

ATS CLINICAL PRACTICE GUIDELINE: SUMMARY FOR CLINICIANS



Series Editors: Carey C. Thomson and Kevin C. Wilson

Severe Asthma

Carey C. Thomson¹, Carolyn H. Welsh², Margaret A. Carno³, Sally E. Wenzel⁴, Fan Chung⁵, Jan L. Brozek⁶, and Kevin C. Wilson⁷; for the ATS/ERS Task Force on Severe Asthma and the American Thoracic Society Implementation Task Force

¹Mt. Auburn Hospital, Harvard Medical School, Boston, Massachusetts; ²University of Colorado, Denver, Colorado; ³University of Rochester Medical Center, Rochester, New York; ⁴University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; ⁵Imperial College, London, United Kingdom; ⁶McMaster University, Hamilton, Ontario, Canada; and ⁷Boston University School of Medicine, Boston, Massachusetts

International ERS/ATS guidelines on definition, evaluation, and treatment of severe asthma. Eur Respir J 2014;43:343–373.

The initial definitions of severe/refractory asthma were published in the *European Respiratory Journal* and the *American Journal of Respiratory and Critical Care Medicine* in 1999 and 2000, respectively (1, 2). Recognizing that substantial new knowledge has accumulated since those publications, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) formed a joint task force that was instructed to: (1) update the definition of severe asthma, (2) identify potential phenotypes of severe asthma, (3) outline the evaluation of severe asthma, and (4) provide evidence-based recommendations on treatment in both adults and children. The collaboration resulted in publication of the *International ERS/ATS Guidelines on the Definition, Evaluation, and Treatment of Severe Asthma* in 2014 (<http://www.thoracic.org/statements/resources/allergy-asthma/severe-asthma-full.pdf>) (3). This summary is prepared for practicing clinicians.

Definition

Severe asthma refers to asthma that: (1) requires treatment with high-dose inhaled corticosteroids (ICS) plus a second controller during the full previous year and/or systemic corticosteroids (CS) during 50% or more of the previous year to prevent symptoms from becoming “uncontrolled,” or (2) remains “uncontrolled” despite this therapy.

Evaluation

The diagnosis of asthma should be confirmed. This may be facilitated by referral for evaluation and management by an asthma specialist for more than 3 months, because misdiagnosis of uncontrolled asthma is as high as 30%. As an example, respiratory symptoms related to obesity are commonly mistaken for asthma. In children, referral to a specialized center results in up to one-half of patients previously classified as having severe asthma being reclassified as having difficult-to-control asthma.

History

Evaluation begins with a careful history emphasizing asthma symptoms, their relationship to exercise, and potential triggers. Conditions that either masquerade as or contribute to severe asthma are also sought. Examples include rhinosinusitis, nasal polyps, psychological factors, vocal cord dysfunction, obesity, smoking, gastroesophageal reflux, medications, and allergies.

Physical Examination

The physical examination should include a complete cardiopulmonary examination, looking for evidence of an alternative diagnosis (e.g., focal wheezing, stridor, crackles); a nasal/sinus evaluation, looking for stigmata of nasal obstruction, nasal polyposis, sinusitis, and allergic rhinitis; an examination of the neck, looking for masses and tracheal deviation; and a skin examination looking for evidence of atopic dermatitis, sarcoidosis, and vasculitis.

Laboratory Confirmation

Spirometry that evaluates both the inspiratory and expiratory loop of the flow–volume curve before and after administration of a bronchodilator is performed in most patients to try to confirm reversible airflow obstruction. Appropriate withholding of medication is necessary to optimally assess reversibility. Spirometry is often normal in children with severe asthma, including the FEV₁ both before and after administration of a bronchodilator; however, the forced expiratory flow in the midexpiratory phase (FEF_{25–75%}) may increase in response to the administration of a bronchodilator in such patients. Lung volumes and the transfer factor for carbon monoxide (DL_{CO}) are measured on a case-by-case basis. Similarly, bronchoprovocation testing (i.e., methacholine challenge or exercise) is performed on a case-by-case basis.

Sputum eosinophil counts (performed in centers experienced in this technique) plus clinical criteria is suggested to guide treatment in adults with severe asthma, rather than clinical criteria alone (conditional recommendation, very low quality evidence). In contrast, it is suggested

A Maintenance of Certification exercise linked to this summary is available at <http://www.thoracic.org/go/severe-asthma-module>.

CME will be available for this article at www.atsjournals.org

Ann Am Thorac Soc Vol 11, No 6, pp 996–997, Jul 2014

Copyright © 2014 by the American Thoracic Society

DOI: 10.1513/AnnalsATS.201405-199CME

Internet address: www.atsjournals.org

that treatment be guided by clinical criteria alone in children with severe asthma, rather than clinical criteria plus sputum eosinophil counts (conditional recommendation, very low quality evidence).

Exhaled nitric oxide testing: it is suggested that clinicians NOT use exhaled nitric oxide testing to guide therapy in adults or children with severe asthma (conditional recommendation, very low quality evidence).

Imaging

High-resolution computed tomography (HRCT) of the chest is suggested in children and adults with severe asthma whose presentation is atypical and who do not have other indications for HRCT based upon history, symptoms, and/or the results of prior investigations (conditional recommendation, very low quality evidence). Examples of atypical presentations include excessive mucus production, rapid decline in lung function, reduced DL_{CO}, and, in children, the absence of atopy.

Assessment of Control

Severe asthma is considered *controlled* if it worsens during the tapering of high doses of ICS, systemic CS, or additional biologics. In contrast, it is considered *uncontrolled* if any one of the following four criteria exists:

- Poor symptom control
 - Asthma Control Questionnaire consistently greater than 1.5, or
 - Asthma Control Test less than 20, or
 - “Not well controlled” as defined by the National Asthma Education and Prevention Program or Global Initiative for Asthma guidelines over 3 months of evaluation;
- Frequent severe exacerbations, defined as needing two or more bursts of systemic CS (>3 d each) during the past year;
- Serious exacerbations, defined as needing one or more hospital or ICU stays, or mechanical ventilation during the past year;
- Airflow limitation, defined as an FEV₁ less than 80% predicted (in the presence of reduced FEV₁/FVC) measured while withholding both short- and long-acting bronchodilators.

Treatment

Anti-IGE Antibody (Omalizumab) Therapy

Omalizumab is suggested for adults and children aged 6 years or older with severe allergic asthma (IgE-dependent allergic asthma [serum IgE of 30–700 IU/ml] that is uncontrolled despite optimal pharmacological and nonpharmacological management and allergen avoidance) (conditional recommendation, low quality evidence in adults, very low quality evidence in children).

Methotrexate

It is suggested that clinicians NOT use methotrexate in adults or children with severe asthma (conditional recommendation, low quality evidence).

Macrolide Antibiotics

It is suggested that clinicians NOT use macrolide antibiotics in adults and children with severe asthma for the treatment of asthma (conditional recommendation, very low quality evidence).

Antifungal Agents

- Antifungal agents are suggested for adults with severe asthma and recurrent exacerbations of allergic bronchopulmonary aspergillosis (ABPA) (conditional recommendation, very low quality evidence).
- It is suggested that clinicians NOT use antifungal agents for the treatment of asthma in adults or children with severe asthma who do not have ABPA irrespective of sensitization to fungi (i.e., positive skin prick test or fungus-specific IgE in serum) (conditional recommendation, very low quality evidence).

Bronchial Thermoplasty

It is recommended that bronchial thermoplasty be performed in adults with severe asthma only in the context of an Institutional Review Board–approved independent registry or a clinical study (strong recommendation, very low quality evidence).

Long-Acting Muscarinic Antagonists (Tiotropium)

Tiotropium improves lung function and symptoms in adults whose moderate to severe asthma is not controlled on moderate- to high-dose ICS, with or without a long-acting β agonist (LABA). In adults taking a high-dose ICS and a LABA, the addition of tiotropium improves lung function and reduces the frequency of severe exacerbations.

Leukotriene Pathway Modifiers

Montelukast is not as effective as LABAs when added to ICS therapy in either preventing exacerbations that require a systemic CS or improving symptoms in moderate asthma. However, it does improve lung function when added to ICS therapy in adults with moderate to severe asthma who are not taking a LABA.

For qualifying remarks related to the recommendations above, see the full clinical practice guidelines (3). ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

- Chung KF, Godard P, Adelroth E, Ayres J, Barnes N, Barnes P, Bel E, Burney P, Chanez P, Connett G, *et al*; European Respiratory Society. Difficult/therapy-resistant asthma: the need for an integrated approach to define clinical phenotypes, evaluate risk factors, understand pathophysiology and find novel therapies. ERS Task Force on Difficult/Therapy-Resistant Asthma. *Eur Respir J* 1999;13:1198–1208.
- American Thoracic Society. Proceedings of the ATS workshop on refractory asthma: current understanding, recommendations, and unanswered questions. *Am J Respir Crit Care Med* 2000;162:2341–2351.
- Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH, Bleecker ER, *et al*. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343–373.