



Management of bronchiolitis and recurrent wheezing in preschoolers

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Wheezing is very common during the preschool years, with nearly 50% of children having at least one episode of wheezing. Preschool wheezing should be considered an umbrella term for distinctive diseases or phenotypes. Despite many efforts, there is a large gap in knowledge regarding preschool wheezing. This paper aims to review the main clinical definitions and updated clinical recommendations for wheezing in preschoolers.

The diagnosis of bronchiolitis is clinical, and the physician should recognize signs and symptoms of respiratory infection and wheezing in young infants. Peak incidence occurs between 3 and 6 months of age. In recent guidelines,⁽¹⁾ the definition includes only young infants. Although the same physiology can occur in toddlers (> 12 months), many clinical trials have excluded these children.⁽¹⁾ Acute bronchiolitis management is largely supportive, focusing on maintaining oxygenation. Supplementation should be recommended if their oxygen saturation is persistently lower than 92%.⁽²⁾ Upper airway suctioning is not routinely recommended. Evidence suggests no benefits from bronchodilator or steroid use in young infants with a first episode of wheezing. Evidence for hypertonic saline is limited and not clearly defined. For infants with severe disease, the available data suggest an important role for high-flow nasal oxygen and noninvasive positive airway pressure ventilation to prevent respiratory failure.⁽¹⁾

Respiratory syncytial virus (RSV) is a leading cause of respiratory disease in infants, especially in prematurely born infants. The use of RSV passive immunization targeting protection during the first 12 months of life may substantially reduce RSV burden. The WHO encouraged the use of preventive interventions for RSV.⁽³⁾ Palivizumab is currently the most widely used prophylaxis for preventing RSV disease in infants. New monoclonal antibodies, such as nirsevimab, as well as maternal immunization, have been developed, which may protect infants during an entire RSV season with a single dose.⁽³⁾

RECURRENT WHEEZING OR REACTIVE AIRWAYS

Viral respiratory infections have been identified as the most frequent trigger of recurrent wheezing episodes in infants and toddlers, typically rhinovirus and RSV infections. Recurrent wheezing associated with infections can subsequently progress to asthma. The variable expression of early-life wheezing phenotypes may hinder the assessment and understanding of these diagnoses.

Recognizing different phenotypic characteristics may help to manage recurrent wheezing in a preschool child (Figure 1). Considering the established efficacy of inhaled corticosteroids (ICs) in the management of asthma, multiple trials have studied the role of ICs in preschool children with recurrent viral wheezing. The use of IC was associated with more episode-free days, fewer exacerbations, and less frequent use of other medications.⁽⁴⁾

Several trials have also examined the role of the azithromycin for the treatment of wheezing episodes. The role of azithromycin in young children with recurrent wheezing remains uncertain, with the greatest evidence for its role leaning toward the prevention of subsequent episodes.⁽⁵⁾ Results of clinical trials⁽¹⁾ showed that prevention is recognized as an important intervention to reduce disease burden, and the use of immunomodulation to improve protection is also gaining importance. In this respect, OM-85 is recognized as the most studied immunomodulatory agent currently available, whose efficacy makes it a valuable tool.⁽⁶⁾ In particular, the combined use of OM-85 and vaccination was recognized as an effective approach to improve prevention strategies in order to reduce the burden of recurrent respiratory infections associated with wheezing episodes.⁽⁶⁾

CHILDHOOD ASTHMA AND OTHER POSSIBLE ETIOLOGIES

Asthma is the most common chronic respiratory condition in childhood worldwide, and children with the disease typically present with wheezing, shortness of breath, and cough. Asthma is triggered by a variety of factors, such as respiratory infections.⁽⁷⁾ Asthma diagnosis in young children can be based on symptoms, presence of risk factors, or therapeutic response to treatment. In young children with a history of wheezing, a diagnosis of asthma is more likely if they present with wheezing or coughing that occurs with exercise or in the absence of respiratory infection; a history of other allergic diseases (eczema, food allergy, or allergic rhinitis); atopy or asthma in first-degree relatives; and clinical improvement within 2 months of IC treatment.⁽⁴⁾ Wheezing episodes in young children with risk factors for asthma should be managed with inhaled short-acting β_2 agonists for relief of symptoms. To control asthma in young children, the use of regular daily low-dose ICs is suggested as the initial treatment.⁽⁴⁾ Wheezing in preschool children can also be associated with other complex diseases, such as lung bronchiectasis, airway abnormality, and chronic infections. Patients with

