reluctant to prescribe maintenance ICS, preferring to use intermittent short-acting β -2 agonists and sometimes ipratropium bromide in younger children, as needed.

If a trial of ICS to prevent symptoms is thought to be indicated, based on atopy, peripheral blood eosinophilia, or because symptoms are so severe in the absence of these findings. A three-step protocol is mandatory to avoid inappropriate use and over-diagnosing transient symptoms as eosinophilic atopic asthma:

- Step 1: trial ICS via a suitable spacer, beclomethasone equivalent 200 μg twice daily for 6 weeks and review.
- Step 2: stop ICS; if there has been no benefit consider poor adherence or an alternative diagnosis; if symptoms have abated, wait and see if they return on stopping ICS.
- Step 3: if symptoms recur, restart ICS and titrate to the lowest effective dose.

Leukotriene receptor antagonists are ineffective in most preschool children, and there is a worryingly high prevalence of neuropsychiatric side-effects.

Studies using oral macrolides for acute wheeze attacks have been conflicting, and because of potential bacterial macrolide

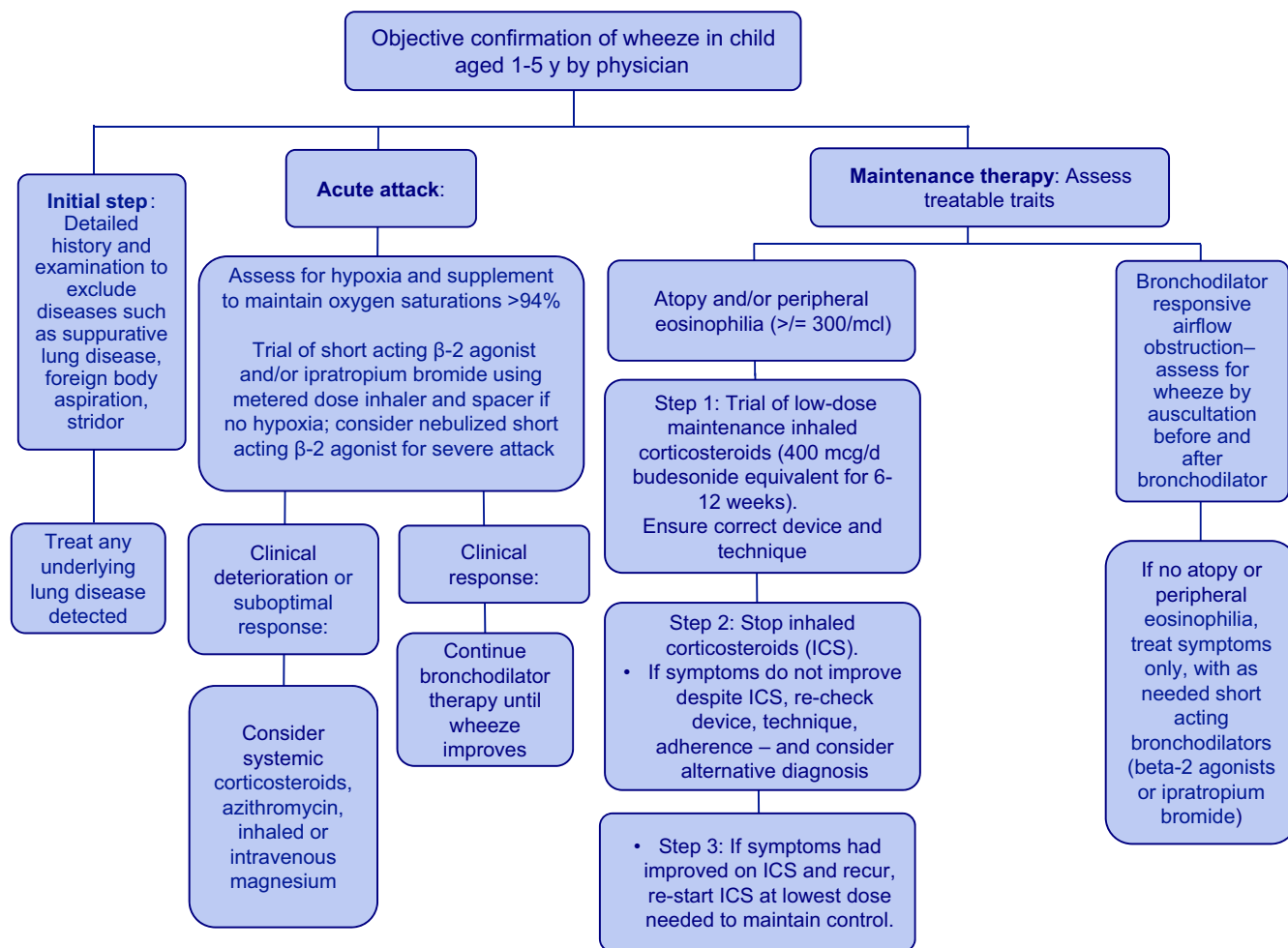


FIGURE 1 Management algorithm for the preschool child presenting with wheezing/asthma

resistance, macrolides should only be used, if at all, intermittently in preschool children with really severe recurrent attacks of wheeze. There is clear evidence that oral prednisolone should only be given to preschool children hospitalized for severe wheeze, and not even for all children admitted to hospital.

Rational management of the preschool child with respiratory symptoms can be achieved by following a logical, stepwise process (Figure 1). However, because of lack of evidence, parts of this algorithm represent personal practice and thus may be controversial.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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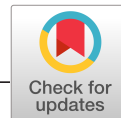
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WILEY

Reply to: Medical algorithm: Diagnosis and treatment of preschool asthma

In their recent educative "Medical Algorithm: Diagnosis and Treatment of Pre-school Asthma" News & Views article, Bush and Saglani propose a clinically useful medical algorithm for the diagnosis and treatment of preschool asthma.¹ The article is welcomed since currently this area, especially related to young wheezing children, is not well covered in guidelines. Asthma guidelines focus on the initiation of regular asthma control medication whereas guidelines on wheezing infants usually focus on the "common" bronchiolitis. Neither of these fit ideally on wheezing preschoolers.

We would like to raise a few topics in support and extension of the treatment algorithm by Bush and Saglani. First, an EAACI Task Force on Clinical Practice Recommendations on Preschool Wheeze has been established, with a mandate to provide more precise diagnostics and more personalized treatment approaches on wheezing illnesses from the first episode onwards (ie, according to virus etiology and other risk factors). According to the survey of the Task Force among caregivers, there is a clear clinical need to improve these aspects.²

Second, the reason, that has limited the progression of the guidelines on wheezing illnesses, is that in most of the children it resolves spontaneously not developing into asthma. Asthma development cannot be predicted to a satisfactory extent and effective prevention cannot be prescribed. As pointed out in the algorithm by Bush and Saglani, recognition of wheezing and atopic characteristics (sensitization or increased blood eosinophil count) or severe episodes suggest response for inhaled corticosteroid treatment. We would like to point out that common use of blood eosinophilia although clinically useful has not been ultimately validated and that aeroallergen sensitization develops gradually during early childhood so additional risk markers are needed. Evidence is accumulating that rhinovirus etiology (a common cold virus detected by a single PCR test) of severe wheezing serves as an effective risk marker for school-age asthma already at the time of the first episodes (odds ratios range between 3 and 10) and has high synergy with atopic characteristics further improving its risk value (with aeroallergen sensitization in atopic families odds ratios reach 40) (for review see³).

Third, there is evidence from at least two trials that young children suffering from severe, first rhinovirus-induced wheezing episode may benefit from traditional asthma medication, including systemic corticosteroid and beta₂-agonists.^{4,5} The efficacy was demonstrated as a shorter duration of hospitalization, shorter duration of cough

after discharge and fewer recurrences. Importantly, clear synergy in efficacy between salbutamol and prednisolone was observed. These findings challenge current bronchiolitis guidelines, all of which do not recommend routine use of beta₂-agonist nor systemic corticosteroid.

Fourth, asthma is considered an incurable disease without any primary or secondary prevention strategies. However, early treatment of rhinovirus-induced severe wheezing episode with systemic corticosteroid has been shown to reduce subsequent asthma inception within the next 6-7 years by 30% (shown in secondary outcomes and in post hoc analyses).^{5,6} Altogether, these findings show that children with early asthma-like inflammation in the airways are more susceptible to rhinovirus infections, which may serve as a good clinical marker. What is more, data support the use of short course of systemic corticosteroid and at least a therapeutic trial with short-acting beta₂-agonists in selected cases of bronchiolitis, in particular those with the rhinovirus-induced severe wheezing episode.

Bronchiolitis and early wheezing episodes are heterogeneous conditions, and we believe as Bush and Saglani suggest their treatment should be administered on a more personalized base than is currently recommended. Here, we emphasize the role of early virological diagnostics (ie rhinovirus etiology of severe wheezing), as a novel, more personalized, identification of those preschoolers who develop asthma and who may benefit from early therapeutic intervention.

CONFLICT OF INTEREST

Dr Papadopoulos reports personal fees from Novartis, Nutricia, HAL, MENARINI/FAES FARMA, SANOFI, MYLAN/MEDA, BIOMAY, AstraZeneca, GSK, MSD, ASIT BIOTECH, Boehringer Ingelheim, grants from Gerolymatos International SA, Capricare, outside the submitted work.

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Recommendations on Preschool Wheeze

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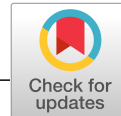
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WILEY

Preschool wheeze: Challenges and research prospects reply to: Dr Jartti and Colleagues; in response to our manuscript entitled: Medical algorithm: Diagnosis and treatment of preschool asthma

To The Editor,

We thank Dr Jartti and colleagues¹ for their interest in our manuscript.² We agree that the INFANT study³ conclusions on blood eosinophil count were *post hoc* and require prospective validation. We also agree that rhinovirus (RV)-triggered attacks have a high predictive value for school-age asthma.⁴ Whether such patients benefit from conventional asthma medication, including prednisolone, is still controversial; no acute benefit of prednisolone is seen in preschool wheeze,⁵ and early use of inhaled steroids in preschool wheeze does not prevent progression to asthma. Admittedly, most studies do not discriminate by viral infection, but given that RV infection is so common, it is surprising that no signal has been seen in big studies if any of these medications were beneficial. Nonetheless, a large prospective randomized trial of management after first acute RV wheeze episode is certainly indicated. However, viral diagnostics for every child with preschool wheeze would prove expensive in the clinical setting, making it important to consider the relevance and clinical application of tests to detect specific viral organisms during attacks. We certainly agree that there is a need to prevent asthma developing, and indeed that is a major focus of our research,⁶ but we were tasked to write mainly about acute management of preschool wheeze, with a limited word count.

KEYWORDS

asthma, eosinophils, epidemiology

CONFLICT OF INTEREST

Dr Saglani has nothing to disclose. Dr Bush has nothing to disclose.

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