Invited review article

Japanese guidelines for childhood asthma 2017* 

Hirokazu Arakawa a,*, Yuhei Hamasaki b, Yoichi Kohno c, Motohiro Ebisawa d, Naomi Kondo e, Sankei Nishima g, Toshiyuki Nishimuta h, Akihiro Morikawa a, i, The Japanese Society of Pediatric Allergy and Clinical Immunology, The Japanese Society of Allergology

a Department of Pediatrics, Gunma University Graduate School of Medicine, Gunma, Japan
b Karatsu Medical and Welfare Center for People with Disabilities, Saga, Japan
c Chiba Rosai Hospital, Chiba, Japan
d Department of Allergy, Clinical Research Center for Allergology and Rheumatology, National Hospital Organization, Sagamihara National Hospital, Kanagawa, Japan
e Heisei College of Health Sciences, Gifu, Japan
f Department of Pediatrics, Graduate School of Medicine, Gifu University, Gifu, Japan
g National Hospital Organization, Fukusuka National Hospital, Fukusuka, Japan
h National Hospital Organization, Shimoshizu National Hospital, Chiba, Japan
i Kita Kanto Allergy Institute, Gunma, Japan

A R T I C L E   I N F O

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

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

A B S T R A C T

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 childhood 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).

Copyright © 2016, Japanese Society of Allergology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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 and airway wall remodeling.

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 hyper-responsiveness, which is a clinical characteristic of asthma, is intensified by airway epithelial damage due to airway...
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 (Fig. 2). Brand et al. reported two subtypes: multi-trigger wheeze and episodic (viral-induced) wheeze. Asthma phenotypes may be recognized to reflect the differential diagnosis and therapeutic strategies.

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. 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
children with a family history of allergic diseases. Children with a higher body mass index (>90th percentile) have a higher prevalence of asthma from infancy to adolescence. The prevalence of childhood asthma in Japan is ranked at the middle of various countries throughout the world.

3.2. Complications

Allergic rhinitis, allergic conjunctivitis, and atopic dermatitis are common coexisting allergic diseases caused by the same mechanism as asthma. Of note, the complication rates of these allergic diseases are >30%. The prevalence of childhood asthma in Japan is ranked at the middle of various countries throughout the world.

3.3. Prognosis

The remission rate is lower in patients with more severe asthma. Remission is defined as an asymptomatic status without any treatment and is thus differentiated from cure. A remission status that continues for 5 years or longer is considered a clinical cure. Furthermore, if respiratory function and airway hyperresponsiveness return to normal levels, the status is determined as a functional cure.

Sixty percent of children who have had wheezing before age 6 experience no more wheezing after 6 years of age. On the other hand, it was demonstrated that 52–72% of children diagnosed as asthmatic at the age of 6 have asthma symptoms at 22 years of age.

3.4. Death from asthma (Fig. 3)

The number of deaths from asthma during childhood has markedly decreased. The following characteristics can be noted: (1) mortality in patients with asthma aged 5–34 years has decreased to ≤0.1 per 100,000 population; (2) mortality in toddler patients aged 0–4 years is higher than that in older children; (3) mortality in young adult patients aged 15–19 years has decreased and is higher among boys and unstable; (4) the most common scenario is severe bronchospasm, with mucus plugging leading to asphyxia; (5) most deaths result in patients with severe persistent asthma, but some patients with moderate or even mild persistent asthma may also die from asthma; (6) sudden and unexpected exacerbation and delayed appropriate consultation are common as causes of death from asthma; and (7) misjudgment of the severity of exacerbation

Table 3

<table>
<thead>
<tr>
<th>Surveillance area</th>
<th>Age (years old)</th>
<th>Surveillance method</th>
<th>Surveillance year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western area of Japan</td>
<td>6–12</td>
<td>ATS-DLD</td>
<td>3.20% 4.60% 6.50%</td>
</tr>
<tr>
<td>Fukuoka Prefecture of Japan</td>
<td>6–7 13–14</td>
<td>ISAAC</td>
<td>17.3% 13.4% 13.0%</td>
</tr>
<tr>
<td>All Japan</td>
<td>0–4 5–9 10–14 15–19</td>
<td>Prevalence rate trend-surveillance</td>
<td>13.6% 12.7% 9.0% 5.4%</td>
</tr>
<tr>
<td>All Japan</td>
<td>3–5 6–7 13–14 16–17</td>
<td>ISAAC</td>
<td>19.9% 13.9% 8.8%</td>
</tr>
<tr>
<td>All Japan</td>
<td>Elementary school Junior high school High school</td>
<td>School health surveillance</td>
<td>6.8% 5.1% 3.6%</td>
</tr>
</tbody>
</table>
and excessive dependence on pressurized metered-dose inhalers (pMDI) of short-acting β₂ agonists of the severity of exacerbation can also lead to death.

To reduce the number of deaths from asthma, early and accurate diagnosis and treatment is necessary, and patients should be thoroughly educated. Instructions about the appropriate use of pMDI of short-acting β₂ agonists against acute exacerbation, early and complete anti-inflammatory therapy with inhaled corticosteroids, and adherence to asthma management are particularly important.

4. Management of acute asthma exacerbation

4.1. Intensity of asthma exacerbation

The intensity of asthma exacerbation is classified into four stages: mild, moderate, and severe exacerbations and respiratory failure. It is based on the degree of impairment of respiratory status and the activities of daily life such as eating, speaking, sleeping, and exercising (Table 4). Because infants cannot complain of dyspnea themselves, the intensity of exacerbation in them is determined on the basis of objective findings. Ill-temper, vomiting, screaming, and difficulty sleeping unless held by the mother are important interview items for identifying severe exacerbation (Table 5).

Supportive indications of the intensity are determined by oxygen saturation (SpO₂) measured using a pulse oximeter and peak expiratory flow (PEF) measured using a spirometer. However, because SpO₂ varies widely among infants compared with school children, caution is needed in the use of SpO₂ to evaluate the intensity of exacerbation in infants.
4.2. History taking in the outpatient department

In the outpatient department, the intensity, duration, and cause of exacerbation must be assessed. The patient's previous history of exacerbation and medical treatment on such occasions should also be evaluated before a treatment plan is determined.

4.3. Treatment of acute exacerbation in outpatient departments (Fig. 4)

Treatment strategies of mild exacerbation. An inhaled $\beta_2$ agonist (salbutamol or procaterol: 0.1–0.3 mL to infants or 0.3–0.5 mL to school children or adolescents, diluted in 2 mL of physiological saline or disodium cromoglycate inhalant solution; 1 ampule = 2 mL) can be administered using a nebulizer. When cough and wheezing disappear, and SpO2 or PEF rates become $\geq 97\%$ or $\geq 80\%$ of predicted values and/or personal best, respectively, 15–30 min after the inhalation, the patient can go home. If a mild cough and wheezing remain even after the inhalation, an additional inhaled $\beta_2$ agonist is administered 20–30 min later. If there is an inadequate response or even exacerbation of symptoms in response to the $\beta_2$ agonist, an additional treatment should be conducted equivalent to that for moderate exacerbation.

Treatment strategies of moderate exacerbation. An inhaled $\beta_2$ agonist can be administered using a nebulizer driven by oxygen in patients with $<95\%$ SpO2. Patients with an insufficient response can receive the inhalation again 20–30 min later. Inhalation can be repeated up to three times. When a favorable response is obtained after the initial treatment, the patient should be observed for an additional hour. If asymptomatic then, the patient is given instructions about future treatment and allowed to go home. If no remission is achieved after two or more inhaled $\beta_2$ agonists, an additional treatment will be conducted. Infants should be treated after hospitalization. Additional treatment for moderate exacerbation includes a steroid and/or aminophylline administration, although aminophylline should be used with caution to prevent adverse effects. If additional treatment results in an unfavorable response or exacerbates symptoms, the patient should be treated after hospitalization.

1. Steroids are administered via an intravenous or oral route (see Table 6 for initial and maintenance doses). Even in patients with moderate exacerbation, an intravenous steroid should be considered for early treatment if they are patients (i) at step 3 or above for stepwise management, (ii) with a history of hospitalization owing to asthma exacerbation within the past year, or (iii) with a history of endotracheal intubation for the treatment of extremely severe asthma exacerbation.

2. Aminophylline is not recommended for the patients shown in Table 7, because unequivocal indications for aminophylline treatment are difficult to secure.

4.4. In-hospital treatments and procedures

Criteria for in-hospital treatment are shown in Table 8.

Treatment strategies of severe exacerbation. An inhaled $\beta_2$ agonist is administered with a nebulizer along with oxygen inhalation. An initial transfusion is performed along with intravenous steroid administration (Table 6). Aminophylline can be administered concomitantly. However, caution should be used in patients aged 0–2 years (Table 9). If symptoms markedly improve, the patient is observed every 4–6 h while receiving inhaled $\beta_2$ agonists and maintenance transfusion. If needed, repeated glucocorticosteroid administration and continuous intravenous aminophylline infusion are concomitantly conducted. If exacerbation does not show any

---

**Table 5**

Symptoms during severe exacerbation in infantile asthma.

| 1. Severe cough (with occasional vomiting) |
| 2. Marked wheezing (occasionally reduced) |
| 3. Depression of suprasternal space and supravacular fossa and between ribs |
| 4. Tachypnea |
| 5. Nasal alar breathing |
| 6. Seesaw breathing |
| 7. Comfort when held upright (orthopnea) |
| 8. Inability to sleep |
| 9. Cyanosis |
| 10. Moaning |
| 11. Tachycardia |
| 12. Ill-temper |
| 13. Scream |
| 14. Lowered level of consciousness |

---

**Fig. 4.** Treatment for acute exacerbation in hospital (2–15 years old). Weak exacerbation usually responds to $\beta_2$ inhalation at home.
occasions per month. Patient should be referred to an expert in cases requiring more
Systemic administration of glucocorticosteroids should be limited to less than three
Hydrocortisone: discontinue within 3
Intravenous injection: infuse for 10

Caution against aminophylline administration for patients younger than 2 years
Indications for hospital admission.
Table 8
Advisable
1. Patients with moderate exacerbation for whom aminophylline administration is not
2. Do not prescribe theophylline for the patients with convulsive disorders, such as
3. If there is fever, carefully refer to indications.
4. Determine dosage based on 10 μg/mL of serum level. Monitor serum level as needed. Adjust dosage as needed, with an upper limit of 15 μg/mL.
5. Theophylline clearance is reduced by fever, viral infection, foods, concomitant

Hydrocortisone
Prednisolone
Methylprednisolone

Table 7
Patients with moderate exacerbation for whom aminophylline administration is not
1. If β2 stimulants or steroids are not effective for severe exacerbation or
2. Do not prescribe theophylline for the patients with convulsive disorders, such as
3. If there is fever, carefully refer to indications.
4. Determine dosage based on 10 μg/mL of serum level. Monitor serum level as needed. Adjust dosage as needed, with an upper limit of 15 μg/mL.
5. Theophylline clearance is reduced by fever, viral infection, foods, concomitant
drugs, etc. In some cases, serum levels are elevated.

H. Arakawa et al. / Allergology International 66 (2017) 190–204
195

Table 6
Formulas for glucocorticosteroids.

<table>
<thead>
<tr>
<th>Intraavenous injection</th>
<th>Initial doses</th>
<th>Maintenance doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>5–7 mg/kg</td>
<td>5–7 mg/kg every 6 h</td>
</tr>
<tr>
<td></td>
<td>5 mg/kg</td>
<td>5 mg/kg every 6–8 h</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>1–1.5 mg/kg</td>
<td>0.5–1 mg/kg every 6 h</td>
</tr>
<tr>
<td></td>
<td>1–1.5 mg/kg</td>
<td>0.5–1 mg/kg every 6–12 h</td>
</tr>
<tr>
<td></td>
<td>0.5–1 mg/kg</td>
<td>(max: 2 mg/kg/day)</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>0.5–1.0 mg/kg</td>
<td>0.5–1.0 mg/kg every 6 h</td>
</tr>
<tr>
<td></td>
<td>0.5–1 mg/kg</td>
<td>0.5–1 mg/kg every 6–12 h</td>
</tr>
</tbody>
</table>

Table 10
Continuous inhalation therapy with β2 agonist.