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AGE	0-12 MONTHS	6-36 MONTHS	2-5 YEARS
MAIN ETIOLOGIC FACTORS	RSV, MATERNAL TOBACCO, PREMATURITY	RESPIRATORY VIRAL INFECTIONS, KINDERGARTEN	ATOPY, HYPERREACTIVITY
			
POSSIBLE PREVENTIVE INTERVENTIONS	RSV MONOCLONAL ANTIBODIES	IMMUNOSTIMULANTS (OM-85), INHALED STEROIDS	INHALED STEROIDS, LEUKOTRIENE ANTAGONISTS
MANAGEMENT OPTIONS	RESPIRATORY SUPPORT, SUPPLEMENTAL OXYGEN	SABA, MACROLIDES ARE CONTROVERSIAL	SABA, ORAL STEROIDS

Figure 1. Common forms of wheezing in preschool children according to age and etiological agent, followed by intervention and treatment recommendations. RSV: respiratory syncytial virus; and SABA: short-acting β_2 agonists.

severe or persistent symptoms should undergo ancillary tests. Chest imaging (low-dose CT) and sweat testing may be important steps in differential diagnosis. In conclusion, wheezing in preschoolers requires careful attention and constant monitoring to ensure respiratory well-being and healthy development.

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AUTHOR CONTRIBUTIONS

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CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Florin TA, Plint AC, Zorc JJ. Viral bronchiolitis. *Lancet*. 2017;389(10065):211-224. [https://doi.org/10.1016/S0140-6736\(16\)30951-5](https://doi.org/10.1016/S0140-6736(16)30951-5)
2. National Institute for Health and Care Excellence (NICE) [Homepage on the Internet]. London: NICE; c2023 [updated 2021 Aug 9; cited 2023 Sep 1]. Bronchiolitis in children: diagnosis and management. Available from: <https://www.nice.org.uk/guidance/ng9>
3. Sun M, Lai H, Na F, Li S, Qiu X, Tian J, et al. Monoclonal Antibody for the Prevention of Respiratory Syncytial Virus in Infants and Children: A Systematic Review and Network Meta-analysis. *JAMA Netw Open*. 2023;6(2):e230023. <https://doi.org/10.1001/jamanetworkopen.2023.0023>
4. Global Initiative for Asthma [homepage on the internet]. Bethesda: Global Initiative for Asthma; c2023 [cited 2023 Jun 1]. Global Strategy for Asthma Management and Prevention (2023 update). Available from: <http://www.ginasthma.org>
5. Bacharier LB, Guilbert TW, Mauger DT, Boehmer S, Beigelman A, Fitzpatrick AM, et al. Early Administration of Azithromycin and Prevention of Severe Lower Respiratory Tract Illnesses in Preschool Children With a History of Such Illnesses: A Randomized Clinical Trial [published correction appears in *JAMA*. 2016 Jan 12;315(2):204] [published correction appears in *JAMA*. 2016 Jan 26;315(4):419]. *JAMA*. 2015;314(19):2034-2044. <https://doi.org/10.1001/jama.2015.13896>
6. Esposito S, Cassano M, Cutrera R, Menzella F, Varricchio A, Uberti M. Expert consensus on the role of OM-85 in the management of recurrent respiratory infections: A Delphi study. *Hum Vaccin Immunother*. 2022;18(6):2106720. <https://doi.org/10.1080/21645515.2022.2106720>
7. Martin J, Townshend J, Brodie M. Diagnosis and management of asthma in children. *BMJ Paediatr Open*. 2022;6(1):e001277. <https://doi.org/10.1136/bmjpo-2021-001277>