Respiratory Medicine (2000) **94,** 299–327
doi:10.1053/rmed.1999.0702, available online at http://www.idealibrary.com on IDEAL®

Report

Nordic consensus report on asthma management

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The work with the Nordic consensus report on asthma management started some years ago. The Nordic countries have common socioeconomic conditions. We acknowledge the international as well as other European guidelines providing valuable recommendations. Nevertheless, we felt the need to combine the common Nordic experiences in order to have a local statement of asthma and asthma care, based upon Nordic clinical science and tradition. The work has been rewarding and we acknowledge many valuable contributions from paediatricians, allergologists and lung physicians in all Nordic countries. The response has so far been positive and we feel that the present material reflects the main opinion of Nordic physicians taking care of asthma patients of all ages. However, the asthma and allergy research field is rapidly developing. Thus, this document should merely be regarded as a time-limited contribution to the continuing scientific discussion of this fascinating field.

Respir. Med. (2000) **94,** 299–327

Introduction

Asthma is a common disease, which affects all age groups. Four to 10% of the population in the western world suffers from asthma.

It is still a matter of dispute whether asthma prevalence really has increased, or if the increase in prevalence reported mainly reflects an increased awareness of the disease. The increase is probably real, and objective measurements such as bronchial hyper-responsiveness to methacholine and exercise tests, have confirmed an increased prevalence over time. Many studies speak in favour of a real prevalence increase, especially in children and young adults, and the number of patients seeking medical help because of asthma has increased. In Scandinavian countries the mortality among young children (<4–5 years) has decreased, probably due to improved acute treatment and monitoring, as well as improved regular treatment.

Alarming periods of sharply increasing asthma mortality have been described in some countries: in the sixties in England and Wales and more recently in New Zealand.

The direct and indirect expenses caused by asthma are considerable and increasing. Asthma, as it manifests itself in the community, is a major healthcare problem. The disease not only demands community action in treatment and care but, also, preventive measures in order to avoid further increase.

Although the basic pathophysiological mechanisms manifesting ultimately as asthma symptoms take place in the airway structures of the lungs, asthma is characteristically a disease with a strong relationship to environmental and living conditions. The classical example is worsening asthma caused by allergens and pollutants. Asthma symptoms are also precipitated by various environmental and physical factors, and respiratory virus infections are major triggers of asthma episodes. In the Nordic countries asthma symptoms caused by cold weather are common and many environmental factors play a key role in the prevention and management of asthma symptoms.

However, air pollution in a broad sense does not explain the increased asthma prevalence. Several studies have

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0954-6111/00/040299+29 $35·00/0

shown a considerably lower prevalence of asthma and allergy in Eastern European countries and in developing countries, despite a high degree of air pollution. Therefore, other factors such as microbial defence, sedentary lifestyle, nutritional status and diet together with other living conditions need to be addressed.

The capabilities of modern asthma management, including preventive measures and early intervention with anti-inflammatory agents, give a better outlook for asthma sufferers. However, asthmatics still have restrictions in daily life such as disturbed night sleep, avoidance of physical and social activities, and loss of school and work days. As a consequence, various national asthma programmes and guidelines have been published during the last few years.

Poor understanding of asthma among healthcare professionals, as well as among patients, is one reason for sub-optimal asthma treatment results. The failure to identify asthma symptoms, over-reliance on bronchodilators, reluctance to use inhaled steroids, insufficient environmental actions and the lack of objective follow-up and appropriate treatment during asthma exacerbations are the problems commonly seen in asthma care. Furthermore, failure to use inhalation devices and bad treatment compliance are often seen among asthmatics. Supervised asthma self-care programmes have been developed to overcome these common problems. Education on different levels is needed before modern asthma treatment can benefit the general asthma population.

The Nordic countries share many similarities in their social, cultural and economical status, and also in their healthcare systems. Therefore it was decided to set up a Nordic Asthma Consensus Group, with the task of preparing common guidelines and suggestions for the Nordic countries to meet the increasing challenges of asthma.

Although this paper is intended mainly for physicians and other healthcare professionals, it is hoped that many important stakeholders such as administrators, environmentalists, politicians involved in healthcare and health educators will find the information useful. Wide national co-operation, not forgetting public opinion, is needed to alleviate the suffering caused by asthma.

Successful asthma management is a combination of good knowledge among professionals and the asthmatic patient. Asthma care needs good facilities, which are useful investments today to make savings for tomorrow.

Definition, diagnosis and early intervention

DEFINITION

Asthma is a chronic airway disease characterized by episodes of wheezing, cough and dyspnoea. It is associated with inflammation of the intrapulmonary airways, which is the main cause of bronchoconstriction. Several inflammatory cells, the eosinophil being one of the most important, and several cellular mediators are involved in the pathogenesis. The airways show increased responsiveness reacting with smooth muscle constriction and inflammation to a variety of stimuli. The airway obstruction may vary spontaneously or can be reversed at least partly by treatment.

PREVALENCE

The prevalence of current asthma in adults is between 2 and 5% in Nordic countries, the highest figures being reported in northern parts of Sweden (1,2). The prevalence among Nordic school children is about 5–10%, with the cumulative incidence another 50% higher (3), implying a doubling of asthma prevalence in 20 years time (4,5). This evolutional pattern seems similar to observations in other countries (6,7,8).

MORBIDITY AND MORTALITY

Despite the increased asthma incidence, a decrease in total days of hospital treatment for asthma in children above 2–3 years of age, as well as in adults, has been noted during the last decade (9,10,11). This mainly reflects the changes in therapeutic approach that has occurred during this time period in active anti-inflammatory treatment, largely in the form of widespread introduction of use of inhaled steroids for children with moderately severe asthma. This is discussed in more detail in the Health economy section.

Mortality has remained unchanged or has decreased in children. In Finland a decrease in mortality in relation to the number of individuals suffering from asthma has been observed during the last 15 years (11).

ALLERGIC SENSITIZATION

Allergic sensitization is the production of specific Ig-E antibodies to an allergen, not necessarily causing symptoms. The term 'allergy' means the presence of both specific Ig-E and concordant symptoms, after exposure to the relevant allergen. Allergic sensitization is more common in children with asthma than in an adult population of asthmatics. At least 70–80% of school children with asthma are sensitized towards one or more common allergens (12), whereas after the age of 40 years, less than 50% of the population demonstrate the presence of specific Ig-E. The frequency of respiratory allergy in the age group from 7–16 years has increased considerably during recent decades (13). The ability to become sensitized depends upon genetic factors and environmental exposure. Our genetic background has not changed and twin studies support the idea that environmental influences are the major contributors to the present situation (14,15).

Increased exposure to environmental allergens such as animal danders, house dust mites and occupational sensitizers may have taken place. However, allergen exposure has always existed and sensitization has not only increased to indoor allergens, but also to outdoor allergens such as grass and birch pollen. These observations imply an effect of some adjuvant factors which facilitate sensitization. Examples of such adjuvant factors are tobacco-smoke,

other environmental pollutants, poor indoor climate and viral infections. Children of smoking parents have a substantially increased incidence of respiratory allergy, as well as increased frequency of upper airway symptoms and infections (16). Children spending their days in nurseries have a considerably higher number of viral respiratory tract infections, which also aggravates symptoms of respiratory allergy. Other contributing factors that have been proposed are general changes in the many aspects of life style associated with urbanization, industrialization, viral and bacterial infections and diet.

The increase in asthma prevalence represents a multifactorial problem threatening our society. New ideas are urgently needed to avoid this health problem escalating further.

Early detection of asthma and early intervention is important. Early intervention does not only mean pharmacological treatment. It is important to identify the environmental exposures. For example, in many cases of occupational asthma, the duration of symptoms caused by work-related agents is directly associated with long-term prognosis of the disease (17).

When obstructive lung disorder is suspected, measurement of lung function is as important as the measurement of blood pressure in patients with hypertension. Any doctor taking care of children and adults with symptoms in the airways should have a peak flow instrument on his desk. Cheap and reliable spirometry equipment is also available. It is highly recommended that forced vital capacity (FVC) and forced expiratory volume in 1 sec (FEV_1) are recorded early in the course of the disease, and that spirometry is performed at least annually in order to detect a decline in lung function over time.

TESTING OF REVERSIBILITY

If obstruction is suspected, a reversibility test should be performed. Peak expiratory volume (PEF) or FEV_1 are recorded before and after bronchodilator treatment. In preschool children, tidal flow volume loops may be used (18). After 400 μg of inhaled salbutamol a maximal, or close to maximal, bronchodilator response is usually achieved within 5–10 min. Especially in middle aged and elderly patients, β_2-agonist treatment may be combined with ipratropium bromide. The onset of bronchodilatation following ipratropium bromide is slower and it is recommendable to wait 25–30 min before a second spirometry is performed. In children not able to inhale from a powder inhaler or pressurized metered dose inhaler (pMDI) with a spacer, a nebulized solution of salbutamol 0.05 mg kg^{-1} may be used.

An improvement from baseline of PEF > 15% (or > 60 l min^{-1}) or preferably $FEV_I > 12\%$ (or > 200 ml) means a clinically relevant reversible airway obstruction. In doubtful cases, with insufficient response, a spirometry after doubling the dose should be performed. When using tidal flow volume loops, a response larger then two SD of the intra-subject baseline variation may be interpreted as a positive response.

In non-responsive patients with persistent obstruction, an oral course of steroids can be instituted (e.g. prednisolone 20–40 mg daily for 2 weeks) and the reversibility test repeated. The increase of $FEV_I > 500$ ml or PEF > 100 l min^{-1} from baseline strongly suggest an asthma diagnosis in adults (19).

A normal lung function at the time of investigation does not by any means exclude asthma. If the history indicates recurrent obstruction, the patient should be instructed to measure PEF at home for a period of 1–2 weeks. PEF should be recorded the morning and evening before and after β_2-agonist inhalation, as well as on demand (e.g. when symptoms occur). This is especially important when environmentally induced obstruction is suspected.

A diurnal variability[1], with or without bronchodilator, > 15% (and more than 60 l) during 2 or more out of 7 days indicates asthma.

BRONCHIAL OBSTRUCTION RELATED TO RESPIRATORY TRACT INFECTION IN ADULTS

Many patients report their asthma as having started at the time of a respiratory tract viral infection. Some viral infections may have a pathophysiological role in the development of asthma and cause exacerbation of already existing asthma (see below).

The presence of airway obstruction in relation to respiratory tract infection is common and should not immediately be regarded as presence of asthma. However, most latent asthmatics, and those at risk of developing asthma, will present with obstruction related to respiratory tract infection. Consequently, a liberal use of spirometry and reversibility testing in patients with infection related airway symptoms is warranted.

Initiation of anti-inflammatory treatment in all patients with airway obstruction induced by infection could lead to unnecessary treatment. A short course of bronchodilator treatment (β_2 and/or ipratropium bromide), sometimes combined with oral acetylcysteine or antitussives, often provides sufficient relief for the vast majority of patients. However, it is important to re-evaluate the situation 1–2 months after the acute episode, in order to pick up those patients who have not fully recovered. In those cases, need for anti-inflammatory treatment (i.e. corticosteroids) should be evaluated.

WHEEZING IN INFANTS

Obstruction of the intrapulmonary airways in connection with respiratory infections is a common paediatric problem. It can be estimated that at least 15% of children have recurrent symptoms of airway obstruction at some point during infancy or at pre-school age. The clinical picture is characterized by wheezing, rhonchi, tachypnoea and chest retractions. The triggering factors are virus infection, most

[1](Highest PEF − Lowest PEF) × 100/Highest PEF

commonly respiratory syncytial virus (RSV), parainfluenza virus and rhino viruses (20,21,22). During the winter season, RSV can be demonstrated in half of the infants and toddlers hospitalized for such airway obstruction (23). At pre-school age, about 50% of children hospitalized because of 'wheezing bronchitis' when below 2 years of age have been found to have asthma (23). At school-age this figure decreases to about 25–30% (20,24,25). Factors correlating to persistence of asthma are atopy, that is other atopic diseases than asthma, usually atopic dermatitis or food allergy, and intense airway obstructive disease (23). On the other hand, total-IgE at birth or at the time of the first hospitalization is a poor predictor for development of asthma during infancy, or persisting asthma, respectively (23,26). Several follow-up studies have failed to demonstrate significant differences in long-term prognosis related to the initial specific virus agent demonstrated at the first hospitalization (20,23,25,27), although it is possible that very early RSV bronchiolitis may induce a process leading to asthma (28).

The implication of wheezing in connection to virus infections and asthma triggered by infections is debated. Recurrent symptoms, or symptoms in a child above the age of 2 years, suggests asthma. The diagnosis asthma can be strongly considered in the following circumstances:

1. From the third attack of airway obstruction during the last year is current asthma.
2. One attack of asthmatic symptoms occurring after the age of 2 years.
3. Irrespective of age in an attack in children with eczema, food allergy or other allergy.
4. If the child does not become free of symptoms when infection has ceased, or has persistent symptoms for more than a month.

Use of the asthma diagnosis from the third attack of airway obstruction is widely accepted. Empirically asthmatic symptoms appearing after the age of 2 years usually reflect hyper-reactive airways, which motivates use of the diagnosis asthma earlier than from the third episode of asthmatic symptoms. Similarly, when asthmatic symptoms with wheeze and rhonchi appear in an infant with other atopic symptoms, odds are high that asthmatic symptoms will recur at least up to school-age. This does not contradict that there are mild as well as severe forms of the disease, and that symptoms may disappear with age. The advantages of early asthma diagnosis according to the above criteria are to promote an active approach in terms of advice to parents, prophylaxis and pharmacotherapy.

'ALL THAT WHEEZES IS NOT ASTHMA'—DIFFERENTIAL DIAGNOSTIC PROBLEMS IN THE INFANT AND YOUNG CHILD

Respiratory infections

Airway symptoms such as stridor, chronic cough, or wheezing can be initiated by many different infectious agents like RSV, parainfluenza and rhino viruses, a least in children. *Bordetella pertussis*, Mycoplasma, *Chlamydia pneumoniae* and Tuberculosis should be considered in patients with chronic cough who are not responding to asthma treatment.

Cystic fibrosis

Cystic fibrosis (CF) in infants can start with symptoms of airway obstruction. Suspicion should arise when the clinical picture does not really fit. Children with CF often have recurrent pneumonias and poor weight gain. The correct diagnosis is obtained from the sweat test. In CF there is an elevated sweat chloride level >60 mmol l^{-1}. Genetic analysis supports the diagnosis.

Vascular anomalies

Usually this is a so-called vascular ring, which is often constituted by a double aortic arch. In the embryo, there is originally a ventral and a dorsal aorta. The ventral aorta should disappear during the fetal period. If this does not occur, the ventral aorta will compress the trachea and oesophagus like a snare. A symptom is more or less continuous stridor, audible in inspiration as well as expiration. A barium swallow will give the correct diagnosis. The vascular ring surrounding the oesophagus and trachea is visualized as a notch in the oesophagus. Treatment is surgical division of the vascular ring.

Laryngo-tracheomalacia

Congenital stridor, especially inspiratory stridor, starts in the neonatal period. The symptoms are aggravated during airway infections and when the child gets upset. The stridor disappears during the first year of life as cartilage in the trachea and larynx becomes firmer.

Cardiac diseases

Cardiac diseases with increased pulmonary blood flow may have symptoms similar to asthma.

Chronic lung disease of the newborn—broncho-pulmonary dysplasia

This lung disease with fibrosis can affect preterm children treated with artificial ventilation with high pressures and oxygen concentrations. The children usually have hyper-reactive airways and asthma-like symptoms with deterioration during respiratory infections. These children usually benefit from the pharmacotherapy given to children with asthma.

Corpus alienum

When suspicion of the diagnosis arises, the parents often start to remember a preceding episode when the child coughed violently while eating peanuts, a carrot, an orange segment or something similar. Pneumonia which recurs at the same location, or changes on chest X-ray which remain following treatment, should raise suspicion.

Tumours

Tumours, such as a lymphoma, leading to bronchial obstruction can produce symptoms similar to those of a corpus alienum.

Hilar lymph gland enlargement

Enlarged lymph nodes in tuberculosis can produce symptoms which can be misinterpreted as asthma.

Operated oesophageal atresia

These children often have asthmatic symptoms with deterioration in connection with viral infections.

Chronic lung disease due to immunodeficiency

Immunodeficiencies, such as deficiency of IgG or IgA, are often associated with respiratory tract infections and the potential development of bronchiectasis, as well as with allergic diseases.

Ciliary abnormalities and impaired mucociliary clearance

Ciliary defects can be misinterpreted as asthma. The clinical picture resembles cystic fibrosis with pneumonias which do not fully resolve. Electron microscopy of cilia obtained via biopsy from nasal or tracheal mucosa can give the diagnosis.

Pulmonary sequestration

This is characterized by non-functioning embryonic lung tissue with a blood supply from the systemic circulation. The tissue usually does not communicate with the functioning lung tissue. The condition is rare but should be considered in cases of recurrent or longstanding pneumonias with the same localization. Treatment consists of extirpation after the diagnosis has been established.

Lobar emphysema

Abnormal lobar distension can produce respiratory distress in an otherwise normal new born or infant. The lobar hyperaeration involves partial bronchial obstruction or intrinsic alveolar disease. Progressive respiratory distress from birth to 6 months of age, especially in the first month, parallels the degree of emphysema. Cough, wheezing, dyspnoea, tachypnoea, tachycardia, stridor and intermittent cyanosis are aggravated with feeding. Excisional therapy should be done when the diagnosis is accompanied by symptoms.

Vocal cord dysfunction

This condition is more likely to occur in adolescence, especially in teenage girls, than in childhood. The symptoms usually appear in connection to physical exercise and appear as stridorous breathing. The symptoms are often perceived as quite dramatic, both for patients and bystanders. The symptoms disappear without treatment when the patient relaxes. Quite naturally the response to anti-asthmatic treatment is poor and there is a risk attached to unnecessary medication. Fiberoptic visualization of the larynx region during exercise can give the diagnosis. Inspiratory and expiratory flow–volume spirometry during attacks is also helpful.

Health economy

Asthma is a common chronic disease which means large costs for the healthcare system (29,30,31,32). The still rising numbers of individuals suffering from asthma emphasizes the economical burden implied by the disease. Total annual costs of asthma in the U.S.A. has been calculated to $US 6206 million (33). For 1993 the society's annual costs for asthma in Sweden was calculated to SEK 3061 million ($US 398 million) for adults and SEK 514 million ($US 67 million) for children, amounting to a total of SEK 3575 million ($US 464 million) (34).

Two economically important consequences of persistent asthma are hospitalizations and lost production due to illness and retirement, and these may be reduced by improving treatment and patient education (11). In Denmark, the costs in 1995 for a 'well treated patient' were

TABLE 1. Costs for asthma in Sweden 1993 [in millions Swedish crowns from Persson *et al.* 1994 (34)]

	Children	Adults
Direct health costs		
Drugs	97·2	226·9
Outpatient treatment	153·6	358·5
Hospitalization	52·9	343·6
Indirect costs, lost production		
Sick leave	183·1	454·6
Supplementary disability pension	7·7	1519·0
Early death	19·1	158·4
Total	513·6	3061

DKK 37 723 and for a 'poorly treated patient' 48 579 per year. The costs for a patient with severe disease were DKK 171 489 and with mild disease 3180 per year. The total annual costs were estimated to be DKK 9.6 billion for an asthmatic population of 212 000.

In Finland it was estimated that 20% of those patients receiving reimbursement for drug costs—caused by regular medication—had severe disease while 60% had mild disease. The severely ill patients however cause 60–70% of the costs. To reduce the costs the patients with severe asthma should be treated more effectively, but in the long run preventing escalation of asthma to become persistent in the patients with mild to moderate disease could be even more cost saving (11,35).

Early diagnosis and appropriate medication of asthma reduces overall morbidity from the disease. Furthermore, optimal care and successful implementation of asthma management plans are valuable, not only for the well-being of the individual asthmatic, but for the profound effect on health economy. Such asthma management strategy involves avoidance of asthma triggers (e.g. passive smoking, house dust mites, indoor pets) and optimal drug therapy, which probably will not only reduce morbidity but also facilitate long-term preservation of lung function (36). In addition, early intervention with anti-inflammatory treatment most likely alters the natural course of the disease (37,38,39). Action plans for acute exacerbations have reduced asthma morbidity, and asthma education for children and adults has demonstrated cost savings in addition to health benefits (40).

During the last 20 years, asthma prevalence in school children in Sweden has doubled to 5–8% (4,41). The same trend has been demonstrated in Norway, which currently has prevalence figures approaching 10% (3), Denmark and Finland. Other European countries show a similar pattern. In some countries, such as the U.S.A., such a trend has led to increased hospitalization. However, during the last decade there has been a major change in the approach to asthma treatment, with a shift of emphasis from bronchodilators towards continuous anti-inflammatory treatment, mainly inhaled steroids. It seems that the net effects have been profound in terms of reduced exacerbation rates, hospital admission rates and number of hospital days for asthma (10). This can be illustrated with figures from Gothenburg, Sweden's second largest town with half a million inhabitants. During the last decade there was a drastic decrease in the total number of hospital days for acute asthma in children. In the age group 2–18 years hospitalization gradually has decreased to a third (9). Both the admission rate and the number of individuals admitted to hospital has decreased. Thus, children less often need hospital treatment, and when they do they need shorter hospital stays. There were no corresponding major changes in emergency unit policies in the treatment of acute asthma during this time period which could account for the observed changes. Although increased efforts in education of parents/patients may have contributed favourably, the major reason for this remarkable decrease in hospitalization is most likely treatment with inhaled steroids, in children with asthma who need more than a few doses of β_2-agonist per week (42,37). This strongly supports the cost-effectiveness of the anti-inflammatory therapeutic approach.

More widespread use of preventive, anti-inflammatory medication, and a reduction in reliance on bronchodilators, are probably the single most effective measure that can be taken in order to reduce the costs implied by asthma.

In 1981, the Finnish Social Insurance Institution recorded 49 259 asthma patients who where entitled to special reimbursement for their drug costs. In 1996 the figures had increased by three-fold, to 159 105 patients (population 5.1 million). Nevertheless, days in hospital per asthmatic population in 1996 were only one quarter of that in 1981, and mortality due to asthma showed a similar trend. In England, Wales and New Zealand the asthma mortality has also dropped since the late 1980s, in spite of an increasing prevalence of asthma (43). However, in the United States and Japan, asthma mortality is low but still increasing. The reason for these differences are obscure.

Although several factors have probably contributed to the positive trend in Finland and many other countries — the disease may even have become milder — early and better treatment of asthma deserves much credit for the favourable development. The consumption of short acting β_2-agonists has been stable in Finland for several years, while the use of inhaled corticosteroids continues to increase. In 1996 the ratio of prescriptions of prophylactic anti-asthmatic medication to β_2-agonists exceeded 1.0 in Finland, the first Nordic country where this occurred (44).

Education

Education on all levels is crucial for successful results when dealing with the problems caused by asthma.

An educated patient with increased knowledge is the key to better compliance, better well-being and better disease control.

SPREADING GENERAL ASTHMA KNOWLEDGE

The general public should have some basic knowledge of asthma. This may facilitate the everyday life of asthmatics. Increased general awareness of environmental factors known to adversely affect asthma may lead to diminished exposure to irritants (e.g. tobacco smoke) and allergens in the home, at work, in school and at day-care centres as well as in public areas. Better general knowledge of asthma is likely to benefit individuals suffering from asthma, because of better understanding and support from family friends and others. There are still misconceptions of asthma in the population. The harmful idea that asthma is psychosomatic is still prevalent. Good general awareness of asthma also facilitates preventive measures and early recognition of the disease. The implementation and development of established community allergy clinics is valuable.

INFORMATION FOR NON-MEDICAL PROFESSIONALS

Sound information about asthma is important when it comes to choice of a suitable profession for a young asthmatic. It is also beneficial for the patients suffering from asthma that many non-medical professionals, including architects, constructors, social workers and employment officials, have a certain knowledge of the disease. Since asthma is common among school children, teachers should be educated and informed about the disease in order to meet the need of the children with asthma. This includes avoiding asthma trigger factors, helping the child with medication when required and aiding the child in normal social relations.

EDUCATION OF THE MEDICAL COMMUNITY

1. The concepts of asthma have changed considerably and this must be taken into account when planning basic educational programs for medical students and nurses as well as post-graduate education for physicians.
2. It must be stressed that the amount and quality of education given should be in balance with the importance and prevalence of this common disease. This is not the fact today. The majority of asthma care today is provided by GPs, and therefore special efforts should be directed to improve primary care. Treatment of asthma is much more than prescription of drugs and includes above all patient-education. In order to implement patient education it is important that not only physicians are involved but that other health providers also take part. Specially trained nurses used for asthma education is one possibility. Experiences with asthma school have been rewarding.

Patient education is a continuous and demanding process which should start when the asthma diagnosis is given and continued indefinitely. The responsibility for successful patient education lies primarily with the physician but must be seen as a general challenge for all healthcare professionals. The family members of an asthmatic are also an important target group for asthma education.

PATIENT EDUCATION

Education and well organized, structured care on all levels are essential for successful results when dealing with the problems caused by asthma.

Recent treatment guidelines (45,46) have emphasized the importance of patient education in the self-management in asthma care. It should begin at the time of diagnosis and be integrated into every step of care. Effective consultations have an essential role in educating patients and provide the opportunity to determine individual levels of disability.

HOW TO IMPROVE COMMUNICATION WITH THE PATIENTS

Research emphasizes a need for health professionals to show a greater understanding of individual patient concerns and their health beliefs, and how these influence compliance with the medical treatment and advice (47). In order to achieve this, health professionals should identify and develop their communication style to improve their own effectiveness during consultations with patients.

Strategies have been identified to improve communication with patients, enhance information exchange and focus medical visits on the patients personal goals (48,49). These strategies may differ somewhat from culture to culture, but comprise good general guidelines:
They are that the professionals:

1. are attentive to the patient (signalled by cues such as using eye contact, sitting rather than standing when communicating with the patient, moving closer to the

TABLE 2. Key points for education of patients in asthma care

- Patient education should begin at the time of diagnosis and be integrated into every step of clinical asthma care.
- It is essential that education be provided by all members of the healthcare team. The principal clinician should introduce the key educational messages and negotiate agreements with patients. These messages should be reinforced and expanded by all members of the healthcare team.
- Teach asthma self-management, tailoring the approach to the needs of each patient. Maintain a sensitivity to cultural beliefs and practices.
- Teach and reinforce at every opportunity:
  Basic facts about asthma;
  Role of medication;
  Skills: inhaler/spacer/holding chamber use, self-monitoring;
  Environmental control measures;
  When and how to take rescue actions.
- Jointly develop treatment goals.
- Encourage an active partnership, provide all patients with a written daily self-management plan and an action plan for exacerbations. Action plans are especially important for patients with moderate-to-severe asthma and patients with a history of severe exacerbations. Provide appropriate patients with a daily asthma diary.
- Encourage adherence by promoting open communication; individualizing, reviewing and adjusting plans as needed; emphasizing goals and outcomes; and encouraging family involvement.

patient, and leaning slightly forward to attend to the discussion);
2. elicit the patient's underlying concerns about the condition;
3. construct reassuring messages that alleviate fears (reducing fear as a distraction enables the patient to focus on what the physician is saying);
4. address immediate concerns expressed by the family (again enabling patients to refocus their attention toward the information being provided);
5. engage the patient in interactive conversation through use of open-ended questions, simple language, analogies to teach important concepts (an interactive dialogue provides richer information);
6. tailor the management plan by eliciting and addressing potential problems in the timing, dosage, or side effects of the medications prescribed;
7. use appropriate non-verbal encouragement (e.g. a pat on the shoulder, nodding in agreement) and verbal praise when the patient reports using correct disease management strategies;
8. elicit the patient's immediate objective related to control of the disease and reaching agreement with the family on a short-term goal (that is, a short-term objective important to the patient, which both provider and patient will strive to reach);
9. evaluate the long-term treatment outcome;
10. help the patients to use the diary information, or guidelines to handle potential disease problems in advance.

KEY CONSTITUENTS OF ASTHMA PATIENT EDUCATION

Patient education can be divided into a basic knowledge and specific skills. Careful consideration is required in planning educational intervention that enables patients to acquire skills and not simply information about asthma.

BASIC KNOWLEDGE OF ASTHMA

This part of patient education includes a knowledge of basic lung anatomy and physiology, the nature of asthma disease, the causes of asthma, the asthma trigger factors and their avoidance as well as basic pharmacology of asthma drugs and basic principles of asthma treatment. The information must be simple and easily adopted.

SPECIFIC SKILLS

The goal for this part of patient education is to facilitate and encourage an asthmatic to live a life as normal as possible despite his disease. The patient should be provided with skills to perform a guided self-management programme. This includes the ability to make home measurement of lung function (PEF and FEV_1) and to interpret the results. The patient should also be well trained to recognize symptoms of asthma deterioration. In many cases symptoms appear before lung function deteriorates. In some cases the opposite is shown, with obvious changes in lung function with few or no symptoms recognized. Thus the individual pattern should be identified. This enables early recognition of the deterioration in asthma. The appropriate use of inhaled devices is fundamental for successful asthma management. The action plan of what to do, when asthma is worsening, should be given both written and verbally.

GUIDED SELF-MANAGEMENT

The goal of the guided self-management of asthma is to prevent asthma exacerbations with early interventions made by the patient and to maximize the benefits of the treatment. Another aim is to make the patient feel responsible and confident so that he/she feels in control of the disease.

Table 3. Key educational messages for patients

Check off or document that the following key messages have been covered:
- Basic facts about asthma
  - The contrast between asthmatic and normal airways
  - What happens to the airways in an asthma attack
- Roles of medications
  - How medications work
    - Long-term control; medications that prevent symptoms, often by reducing inflammation
    - Quick relief; short-acting bronchodilator relaxes muscles around airways
  - Stress the importance of long-term-control medications and not to expect quick relief from them
- Skills
  - Inhaler use (patient demonstrates)
  - Spacer/holding chamber used
  - Symptom monitoring, peak flow monitoring and recognizing early signs of deterioration
- Environmental control measures
  - Identifying and avoiding environmental precipitants or exposures
- When and how to take rescue actions
  - Responding to changes in asthma severity
  - (daily self-management plan and action plan)

Well recognized medical societies have developed a six-step plan for self-management (Table 4).

Action plans and self-monitoring should be tailored to patient's skill levels and life-style and may be based on either peak flow or symptoms. Recent research on guided self-management of asthma suggests that it is most suitable for patients suffering from severe or moderate asthma. However, patients who are unsuitable for self-management education or do not want to take the full responsibility for their condition can still achieve benefit from a structured program of regular medical review (51,52).

PATIENT FOCUSED CONSULTATION

Consultations may have either a health professional or patient centred approach. During a health professional centred consultation the patient is asked a series of questions in order to identify problems and is prescribed treatment or management considered appropriate by the health professional.

While this approach may be preferred by some patients, it can be associated with a number of drawbacks. Over-directed interviewing and frequent interruptions by the health professionals may mean that the consultation is not focused on the patients personal goals and needs, and important emotional or psychological problems may not be elicited. Patients with expectations left unfulfilled following consultation are less likely to comply with treatment, particularly if they feel it has been prescribed without sufficient attention being paid to their own concerns.

In contrast, in a patient centred approach, the patient takes the lead and directs the consultation. The patient is given the opportunity to discuss their own personal concerns and those aspects which cause the most difficulties. The objective is for the patient to understand the problems and reach agreement or consensus by negotiation with the health professional on the management of their condition.

The patient centred approach may often be more appropriate for asthma care allowing improved self-management and enabling the patients to acquire the knowledge, conviction and ability to make informed choices and enhance their quality of life.

EDUCATION IN A STEPWISE MANNER

All patients with asthma should receive appropriate information. It is important not to overwhelm the new patient with too much information. It is better to provide small amounts of information at more frequent intervals.

Table 5 gives recommendations for the context of both initial visits and follow-up for asthma patients. They offer suggestions on how to structure each consultation including assessment questions, specific information and examples of educational interventions in order to provide the patients with appropriate skills to manage the condition.

TABLE 4. Asthma self-management (50)

Step 1: Know how severe your asthma is
Step 2: Achieve your best lung function
Step 3: Avoid asthma triggers
Step 4: Stay at your best
Step 5: Have an action plan
Step 6: Educate and review regularly

DIFFERENT SETTINGS FOR PATIENT EDUCATION AND SELF-MANAGEMENT

A large number of studies have been carried out in order to provide evidence that one setting is more effective than another for patient education. Overall, for adults and children, there is no clear evidence that one setting is better than another. Some studies have shown benefits in one setting where others have not. Many of the studies have evaluated educational outcomes rather than morbidity. The population and the severity of the disease differs from secondary care to primary care.

It is both possible and effective to educate patients in many kinds of settings such as primary care, emergency departments, inpatient wards, clinics, community organizations and pharmacies and, last but not least, at schools.

Each setting offers specific advantages and limitations that should be viewed as shaping the educaional goals that can be attained. Therefore the best setting is probably the one where the patient actually attends, wants to learn most and is most receptive to behaviour alteration.

THE VALUE OF DIFFERENT KINDS OF EDUCATIONAL MATERIALS

Patient education can be accomplished through several different mediums. Pamphlets, books, videos, audiocassettes, asthma educational courses, support groups, television programs, the Internet, video games and direct contact with the healthcare professional are all methods that can be utilized in order to spread information. Nevertheless research has demonstrated these approaches to be differentially effective.

It does appear that the most preferred and effective methods for controlling asthma are those which emphasize personal interaction and opportunities for personalized advice (53). Thus, it has been suggested that information should first be relayed to the patient verbally with direct opportunity for feedback, followed by reinforcement through various techniques. In order to give patients appropriate information it is important to realize that a patient's sense of control appears to depend as much on information about life implications of the disease process as on information about diagnosis and treatment (54).

There is a high patient demand for written information that gives clear advice on what action to take to supplement what they are told in health consultations. Another important issue to consider is the appropriate readability level. Studies give evidence that both high and low education groups understand, remember and prefer simply

TABLE 5. Delivery of asthma education by clinicians during patient care visits

Assessment questions	Information	Skills
	Information for initial visit	
Focus on: Expectations of visit Goals of treatment Medications Quality of life	Teach in simple language What is asthma? A chronic lung disease. The airways are very sensitive. They become inflamed and narrow. Breathing becomes difficult.	Teach or review and demonstrate: Inhaler and spacer/holding chamber use. Check performance. Self-monitoring skills that are tied to an action plan: Recognize intensity and frequency of asthma symptoms. Review the signs of deterioration and the need to reevaluate therapy: Waking at night with asthma. Increased medications use Decreased activity tolerance.
'What worries you most about your asthma' What do you want to accomplish at this visit? 'What do you want to be able to do that you can't do now because of your asthma?'	Asthma treatments. Two types of medicines are needed: *Long-term control*: Medications that prevent symptoms, often by reducing inflammation. *Quick relief*: short-acting bronchodilator relaxes muscles around airways.	
'What do you except from treatment?' 'What medicines have you tried?'	Bring all medications to every appointment.	Use of a simple written self-management plan and action plan.
'What other questions do you have for me today?'	When to seek medical advice. Provide appropriate telephone number.	
	Recommendations for first follow-up visit (2 to 4 weeks or sooner as needed)	
Focus on: Expectations of visit Goals of treatment Medications Quality of life	Teach in simple language. