Canadian consensus on the treatment of asthma in children

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In recent years there has been considerable publicity about the management of asthma since the recognition that in many countries the rates of death and illness associated with this disease are increasing. Attempts have been made internationally to standardize treatment guidelines, but these appear to have had limited impact in Canada. Furthermore, discussions of the management of asthma frequently ignore the unique requirements of children.

To address these concerns a 2-day roundtable meeting was held in Toronto in September 1990. The participants represented several specialties but were all experts in the treatment of pediatric asthma. The meeting focused on pediatric asthma in Canada and had the objective of formulating simple management guidelines to be applied by primary care physicians.

The guidelines were drawn up only after several presentations and discussions. The presentations were essentially extensive reviews of topics, from the definition and epidemiologic and pathophysiologic features of asthma to the various therapeutic methods in use. After each presentation an exhaustive roundtable discussion took place, and during the final stages the resultant conclusions were framed as rough guidelines.

After the meeting the guidelines were synthesized and refined by the chairman and then sent to the other participants for their approval. The final recommendations were incorporated and form the substance of this article. The main findings are summarized in the treatment algorithms.

Definition

The various pathophysiologic mechanisms and clinical manifestations of asthma make it difficult to formulate a clear-cut definition. In the case of children the difficulty is magnified because of the overlap of symptoms of asthma with those of related respiratory disorders and because of the limitations of the available diagnostic tools. Misdiagnosis is all too common: asthma is often confused with conditions such as chronic bronchitis and bronchiolitis.[1] A

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proper definition is crucial if asthma in children is to be diagnosed and treated appropriately. We therefore use the definition of Canny and Levison,[2] who proposed that "any child, regardless of age, with recurrent (three or more) episodes of wheezing and/or dyspnea be considered as having asthma until proven otherwise."

About 5% of children with asthma present with a chronic cough without wheezing. Some children are misdiagnosed as having recurrent pneumonia on the basis of radiographic examination, whereas the infiltrates seen represent recurrent atelectasis due to plugging of the peripheral airways by mucus.[3]

Asthma is much more likely in children than in adults to involve acute and severe episodes, which may develop in a few days or even hours. Asthma is often initiated by a viral infection, and prompt, effective treatment is necessary to prevent frequent visits to the emergency department or readmissions to hospital. The diagnosis may be more difficult in children than in adults, since young children are unable to undergo pulmonary function and bronchial provocation tests.

Pathophysiologic features

In the past few years much has been learned about the mechanisms and mediators involved in asthma. Undoubtedly, inflammation has an important role in most cases, as do bronchospasm and hyperresponsiveness of the airways to physical and environmental stimuli.[4-7] However, no single mechanism can be shown to be present in all cases. Asthma is a complex disease expressed in various ways and with various degrees of severity; much depends on the individual patient and the trigger. Certainly, the distinct responses to the different types of pharmacotherapy underline this point. Although each antiasthmatic drug has been shown to act on one or more of the pathophysiologic mechanisms none is universally efficacious. Thus, therapy can never be of a "cookbook" nature; instead, it must be tailored to each patient.

Table 1: Asthma history*

Nature of symptoms
Pattern of symptoms (severity, frequency and seasonal and diurnal variation)
Precipitating or aggravating factors
Profile of typical acute episode (including visits to the emergency department, hospital admissions and admissions to the intensive care unit)
Previous and current drug therapy (response, dosage, delivery and side effects)
Impact of disease on child and family (e.g., exercise intolerance, sleep disturbance and financial difficulties)
Atopic history
School performance and attendance
Psychosocial evaluation of patient and family
Environmental history (including active or passive smoking and housing conditions)
Family history
General medical history of child

*Reproduced with permission and modifications from Canny and associates.[9]

Prevalence

Although asthma is common there are few, if any, studies of the prevalence of childhood asthma and its treatment in Canada. Most of the data are obtained from records of emergency department visits and hospital admissions and therefore reflect treatment failures rather than successes. The available data do indicate that rates of asthma-related hospital admissions continue to increase, as seen in other developed countries. There was a slight increase in the death rate among young people with asthma between 1971 and 1988.[8]

Diagnosis

Regardless of the patient's age the primary diagnostic indicators stem from the history and the physical examination. The history should profile the family and the patient's symptoms (Table 1); the information derived could help rule out other severe conditions that might present in a similar fashion, including cystic fibrosis, heart disease and an inhaled foreign body. The diagnosis of asthma is frequently one of exclusion and is confirmed by a therapeutic trial.