Nebulizer
Inspiron nebulizer & face mask (or O2 tent)
Inhalation liquid
R/L-isopolotenol (0.5%) 2–5 mL (or L-isopolotenol 10–25 mL) + 0.9% NaCl 500 mL (double dose of R/L-isopolotenol [0.5%] can be used according to symptoms)
Methods
1. Start with 50%O2 at 10 L/min.
2. Adjust O2 concentration and flow in order to maintain SpO2 over 95%.
3. If patient’s status is not improved after 30 min, step up the inhalation condition, or consider management with respirator.
4. When patient’s status is improved, step down the inhalation condition and stop continuous inhalation therapy; then change to intermittent inhalation with β2 stimulant.

Monitoring
1. SpO2 with pulse oximeter, ECG, blood pressure, respiratory rate
2. Electrolytes, CPK, LDH, GOT, blood gas
Cautions
1. Keep in mind the timing to change to management with respirator.
2. Regular sputum cough-up, body position change and body movement are encouraged.
3. Watch out for obstruction in tubes and failure of inhalation devices (give special attention to clogging of Inspiron nebulizer).
4. Watch out for signs of myocardial infarction: abnormal ECG findings and chest pain Check cardiac enzymes (CPK, GOT and LDH), and consider changing to therapy with management with respirator.

Table 9
Cautions against aminophylline administration for patients younger than 2 years old.

improvement at 30 min after the start of treatment, additional treatments are considered. Continuous isopolotenol (e.g., Asthpul) inhalation can be conducted.17–19 During this treatment, parameters such as blood pressure, heart rate, respiratory rate, and SpO2 should be monitored. The continuous inhalation is usually very effective, and effects can be observed within 30 min. Intravenous glucocorticosteroid administration is carried out periodically (Table 6) and can be stopped within several days after recovery (Table 10).

4.5. Treatment of respiratory failure
Patients with respiratory failure require intensive care with the assistance of emergency specialists and anesthesiologists. Respiratory failure results in the alleviation and disappearance of wheezing and causes severe cyanosis. In addition, it may be accompanied by urinary and fecal incontinence and unconsciousness. Arterial blood gas analysis is needed to assess respiration status, and the presence of complications (such as subcutaneous emphysema, mediastinal emphysema, atelectasis, pneumonia, and pneumothorax) to preclude treatment has to be carefully assessed. Although there is no definite indication for artificial respiratory management, it should be considered when one or more of the following signs are apparent: (1) reduced respiratory sounds and wheezing in the presence of cyanosis, (2) impaired consciousness resulting in somnolence or coma; (3) <60 mmHg PaO2 (<90% SpO2) even after sufficient oxygen inhalation; and (4) elevated PaCO2 (>65 mmHg or >5 mmHg/h).

The usefulness of noninvasive positive ventilation is still under investigation for childhood asthma.

4.6. Complications with acute asthma exacerbation
Air leak syndromes such as mediastinal emphysema, subcutaneous emphysema, and pneumothorax are major complications with acute exacerbation. Patients with pneumothorax complain of chest pain that worsens with exertion and deep respiration. Cough and dyspnea are often observed. Leaked air is usually absorbed spontaneously. In acute asthma exacerbation, airway obstruction often occurs with airway constriction, mucus hypersecretion and
Table 11: Definition of asthma severity in Japanese Pediatric Guideline.

<table>
<thead>
<tr>
<th>Asthma severity decided from patient's symptoms without considering current treatment step</th>
<th>Current treatment step</th>
</tr>
</thead>
<tbody>
<tr>
<td>intermittent, mild persistent, moderate persistent, and severe persistent, including most severe persistent as a subgroup.</td>
<td>Step 1</td>
</tr>
<tr>
<td>intermittent, mild persistent, moderate persistent, and severe persistent, including most severe persistent as a subgroup.</td>
<td>Step 2</td>
</tr>
<tr>
<td>intermittent, mild persistent, moderate persistent, and severe persistent, including most severe persistent as a subgroup.</td>
<td>Step 3</td>
</tr>
<tr>
<td>intermittent, mild persistent, moderate persistent, and severe persistent, including most severe persistent as a subgroup.</td>
<td>Step 4</td>
</tr>
</tbody>
</table>

5. Basics of long-term management of childhood asthma

5.1. Severity determination

Asthma severity is classified into four levels: intermittent, mild persistent, moderate persistent, and severe persistent, including most severe persistent as a subgroup.

The severity of disease in patients not taking long-term management drugs is shown in Table 11. If long-term management drugs are already administered, the “true” severity is determined under consideration of the present treatment step (Table 12). For example, if the “apparent” severity in a patient being treated at step 2 is mild persistent, the “true” severity is determined as their intersection point, i.e., moderate persistent asthma. In patients with symptoms not controlled at step 4, whose “apparent” severity is moderate or severe persistent, the “true” severity is determined as the most severe persistent asthma.

Comparison of asthma severity between children and adults demonstrates one-level differences: intermittent, mild persistent, and moderate persistent in adults correspond to mild persistent, moderate persistent, and severe persistent in children, respectively.

5.2. Treatment goals of childhood asthma

The treatment goals of childhood asthma are shown in Table 13. Although the ultimate goal of childhood asthma treatment is complete remission or cure, practical targets in daily life are controlling symptoms, restoring and/or maintaining normal respiratory functions, and maintaining a good quality of life (QOL).

5.3. Control level

Control levels are determined by symptoms, interference with daily activities, and frequency of using inhaled β2 agonists (Table 14).

5.4. Control of asthma

This guideline intends to help non-specialist physicians to aim at reaching the level of complete control in asthma treatment and management. Important factors to attain this goal are appropriate use of anti-inflammatory drugs, elimination of environmental risk factors, and educational and enlightening activities for patients and caregivers regarding adequate asthma management in daily life. The first factor is the most efficient and effective strategy along with the recent development of anti-inflammatory drugs for chronic airway inflammation. Favorable control can be achieved by selecting an appropriate step based on asthma severity. However, insufficient treatment, inappropriate drugs, and unavoidable exacerbation factors result in poor control. The asthma control test was devised for the evaluation of control levels, which would help to adjust treatment and management toward favorable control.

5.5. Evaluation methods of asthma control levels

(1) Asthma diary. A diary kept by a patient would be useful for doctors to gain access to the information pointing to asthma control through the patient’s own description of respiratory symptoms and daily activities such as sleeping, eating, and exercising. The information about drug use and the values of peak flow meter monitoring would also be important for the evaluation of control. In addition, assessment of respiratory functions using a spirometer is important.

(2) Childhood Asthma Control Test (C-ACT). The C-ACT is used in many countries for children aged 4–11 years. The test consists of seven questions, the first four of which are answered by the children with asthma and the remaining three answered by their parents. The first four questions use a faces scale to allow children to answer them easily. Scoring is as follows: 27, 20, and 20 points indicate complete, favorable, and poor control, respectively. For children aged >12 years, the Asthma Control Test (ACT) for adults can be used.

(3) Japanese Pediatric Asthma Control Program (JPAC). Severity and control status can be assessed using the JPAC program. It allows the selection of treatment step according to this guideline. Step-up and step-down may also be determined.

Table 12: How to determine true asthma severity in patients under treatment with anti-asthma drugs.
Although final goal is remission or cure, the aims of daily control are:

1. Complete control of asthma symptoms
   - Reduced or no need for β2 stimulants in exacerbation.
   - No symptoms day and night.

2. Normal respiratory functions
   - Stable PEF rate. Stable pulmonary function tests.
   - Improved airway hyper-responsiveness (no symptom aggravation after exercise, cold air inhalation, etc.).

3. Improved QOL
   - Normal daily life, including sports. No absence from school.
   - No side effects associated with drug therapies.

### Table 13
Treatment goal of childhood bronchial asthma.

<table>
<thead>
<tr>
<th>Component of control</th>
<th>Classification of asthma control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well-controlled</td>
</tr>
<tr>
<td>Mild symptoms</td>
<td>None</td>
</tr>
<tr>
<td>Apparent symptoms</td>
<td>None</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>SABA use for symptom control</td>
<td>None</td>
</tr>
</tbody>
</table>

Control levels are evaluated by conditions during the recent 4 weeks. Mild symptoms indicate transient cough and/or wheezing induced by exercise, laughing and crying. Also included are short periods of coughing at the time of awakening and during sleep.

Apparent symptoms indicate continuous coughing and wheezing with dyspnea and chest tightness. >80% of predicted/personal best in PEF and/or FEV1. 0%, <20% of circadian changes in PEF, and <12% of FEV increase by β2 stimulant inhalation are preferable as well-controlled conditions.

At the time of assessment, hospital admission due to severe exacerbation, use of oral glucocorticosteroid for symptom control, and seasonal exacerbation in recent 12 months should be considered.

Scoring is as follows: 15, 12–14, and ≤11 points show complete, favorable (but still insufficient), and poor control, respectively. Full scores in both the C-ACT and JPAC correspond to a well-controlled state in JAGL 2017.

### 5.6. Avoidance of exacerbation factors

Most patients with childhood asthma have atopic diathesis and produce specific IgE antibodies to house dust mites. Tests are needed to determine the specific IgE antibodies to house dust mites and other possible allergens, and the elimination of these allergens from the patient's living environment is necessary.

### 5.7. Allergy tests and assessment

Total serum IgE values vary with age. High values are those that exceed the mean ± 2 standard deviations. The first step to identify the allergens of children with asthma is to take carefully past history of episodic symptoms after a particular antigen exposure. Routine examinations include skin tests and measurement of specific IgE antibodies in serum. However, the results of positive skin test or positive specific IgE do not mean that allergen is causing symptoms.

### 5.8. Instructions for environmental improvement (Table 15)

Cleaning rooms with a vacuum cleaner is an important measure against mite antigens. Using a wood or cushioned floor as a flooring material is effective. Because measures for bedclothes are also important, bedclothes should preferably be cleaned by a vacuum cleaner at least once a week. As sensitization to pets (e.g., cats, dogs, and rodents) may induce exacerbation, contact with these animals should be avoided.

### 5.9. Instructions for smoking cessation

Active or passive smoking is an important exacerbation factor for asthma. Smoking by pregnant mothers affects the respiratory function of their children after birth. Parents with smoking habits must be instructed about the need for smoking cessation as a vital component of childhood asthma treatment. If children themselves are smokers, they should be educated about the adverse influences on treatment and smoking cessation therapy.

### Table 15
Points for improvement in environmental conditions.

<table>
<thead>
<tr>
<th>Component of control</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedding</td>
<td>Use anti-mite sheets and covers; wash bedding frequently and hang it outdoors to dry in the sun</td>
</tr>
<tr>
<td>Mattress</td>
<td>Do not use mattresses; wooden floors are preferable</td>
</tr>
<tr>
<td>Sofa</td>
<td>Use sofas made of leather or artificial leather; no fabric-made sofas</td>
</tr>
<tr>
<td>Stuffed toys</td>
<td>Do not use stuffed toys; use washable ones if necessary</td>
</tr>
<tr>
<td>Furniture</td>
<td>Use easily cleanable furniture only</td>
</tr>
<tr>
<td>Drapes</td>
<td>Use window shades instead of curtains; washable curtains if necessary</td>
</tr>
<tr>
<td>Pet animals</td>
<td>Do not keep mammals and/or birds inside rooms</td>
</tr>
<tr>
<td>Vacuum cleaner</td>
<td>Use one equipped with 2-layered dust bag</td>
</tr>
<tr>
<td>Potted plants</td>
<td>Do not grow plants inside rooms</td>
</tr>
<tr>
<td>Laundry</td>
<td>Do not hang the laundry inside rooms</td>
</tr>
<tr>
<td>Heating appliances</td>
<td>Exhaust gas must be ducted outdoors if kerosene or gas heater is used</td>
</tr>
<tr>
<td>Materials for building houses</td>
<td>Eliminate architectural materials containing volatile chemicals such as aldehyde and phenol</td>
</tr>
<tr>
<td>Tobacco-smoking</td>
<td>Persuade family members to discontinue smoking inside rooms</td>
</tr>
</tbody>
</table>

### 6. Long-term management by medication

#### 6.1. Formulations and characteristics of long-term management drugs (controllers)

Long-term management drugs (controllers) are continuously used to reduce and eliminate asthma symptoms, improve QOL, and normalize and maintain respiratory function. Controllers with anti-inflammatory effects include inhaled corticosteroids (ICSs), leukotriene receptor antagonists (LTRAs), and theophylline. Oral steroid administration for long-term management should be limited to the most severe cases because of systemic side effects. ICSs are routinely used for patients with a level of severity that is higher than mild persistent, because ICSs have strong anti-inflammatory effects with relatively low systemic adverse effects. Long-acting β2 agonists (LABAs) are concomitantly used with ICSs for long-term management. LABAs should not be used alone.

**Inhaled corticosteroids** potently suppress airway inflammation and play an important role in long-term asthma control. The amelioration of airway inflammation by ICSS leads to improvement in subjective symptoms, respiratory function, and airway hyper-responsiveness. Hospitalization owing to acute exacerbation and deaths from asthma also decrease. However, no evidence has been obtained regarding alteration in the natural history of asthma resulting from the persistent use of ICSS for long periods. A combination of the drugs ICS and LABA can be used for children aged >5 years. An adequate drug formulary should be selected depending on the patient's age and/or inhalation techniques to maximize the efficiency of drug inhalation.

**Leukotriene receptor antagonists** inhibit bronchoconstriction and airway inflammation, and are effective for long-term...
management. In many cases, LTRAs improve respiratory function and reduce the frequency of exacerbations within 1–2 weeks after administration of LTRAs. In patients with mild persistent asthma, LTRAs are as effective as ICSs. Efficacy of LTRAs as add-on therapy to ICSs has also been demonstrated.32–34 Sustained-release theophylline (SRT) has a bronchodilator action and an anti-inflammatory effect and is used as a controller. The dosage of theophylline is determined by factors that influence metabolism such as individual differences, infections, meal contents, and concomitant drugs. It should be noticed that fever during a viral infection causes an elevated serum theophylline level owing to decreased clearance. An intractable convulsion associated with theophylline administration can occur as a severe side effect particularly in infants.35

Table 16
Asthma management in children under 2 years of age.

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal therapy</td>
<td>SABA as needed</td>
<td>LTRA and/or DSCG</td>
<td>ICS (medium dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS (high dose) possibly add LTRA</td>
</tr>
<tr>
<td>Additional therapy</td>
<td>LTRA and/or DSCG</td>
<td>ICS (low dose)</td>
<td>LTRA LABA (p.o. or adhesive skin patch)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Theophylline (maintain at 5–10 mg/mL in blood conc.) can be considered</td>
</tr>
</tbody>
</table>

LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; DSCG, disodium cromoglycate; LABA, long-acting beta agonist.
LABA is discontinued when good control level is achieved. LABA (p.o.) is defined as the $\beta_2$ stimulants prescribed as twice a day.
Theophylline is not used for patients under 6 months of age. Theophylline is not recommended for patients with history of convolution. Prescription of theophylline for patients with fever should be with caution.
Strongly recommend that uncontrollable patients with step 3 or step 4 management strategy be referred to experts in treating severe childhood asthma.

Table 17
Asthma management in children 2–5 years of age.

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal therapy</td>
<td>SABA as needed</td>
<td>LTRA and/or DSCG</td>
<td>ICS (medium dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS (high dose) possibly add one or more of the following drugs</td>
</tr>
<tr>
<td>Additional therapy</td>
<td>LTRA and/or DSCG</td>
<td>LTRA LABA or SFC Theophylline (consider)</td>
<td>Consider the following: Increase ICS/SFC to higher doses or p.o. steroid</td>
</tr>
</tbody>
</table>

LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; DSCG, disodium cromoglycate; LABA, long-acting beta agonist; SFC, salmeterol/fluticasone combined drug.
LABA is discontinued when good control level is achieved. LABA (p.o.) is started, oral and percutaneous LABA should be discontinued.
Addition of SFC to ICS is acceptable; however, total dose of steroid is limited within the dose of basal therapy. SFC should be used for patients 5 years or more of age.
Uncontrollable patients with step 3-management strategy are recommended to be referred to experts in treating severe childhood asthma.
As an additional therapy at step 4, an increase of ICS/SFC to higher doses or p.o. steroid therapy or long-term admission management is considered. Patients should be controlled under experts in treating severe childhood asthma.

Table 18
Asthma management in children 6–15 years of age.

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal therapy</td>
<td>SABA as needed</td>
<td>ICS (low dose) and/or LTRA and/or DSCG</td>
<td>ICS (medium dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS (high dose) possibly add one or more of the following drugs</td>
</tr>
<tr>
<td>Additional therapy</td>
<td>LTRA and/or DSCG</td>
<td>Theophylline (consider)</td>
<td>LTRA Theophylline LABA or SFC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider the following: Increase ICS/SFC to higher doses or p.o. steroid</td>
</tr>
</tbody>
</table>

LTRA, leukotriene receptor antagonist; ICS, inhaled corticosteroid; DSCG, disodium cromoglycate; LABA, long-acting beta agonist; SFC, salmeterol/fluticasone combined drug.
LABA is discontinued when good control level is achieved. When SFC is started, oral and percutaneous LABA should be discontinued.
Addition of SFC to ICS is acceptable; however, total steroid dose is limited within the dose of basal therapy.
It is recommended that uncontrollable patients with step 3-management strategy be referred to experts in treating severe childhood asthma.
As an additional therapy at step 4, an increase of ICS/SFC to higher doses or p.o. steroid therapy or long-term admission management is considered. Patients should be controlled under experts in treating severe childhood asthma.

Long-acting $\beta_2$ agonists may be used concomitantly with ICSs or other anti-inflammatory drugs, because $\beta_2$ agonists have no inhibitory effects on airway inflammation. Besides inhaled LABAs, transdermal patches are and per oral medicines are available as LABAs in Japan. The serum tulobuterol level is maintained at a therapeutic range for 24 h after application of a transdermal tulobuterol patch.

6.2. Long-term management plan
In a pharmacotherapy plan for long-term control of asthma, a long-term management drug for the treatment step determined by the severity should be selected (Table 12). The severity is determined on the basis of symptoms and their frequency during the most recent month (see Table 11). The pharmacological stepwise

management.
management is divided into three age groups <2, 2–5, and 6–15 years old (Table 16–18). Table 19 indicates the doses of different products of ICS at steps 1–4.

The control status can be evaluated by monitoring subtle asthma symptoms, apparent asthma exacerbation, frequency of using inhaled β2 agonists during treatment, and restrictions of daily life such as sleeping, feeding, and speaking (Table 14). Favorable control is indicated by ≤20% diurnal variation in the PEF rate or ≥80% of the patient’s personal best rate. C-ACT, JPAC, and/or an asthma diary are also useful for evaluating asthma control. Table 20 lists criteria that indicate the status of favorable asthma control.

If control is insufficient or poor, additional or step-up therapy is conducted to achieve complete control. It is also important to reexamine an adherence of medication, allergen avoidance, and the effects of psychosocial factors. If there are no positive effects even at step 4 in the case of most severe persistent asthma, hospitalization for further treatment or oral steroid administration can be considered.

If complete control has been achieved for 3 months or longer, a step-down is recommended depending on the severity, history of disease, respiratory function, and medication. An applicable step-down therapy reduces the dosage to the lowest recommended dose to maintain the control level. When asthma symptoms are controlled below the intermittent level and respiratory function is favorable after reduction to the lowest recommended dose at the same time, treatment can be discontinued (Fig. 5). At present, there are no explicit criteria for discontinuation of drugs. Even if symptoms are no longer apparent, the patient should be followed up because remission does not mean cure.

### 7. Diagnosis and treatment of persistent cough

#### 7.1. Persistent cough and asthma

No definite criteria exist for persistent cough in children. The Japanese Respiratory Society defines three types of coughs in adults: acute cough, prolonged cough, and chronic cough indicating persistent symptoms for <3 weeks, 3–8 weeks, and ≥8 weeks, respectively. Patients with underlying diseases that cause persistent cough for over 8 weeks are diagnosed as having chronic cough in a broad sense. Asthma is the leading cause of chronic cough. Other causes are postnasal drainage and gastroesophageal reflux. Cough-variant asthma is a unique condition demonstrating persistent cough with airway hyper-responsiveness but no history of wheezing. Inhaled β2 agonists are effective as its treatment. Some patients with cough-variant asthma will develop bronchial asthma.

Underlying mechanisms of persistent cough are airway inflammation due to infection and allergy, direct and/or indirect stimulation with sputum, nasal discharge, and gastric juice, and stimulation by airway smooth muscle constriction and mucosal edema in various pathological conditions.
Table 21
Combination of inhalation device and aiding tools.

<table>
<thead>
<tr>
<th>Age</th>
<th>Drug</th>
<th>Inhalation devices and aiding tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baby</td>
<td>pMDI</td>
<td>pMDI + mask</td>
</tr>
<tr>
<td>Infant</td>
<td>pMDI</td>
<td>pMDI + mask or mouth piece</td>
</tr>
<tr>
<td>School children</td>
<td>pMDI</td>
<td>pMDI + mouth piece</td>
</tr>
<tr>
<td></td>
<td>DPI</td>
<td>DPI with mouth piece or spacer with mouth piece</td>
</tr>
</tbody>
</table>

Table 22
Check list of inhalation therapy.

- Nebulizer
  - Bite mouth piece firmly
  - Expectorate salivary fluid without reversing from time to time
  - Can ventilate through mouth
  - Adhere mask tightly on the face
  - Can ventilate without crying
  - Can synchronize actuation and inhalation
  - Can ventilate through mouth
  - Can ventilate slow and deep
  - Can hold breath for certain periods of time
  - pMDI + spacer
    - When using mouth piece, can bite mouth piece firmly
    - When using mask, can adhere mask tightly on the face
    - Can ventilate without crying
    - Can hold breath for certain periods of time
  - DPI
    - Keep device in appropriate position
    - Do not blow away drug-powder before inhalation
    - Can ventilate with strong inspiration
    - Can ventilate deep
    - Can hold breath for certain periods of time
- Other points
  - Gargle or drink water after inhalation (in the case of using ICS)

7.2. Treatment of persistent cough
The fundamental strategy for the treatment of persistent cough is to first determine the underlying mechanisms. If the underlying mechanism of persistent cough is asthma, the patient can be treated according to the asthma guideline. In the case of poor control, stepping-up of the treatment level, elimination of exacerbation factors from the patient’s environment, and educating the patient about asthma control should be considered.

8. Inhalers and spacers
Inhalation therapy is critical and effective for the daily management and treatment of asthma exacerbation in children, including infants. A good understanding of the characteristics of inhalers is important for the selection of an appropriate inhaler based on the child’s status.

8.1. Inhalers
Inhalers are classified into nebulizers and metered-dose inhalers. Three types of nebulizers are available based on their drive systems: jet, ultrasonic, and mesh. Metered-dose inhalers include the pMDI and the dry powder inhaler (DPI). In Table 21, combinations of nebulizers or spacers with and without a face mask and inhaled drugs for different age groups are demonstrated. The appropriate combination can be selected by assessing various conditions such as efficiency of inhalation, compliance, patient preference, and financial matters.

(1) A nebulizer can be used regardless of age if a mask is used. Jet nebulizers are the most widely used for inhalation therapy of asthma. Mesh nebulizers, a subtype of ultrasonic nebulizers, are lightweight, save power, and have a high vaporizing capacity. Ordinary ultrasonic nebulizers are unsuitable for inhaling anti-asthma drugs because of thermal denaturation and concentration changes of drugs in the reserve tank.39

When children use nebulizers, they should inhale at a resting respiratory rate in a sitting position. In children old enough to breathe orally, soluble drugs are inhaled with a mouth piece attached to the nozzle of the nebulizer. In infants, a nebulizer is used with a face mask attached to the nozzle, to cover the mouth and nose. Adhesion of the mask to the patient’s face is important to optimize inhalation efficiency, which is reduced by nasal inhalation or crying.40-41

(2) Both pMDIs and DPIs are available. In pMDIs, spray and inhalation need to be synchronized. Even in infants for whom spray and inhalation cannot be synchronized, a pMDI can be employed by using a spacer with a face mask. When using a DPI, a patient inhaled a drug through self-respiration. School children or adolescents can use DPIs because they can generate the certain amount of inspiratory force required.

8.2. Spacers
A spacer is an indispensable aiding instrument for pMDIs in infants who cannot accurately perform the procedures for the synchronization of spray and inhalation. Concomitant use of a spacer allows inhalation at a normal respiratory rhythm even without synchronizing spray and inhalation, thus increasing inhalation efficiency. In addition, a spacer is useful in adsorbing large particles (≥5 μm) onto the inner wall of the spacer to prevent deposition of excess drugs in the oral cavity and reduce adverse effects. In infants who cannot breathe through the mouth, the nose and mouth are covered with a face mask without leakage to maintain inhalation efficiency and maximize the benefit from a spacer.

Many types of spacers are available. A spacer with data assuring aerodynamic properties, clinical usefulness, and safety should be selected. The effectiveness of a spacer is greatly influenced by concomitant agents and procedures as well as its shape, structure, and physical properties.

Technical mastery in the adequate use of inhalation devices and aiding accessories is essential to obtain maximal efficacy of inhalation drugs (Table 22).

9. Patient education
To perform asthma treatment effectively, patients and their caregivers need to be educated and actively involved in the treatment.42-43

(1) The caregivers must ensure that infants do not experience discomfort during treatment. The caregivers should also help the infant to be interested in the treatment and stay motivated. They should encourage and compliment them on their good performance in inhalation and habituate them to the treatment gradually.

(2) School-age children should have the pathophysiology of asthma explained to them, using simple terms and metaphors, to understand the need for treatment. They should be cheerfully instructed about the abdominal breathing technique, PEF measurement, and other matters as if they were playing some kind of game.

(3) Prepubertal children should be instructed about the need for continuing treatment without interruption. According to their level of understanding, they should be educated about
the pathophysiology of asthma and its treatment. Because it is difficult to make such young patients take charge of the part of treatment and management that their parents had been taking care of, compliment them on their efforts to achieve self-fulfillment and eventually self-management.

(4) Children in puberty are more likely to disobey their parents because of parent–child conflicts during puberty. Treatment and management will be interrupted if the education and instruction are insufficient, which results in poor control and increased risk of death from asthma. Children are directly instructed at their consultation. As it is often the case that not enough time may be taken in outpatient departments, it is far more effective to hospitalize children with severe persistent asthma for education and instruction during a summer vacation or when they can take time off from schoolwork without difficulty.

(5) Pubertal and adolescent patients have problems such as low compliance, remodeling, and death from asthma. Understanding the characteristics and problems of pubertal asthma on the patient’s part is important for treatment and management (Fig. 6). Points of management and treatment for pubertal asthma are demonstrated in Table 23.

9.1. Improvement in adherence
Sharing a treatment goal and establishing a partnership are important to both patient and doctor. The patient’s basic knowledge and skills should be checked repeatedly at consultations to help him/her take a positive attitude toward treatment and high adherence.

10. Exercise-induced asthma
EIA is a phenomenon in which wheezing and dyspnea occur temporarily during or after exercise. Its pathology is yet to be clarified. Cooling in the airway caused by hyperventilation during exercise and elevated osmolality in the airway epithelium due to water loss are potential mechanisms responsible for the underlying pathophysiology. Increased airway temperature after exercise may also be involved.

If coughing, wheezing, and dyspnea occur during or after exercise, a diagnosis of EIA may be easily made. An exercise stress test is conducted to quantitate the EIA. If the maximal percent decreases of the forced expiratory volume in 1 s (FEV1) and PEF are larger than 15% and 20%, respectively, a diagnosis of EIA is confirmed. The maximum decrease in the rate of FEV1 after exercise is higher in patients with more severe asthma. This serves as a parameter in the determination of the severity of asthma. Because EIA is also associated with airway hyper-responsiveness, the patient’s history with respect to EIA provides clues as to whether the current treatment step is appropriate.

To prevent EIA, the appropriate treatment step should be selected based on severity. If in fact EIA has occurred, the procedures shown in Table 24 may prevent its repetition.

Exercise does not have to be restricted because it otherwise benefits the child’s growth in various ways. Parents, teachers, school officials, school physicians, and attending physicians should collaborate to take measures so that children with asthma can safely participate in exercise at preschools and schools.

11. Participation in events at preschools and schools
Parents of children with asthma and their attending physicians should help to make supportive plans for their extra curricular activities such as school trips, camps, and excursions, in cooperation with preschools and schools so that those children can participate in these events whenever possible. Methods of treatment for acute exacerbation must be provided to children with asthma and their parents beforehand when taking part in such events.

If children with asthma develop acute exacerbation while participating in an event, a β2 agonist should be given earlier than it would be in a regular treatment schedule because of the special situation. Likewise, depending on the status of daily symptoms, an increase of the daily dose of ICS and/or short-term oral administration of a corticosteroid should be considered. In case acute
1. Recognition of features and pathophysiology in adolescent asthma
2. Evaluation
   - Adherence
   - Disincentive factors
   - Motivation to adherence
   - Ease of access to medical facilities
3. Control levels
   - Asthma diary
   - PEF (peak expiratory flow) monitoring
   - EIA
   - JPAC (Japanese Pediatric Asthma Control Program)
   - C-ACT (Childhood Asthma Control Test)
   - Remodeling, small airway obstruction and airway inflammation
   - Circadian variation of PEF
   - Flow volume curve
4. Support for increasing self-management ability
   - Establishment of good relationships between medical staff and patients and family members
   - Easy and sufficient explanation for asthma pathophysiology
   - Provision of education programs
   - Sufficient advice for cessation of smoking, school activities, work, marriage, child birth, etc.
   - Raise awareness of asthma-death
5. Establishment of medical support in various places
   - Provision of specific action plan for asthma management
   - Reconfirmation of own management and treatment goal
6. Reevaluation of treatment and management
   - Evaluation of current medical plan
   - Step-up therapeutic plan if necessary

<table>
<thead>
<tr>
<th>Adherence</th>
<th>Disincentive factors</th>
<th>Motivation to adherence</th>
<th>Ease of access to medical facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma diary</td>
<td>PEF (peak expiratory flow) monitoring</td>
<td>EIA</td>
<td>JPAC (Japanese Pediatric Asthma Control Program)</td>
</tr>
<tr>
<td>C-ACT (Childhood Asthma Control Test)</td>
<td>Remodeling, small airway obstruction and airway inflammation</td>
<td>Circadian variation of PEF</td>
<td>Flow volume curve</td>
</tr>
<tr>
<td>Support for increasing self-management ability</td>
<td>Establishment of good relationships between medical staff and patients and family members</td>
<td>Easy and sufficient explanation for asthma pathophysiology</td>
<td>Provision of education programs</td>
</tr>
<tr>
<td>Sufficient advice for cessation of smoking, school activities, work, marriage, child birth, etc.</td>
<td>Raise awareness of asthma-death</td>
<td>Provision of specific action plan for asthma management</td>
<td>Reconfirmation of own management and treatment goal</td>
</tr>
<tr>
<td>Establishment of medical support in various places</td>
<td>Provision of medical information about patients</td>
<td>Preparation of instruction forms in acute exacerbation</td>
<td>Preparation of referral forms in school trips, extra curricular activities and travels</td>
</tr>
<tr>
<td>Support to enhance understanding in workplace</td>
<td>Assessment of complications</td>
<td>Allergic rhinitis, sinusitis</td>
<td>Pneumothorax, subcutaneous emphysema, mediastinal emphysema</td>
</tr>
<tr>
<td>Psychosomatic diseases</td>
<td>Reevaluation of treatment and management</td>
<td>Evaluation of current medical plan</td>
<td>Step-up therapeutic plan if necessary</td>
</tr>
</tbody>
</table>

Children with any of the five allergic diseases are required to submit the form when entering preschool and school in Japan. This form provides information on the treatment for the child’s allergic diseases, with precautionary measures to take on the part of the administration. The form also gives emergency contact telephone numbers and names of consulting medical institutions and physicians in emergency for the patient’s safety.

11.3. Precautions for vaccination

Conditions such as bronchial asthma, atopic dermatitis, allergic rhinitis, urticaria, or allergic predisposition alone do not preclude vaccination. However, attention should be paid as to whether patients are potentially allergic to vaccine components including vaccine additives. A preliminary diagnosis considering previous allergic symptoms may be conducted. ICS and topical use of glucocorticosteroid do not exclude vaccination.

11.4. Vaccine additives and inoculum components for allergy

Reportedly, gelatin (stabilizer), thimerosal (antiseptics), egg ingredients (culture components), and antimicrobials included in vaccines can cause allergy. The physician should carefully refer to the attached document before giving an injection because constituents may differ in formulations produced by different pharmaceutical companies.

11.5. Major vaccines for children with asthma

1. Warm-ups before exercise
2. Drugs
   - β2 stimulant
   - DSCG
   - LTRA
   - Other medications
3. Others
   - Mask
   - Training regularly

| Light exercise causing mild EIA reduces EIA that is induced subsequent to hard exercise because of the refractory period.
| Inhalation or intake of β2 stimulant 15 min or 60 min before exercise inhibits EIA. However, use of β2 stimulant should be limited, because β2 stimulant may induce airway hyper-responsiveness. Reduction of EIA by training regularly is preferable.
| Inhalation of DSCG 15 min before exercise prevents reduction of FEV1 and PEF.
| LTRA inhibits EIA.
| EIA indicates poor control of asthma. Adequate treatment with controller drugs including ICS and LTRA prevents EIA.
| Wearing mask prevents EIA because it helps inhalation of air with adequate moisture and temperature.
| Regular training reduces severity of EIA.

Prevention in acute exacerbation: Prophylaxis of exercise-induced asthma (EIA).
11.6. Considerations for surgery

Because asthma is a risk factor in patients undergoing general anesthesia, especially inhalation anesthesia, attention must be paid to the management of physical conditions before and during surgery and also for respiratory management after surgery.

For non-emergency surgery, a period of at least 2 weeks of no paroxysmal symptoms is required after exacerbation even in patients with mild persistent asthma. If asthma exacerbation occurs within 2 weeks of the previous exacerbation, surgery should be postponed. In cases of non-emergency surgery, a period of 2 or 3 months with no exacerbation before surgery is recommended, because it takes several months before airway hyper-responsiveness becomes sufficiently reduced.

Complications and allergic reactions to drugs, medical materials, latex, foods, among other things, must be investigated before surgery. Caution to avoid adrenocortical insufficiency is needed in patients administered systemic steroid for 6 months or longer. Systemic steroids should be administered after surgery as well.

12. Conclusion

A new edition of JAGL has been introduced that reflects recent progress in strategies of asthma treatment and management for children. Long-term management with anti-inflammatory controller drugs, elimination of airborne antigens from the patient's living environment, and enlightenment and education about bronchial asthma including pathophysiology are three fundamental factors for the treatment and management of childhood asthma. It is important to maintain a well-controlled state for a sufficient period of time, which in turn affords a good QOL and may ultimately result in remission and cure. A well-controlled state is defined as a completely controlled status without subtle symptoms including even a short period of wheezing. Essential information is summarized in this review.

Acknowledgements

We, finally, appreciate very much the great support from the following committee members of JAGL 2012: Yukoh Aihara, Akira Akasawa, Yuichi Adachi, Toshihlike Ikebe, Kunio Ichikawa, Toshishige Inoue, Totsuom Inoue, Atsuo Irisu, Yukihito Obaya, Kenji Okada, Hiroshi Odajima, Toshio Katsunuma, Makoto Kameda, Kazuyuki Kurihara, Tatsuo Sakamoto, Naoki Shimoji, Yutaka Suehiro, Kenichi Inoue, Tsutomu Iwata, Atsuo Urisu, Yukihiro Ohya, Kenji Okada, and Tsutomu Iwata.

Conflict of interest

The authors have no conflict of interest to declare.

References


