Allergology International 66 (2017) 190–204

Contents lists available at ScienceDirect

Allergology International

journal homepage: http://www.elsevier.com/locate/alit

Invited review article

Japanese guidelines for childhood asthma 2017☆

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ARTICLE INFO

Article history:
Received 6 September 2016
Available online 18 January 2017

Keywords:
Acute exacerbation
Anti-inflammatory drugs
Childhood asthma
Guideline
Long-term management

ABSTRACT

The Japanese Guideline for the Diagnosis and Treatment of Allergic Diseases 2017 (JAGL 2017) includes a minor revision of the Japanese Pediatric Guideline for the Treatment and Management of Asthma 2012 (JPGL 2012) by the Japanese Society of Pediatric Allergy and Clinical Immunology. The section on child asthma in JAGL 2017 provides information on how to diagnose asthma between infancy and adolescence (0–15 years of age). It makes recommendations for best practices in the management of childhood asthma, including management of acute exacerbations and non-pharmacological and pharmacological management. This guideline will be of interest to non-specialist physicians involved in the care of children with asthma. JAGL differs from the Global Initiative for Asthma Guideline in that JAGL emphasizes diagnosis and early intervention of children with asthma at <2 years or 2–5 years of age. The first choice of treatment depends on the severity and frequency of symptoms. Pharmacological management, including step-up or step-down of drugs used for long-term management based on the status of asthma control levels, is easy to understand; thus, this guideline is suitable for the routine medical care of children with asthma. JAGL also recommends using a control test in children, so that the physician aims for complete control by avoiding exacerbating factors and appropriately using anti-inflammatory drugs (for example, inhaled corticosteroids and leukotriene receptor antagonists).

1. Definition and pathophysiology of childhood asthma (Fig. 1)

Childhood asthma causes recurrent dyspnea accompanied by paroxysmal whistling/wheezing. The dyspnea is spontaneously or therapeutically remitted or cured and rarely lethal. Like adult asthma, childhood asthma is pathologically characterized by chronic airway inflammation[1,2] and airway wall remodeling.[3–7]

Chronic airway inflammation is caused by the activation of eosinophils, mast cells, and lymphocytes and by airway mucosal damage. The viewpoint that asthma is a condition of chronic inflammation has an important implication for asthma treatment and management. It is fundamental to understand the necessity of anti-inflammatory drugs for basic treatment of persistent asthma. Many aspects of airway wall remodeling, which may influence the prognosis of asthma, are still unknown, including its causes, onset time, and effects of anti-inflammatory treatment. Airway hyperresponsiveness, which is a clinical characteristic of asthma, is intensified by airway epithelial damage due to airway

☆ This article is an updated version of "Japanese guideline for childhood asthma 2014" published in Allergol Int 2014:63:335–56.

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Peer review under responsibility of Japanese Society of Allergology.

http://dx.doi.org/10.1016/j.alit.2016.11.003

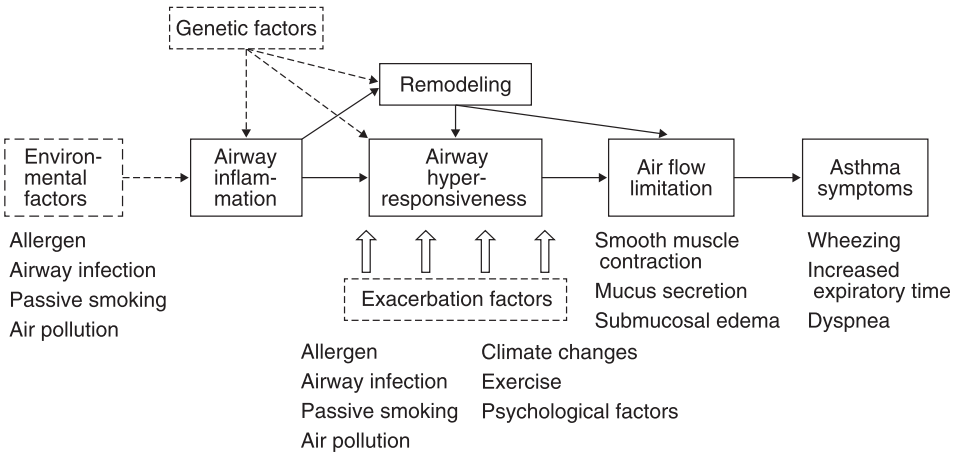

Fig. 1. Pathophysiology of bronchial asthma.

inflammation. Airway hyper-responsiveness can be assessed by a patient's responses to non-specific stimuli such as inhaled histamine or methacholine. Exercise-induced asthma (EIA) is also associated with airway hyper-responsiveness.

2. Diagnosis and differential diagnosis of childhood asthma

The typical symptoms of asthma are dyspnea accompanied by whistling/wheezing, coughing, and chest tightness. Expiratory dyspnea occurs mainly during asthma exacerbation. As symptoms progress, however, inspiratory dyspnea may coexist. If such symptoms recur, it is reasonable to diagnose symptomatic asthma. However, some patients present with misleading symptoms. Table 1 summarizes the physiological and immunological examinations and allergy tests that may support the accuracy of diagnosis.

2.1. Differential diagnosis

The differential diagnosis of asthma in children is shown in Table 2. Children with wheezing symptoms, particularly those with acute wheezing, must be differentially diagnosed. In infants, an accumulation of secretion in the lower respiratory tract resulting from conditions such as bronchitis, bronchiolitis, or pneumonia may cause recurrent episodes of wheezing. In addition, recurrent wheezing can be seen in children with complications of underlying conditions such as congenital anomalies (for example, vascular ring), immotile cilia syndrome, gastroesophageal reflux disease, and congenital heart disease.

2.2. Atopic asthma and non-atopic asthma

There are two types of childhood asthma: atopic asthma and non-atopic asthma. Most cases of childhood asthma are atopic, in which patients exhibit elevated specific immunoglobulin E (IgE) levels for house dust mites.

2.3. Asthma phenotype

Recently, asthma phenotypes during childhood have been discussed. Martinez *et al.* classified wheezy infants into three subtypes: transient early wheezers, non-atopic wheezers, and IgE-associated wheezers[8] (Fig. 2). Brand *et al.* reported two subtypes: multi-trigger wheeze and episodic (viral-induced) wheeze.[9] Asthma phenotypes may be recognized to reflect the differential diagnosis and therapeutic strategies.

Table 1
References for asthma diagnosis.

1. Respiratory functions: spirogram, flow volume curve, peak flow (PER) rate, and reactivity and reversibility for β_2 stimulants
2. Airway hyper-responsiveness test: acetylcholine and histamine thresholds and exercise stress test
3. Data indicating airway inflammation: eosinophils, mast cells (basophils) in rhinorrhea and sputum, and concentration of nitric oxide (FeNO) in exhaled breath
4. IgE: total serum IgE level, specific IgE antibody, immediate skin response, and antigen inhalation test
5. Family and patients' past histories of allergic diseases

Table 2
Differential diagnosis.

Anomalies	*Others*
Chest vascular malformation	Hypersensitive pneumonitis
Congenital heart diseases	Bronchial foreign bodies
Anomalies of airway	Psychogenic cough
Laryngomalacia	Vocal cord dysfunction
Bronchomalacia	Compression of airway
Tracheomalacia	Pulmonary edema
Immotile cilia syndrome	Allergic bronchopulmonary aspergillosis
Infection	Cystic fibrosis
Nasopharyngitis, sinusitis	Sarcoidosis
Croop (acute laryngitis)	Pulmonary embolism
Bronchitis	
Bronchiolitis	
Pneumonia	
Bronchiectasis	
Pulmonary tuberculosis	

3. Epidemiology of childhood asthma

3.1. Prevalence

The International Study of Asthma and Allergies in Childhood and the American Thoracic Society–Division of Lung Diseases (ATS–DLD) with modification are used to survey the prevalence of childhood asthma in Japan.[10,11] The prevalence of asthma as determined by ATS–DLD is 3.2–6.5% in Japan. Asthma prevalence in school children has been increasing during the last two decades according to a survey targeting children in the same primary schools within the same given area. However, a very recent survey indicates that asthma prevalence tends to be declining (Table 3) with the following characteristics: (1) it is more common among male children, more specifically male infants; (2) it varies twofold or more among regions; and (3) it shows a higher prevalence in