The initial evaluation should include pulmonary function studies — of either the peak airflow rate or the forced expiratory volume in 1 second — to establish a baseline before treatment is begun. If the child is symptom-free the test results may be normal. However, if airway obstruction is present a diagnosis of asthma can be confirmed by the demonstration of a significant improvement in airflow rates after inhalation of a β_2 agonist. Most children over 6 years of age can undergo these studies well enough to justify the use of these agents. However, airflow studies are generally not possible in younger children except in highly specialized laboratories.

A brief therapeutic trial with antiasthmatic medication may confirm the diagnosis of asthma much more efficiently than pulmonary function studies. A record of the changes in airflow rates measured at home or a symptom diary that is carefully kept (by the parents), or both, can adequately show the response to medication and probably yields as much definitive information as would an exercise, methacholine or histamine challenge. Up to 30% of healthy children without asthma have an abnormal response

to these challenges. If the diagnosis is still in doubt other investigations, such as a radiographic examination, are indicated.

Environmental control

Most asthmatic children over the age of 3 are atopic, and limited skin testing to determine possible sensitivity to environmental allergens is a reasonable measure. Once the offending allergen has been identified the patient and his or her parents can be counselled on ways to avoid or limit exposure to it. The recommended skin prick tests are for the two most common dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*), cats, dogs and a saline control. Sometimes additional tests are indicated (e.g., for pollens). A histamine control test should be performed in case the child has recently received antihistamines. Radioallergosorbent tests are an alternative if skin prick tests cannot be performed.

If there is a demonstrated sensitivity to a household allergen avoidance measures — if performed correctly — can be effective in ameliorating symptoms of asthma (Table 2).[10,11] The importance of environmental manipulation should be explained to the child's parents and reinforced with written instructions that clearly detail effective methods of avoidance. Too often parents waste time and effort on useless measures. For example, they may scrub the bedroom walls in the mistaken belief that this will reduce the child's exposure to house dust mites; however, mites do not live on walls!

Smoking

Exposure to smoke increases the risk of asthma in children who have atopic dermatitis;[12,13] parents of all such children should therefore be encouraged not to smoke. The need to eliminate or drastically reduce an asthmatic patient's exposure to smoke from cigarettes, cigars and pipes cannot be emphasized strongly enough. Exposure to tobacco smoke aggravates symptoms of asthma, increases bronchial irritability and decreases pulmonary airflow rates.[12] There should be no smoking in the home or, if the child is present, in the car.

Household pets

Cat dander and, to a lesser extent, dog dander are key culprits in triggering asthmatic symptoms; they also increase bronchial hyperresponsiveness, which results in a low threshold for symptoms provoked by exercise or cold air. Therefore, the child's bedroom should be off limits to pets that have fur or feathers. Complete removal of a pet is indicated if it is of a species to which the child is allergic, as demonstrated by a skin test or symptoms. Even if the pet were confined to the basement its dander would continue to circulate throughout the house. Parents should be informed that it may take several months after a pet is removed from the house to eliminate all traces of animal hair and dander, even with steam-cleaning of the carpets and upholstery.[14] Families who are considering acquiring a pet should definitely be advised against this.

Education

Education of the parents and child (when he or she is old enough) is essential to convey the nature of asthma, the factors that aggravate it and the methods of treatment. There must be an understanding of how medications are administered and how they work and of possible side effects; physicians should emphasize these points routinely. Written instructions should be provided to explain methods of drug administration during an acute asthmatic episode and to describe the conditions under which medical help should be promptly sought.

Children should be included in the management program as soon as they are able to understand it, and they must be encouraged to assume the responsibility of managing their condition as they approach adolescence.

Psychologic management

Though psychologic factors do not cause asthma

Table 2: How to create an allergen-free bedroom*

Install zippered plastic or vinyl covers that completely enclose the mattress and box spring; the pillows should be encased in plastic or laundered once a month
Remove fluffy stuffed animals and upholstered furniture
Remove carpeting
All bedding should be laundered every 2 weeks, preferably at water temperatures of 68°C
If there is a family pet keep it out of the child's bedroom or outside the house if possible; if an allergic reaction has been demonstrated through exposure to any animal of the same species or through a positive skin prick test, removal of the pet from the household is mandatory
No smoking in the house
If humidifiers are in use during the winter months keep the humidity well below 50%; higher levels permit growth of dust mites
Air conditioning is helpful if the patient is allergic to mites or pollens since it will lower the relative humidity; windows can be kept closed to stop pollens from drifting in

*Reproduced with permission and modifications from Murray and Ferguson.[10]

they can have a significant effect on the frequency and severity of attacks. Stress and anxiety can trigger symptoms of acute asthma. If a child does not respond to management as well as would be expected the possibility of underlying psychologic and family problems, difficulties with compliance or physical changes should be considered. Teachers should be made aware of the child's asthma and its treatment and should have written instructions on how to handle emergencies.

Immunotherapy

There is evidence that specific hyposensitization (immunotherapy) lessens bronchial sensitivity to certain allergens (e.g., cat hair); however, its value in asthma remains controversial.[15,16] If implemented, immunotherapy should be used in conjunction with medication and never as the sole form of treatment.

Pharmacotherapy

Pharmacologic agents in the treatment of asthma fall into two categories: bronchodilators, which include the β_2 agonists, anticholinergics and methylxanthines, and the anti-inflammatory prophylactic agents, which include sodium cromoglycate, ketotifen and corticosteroids (inhaled and taken orally).

The role of new and old drug therapies

The methylxanthines or theophylline preparations have a low therapeutic index and significant side effects. Recently there have been suggestions that theophylline affects cognition and behaviour;[17] however, the findings are controversial, and many people feel that the data are still inconclusive. Although no longer considered a first-line therapy for asthma theophylline may still be a useful medication in patients (a) who have moderate to severe asthma but do not benefit from β_2 agonist and inhaled steroid therapy, (b) who cannot take inhaled medications (small children) or (c) who have nocturnal asthma. Persistent nocturnal symptoms probably warrant consideration of other prophylactic therapies.

Ipratropium bromide is a bronchodilator that has a different mechanism of action from a β_2 agonist. Some studies[18-20] but not all[21,22] suggest that a combination of these two agents may provide increased bronchodilation in acute episodes of asthma. However, ipratropium bromide is not indicated as first-line therapy, and its role in the treatment of chronic asthma is not clearly defined.

First developed as an antihistamine ketotifen is now recognized to have anti-inflammatory properties. It has demonstrated a prophylactic, anti-asthmatic effect comparable to that of sodium cromoglycate in selected patients.[23-26] In asthmatic patients with coexisting allergic rhinitis ketotifen may provide an additional antirhinitic effect. Ketotifen takes up to 8 to 12 weeks to achieve its full effect.

Modes of drug delivery

Whenever possible inhalation of the drug by means of a metered dose inhaler (MDI) or one of the powder inhalers is preferred. Unlike oral or parenteral administration, inhalation allows for direct delivery of the medication into the airways;[27] this maximizes drug efficacy and minimizes the total dose required. As well, there is a correspondingly lower incidence of side effects.[27]

Portable and inexpensive, MDIs and dry-powder inhalers are probably ideal for use in children over 7 years of age. With careful and regular instruction even children as young as 3 years can benefit from them. These younger children, along with older children who have a poor inhalation technique, should use a spacer with the MDI. For children under 3 years of age a masked aerochamber can be used.

Nebulizers are used in hospitals and at home with increasing (and sometimes disturbing) frequency and have a specific place in the management of asthma. They are of great benefit to children with severe, chronic asthma, a history of life-threatening attacks or a demonstrated inability to use MDIs or dry-powder inhalers (e.g., very young children).

Treatment

Asthma therapy is aimed at achieving a level of symptom control that will allow for a normal quality of life for the child: participation in regular sports activities, unimpaired school performance and uninterrupted sleep. Treatment strategies will vary depending on the degree of severity and the frequency of symptoms. As the use of medications becomes more complex greater attention should be paid to short-term and long-term side effects (e.g., effects on growth and cognition).

Mild, infrequent asthma

Most children (75%) with asthma experience only mild and sporadic episodes of coughing and wheezing in the course of a year. Generally, their quality of life is unaffected, and their symptoms are controlled by the intermittent administration of a β_2 agonist (Fig. 1). For these children prophylactic agents are only indicated if a precipitating event such as exercise or exposure to cold air, animals or pollen is expected. Asthma symptoms that occur

seasonally may be treated with an agent such as sodium cromoglycate or ketotifen, administered 6 to 8 weeks before the start of the pollen season and continued until the end of it.

Frequent, episodic asthma

Approximately 20% of asthmatic children have symptoms that are frequent (more than six episodes per year) or severe enough, or both, to affect schooling, interrupt sleep and often obstruct airways. As a result, there may be a growing and unhealthy dependence on bronchodilator use for normal functioning. "Unhealthy dependence" may be described as the routine use of bronchodilators twice a day or more (Fig. 2). Daily prophylactic therapy is indicated in these children. A trial of sodium cromoglycate (which has a good safety profile) or of ketotifen should be implemented.[22-25] Although inhaled corticosteroids are highly efficacious they are not first-line prophylactic medications in this context, since their long-term effects are as yet undetermined.

Sodium cromoglycate can be administered four times daily initially and then three times or twice daily when the patient's condition is stable. Ketotifen is given orally twice daily; this mode of delivery is particularly advantageous, especially in young children. If no therapeutic effect can be seen after 6 to 8 weeks with sodium cromoglycate or 8 to 12 weeks with ketotifen, inhaled corticosteroid treatment should be introduced. Once corticosteroid therapy is begun sodium cromoglycate or ketotifen therapy should be stopped.

Although there has long been concern regarding the systemic side effects of oral corticosteroid treatment many short-term studies have shown that low doses of inhaled corticosteroids are safe for use in children.[29-31] Initially, doses of 400 μg/d (200 μg twice daily to encourage compliance) should be administered in conjunction with a β_2 agonist. Depending on the clinical response the dose can be modified. The corticosteroids should be administered with the use of a spacer to increase their effectiveness and to minimize the risk of oropharyngeal candidiasis.

Before prophylaxis is begun the patient's condition must be stabilized through the use of β_2 agonists combined, if necessary, with corticosteroids given orally.

Severe, chronic asthma

Children with severe, chronic asthma constitute a small minority (5%). Aggressive therapy is warranted to alleviate persistent daily symptoms, chronic airway obstruction, constantly interrupted sleep and poor exercise tolerance (Fig. 3). Inhalation of larger doses of corticosteroids (more than 1000 μg/d, upper limit 1600 μg/d) may be considered. At present it is unclear how well these larger doses will be tolerated

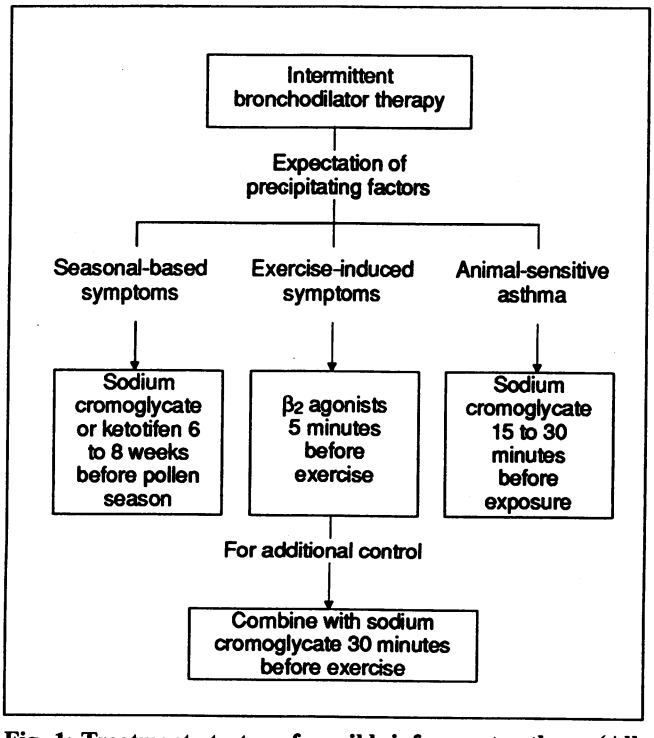

Fig. 1: Treatment strategy for mild, infrequent asthma. (All four figures are reproduced with permission and modifications from Levison.[28])

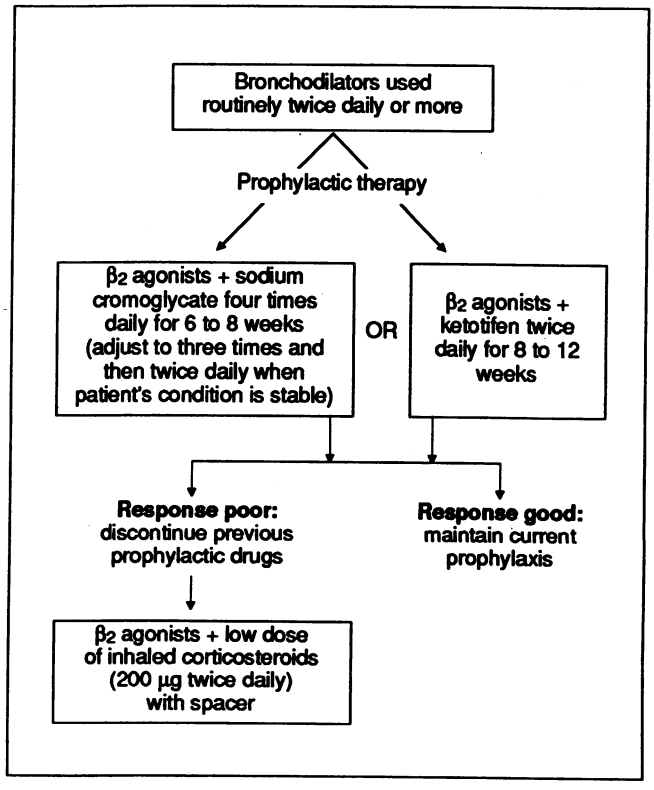

Fig. 2: Treatment strategy for frequent, episodic asthma.

before adrenal suppression, bone demineralization or cataracts occur. If bronchodilation is insufficient with standard β_2 agonist therapy alone a sustained-release theophylline preparation or ipratropium bromide should be added.

A short course of oral therapy with corticosteroids (e.g., prednisone, 1 mg/kg daily for 5 to 7 days) can be recommended in cases of acute, severe episodes of asthma at home. Such a measure may reduce the need for admission to hospital.[32-34] An alternate-day regimen that calls for the lowest possible dose of prednisone or prednisolone is desirable to minimize systemic side effects. A gradual reduction of the dose should be attempted once the patient's condition is stable.

With the use of corticosteroids in general the patient's height, weight and blood pressure need to be monitored; in addition, a slit-lamp examination should be performed at intervals of 6 to 12 months to check for early cataract formation.

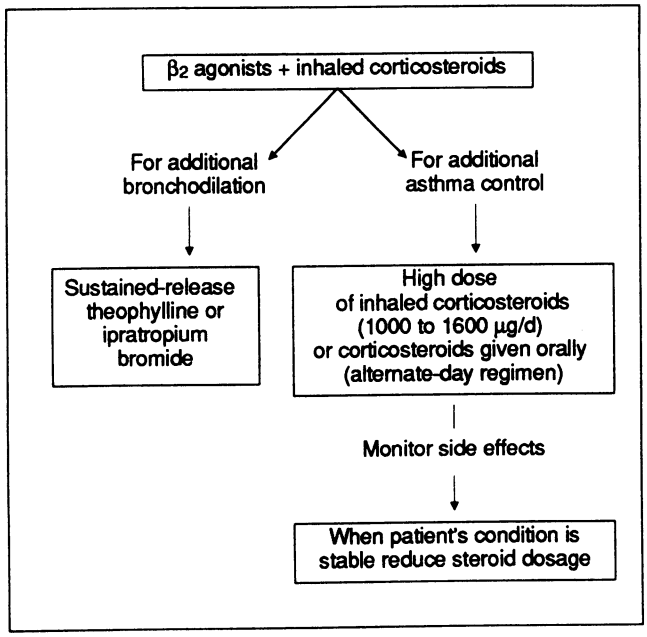

Fig. 3: Treatment strategy for severe, chronic asthma.

Asthma in infants and young children

Because of the difficulties in treating very young children a number of pharmacotherapeutic options should be pursued in sequence (Fig. 4). However, these options must take into account that a nebulizer with a mask attachment is probably the only effective means of drug delivery. The exception to this is in cases of very mild asthma, for which a trial of oral therapy with a β_2 agonist should be attempted first.

As a rule a nebulized β_2 agonist constitutes the first line of therapy. If no clinical benefit is seen nebulized ipratropium bromide may be added, and if symptoms persist nebulized sodium cromoglycate or oral therapy with ketotifen could be attempted. Therapy should be supplemented with a sustained-release theophylline preparation if there is still inadequate control. As a last line of therapy corticosteroids may be administered orally (using the alternate-day regimen), particularly in cases of severe, chronic asthma. It is hoped that nebulizing solutions of corticosteroids will soon be available.

Exercise-induced asthma

Exercise-induced asthma is most effectively controlled with a β_2 agonist inhaled approximately 5 minutes before exercise.[35] Sodium cromoglycate taken half an hour before exercise is effective in about 60% of children and can be used with the β_2 agonist if necessary. A lack of response to these measures implies poor asthma control, and other prophylactic agents should be considered.

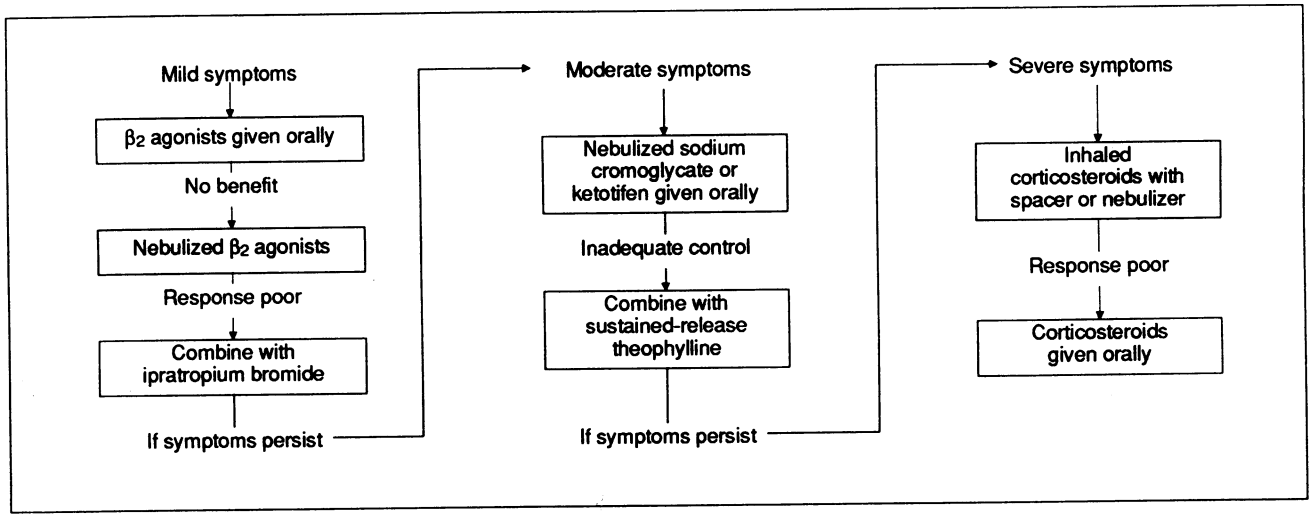

Fig. 4: Treatment strategy for asthma in infants and young children.

Nocturnal asthma

Disruptive symptoms of coughing and wheezing during the night are indicative of poor asthma control and, hence, inadequate therapy. Daytime therapy should first be corrected with the use of an inhaled bronchodilator and a prophylactic agent. If nocturnal symptoms persist a long-acting theophylline preparation taken at bedtime is often effective.[36,37] Environmental control measures should be considered for patients with a demonstrated sensitivity to household allergens.

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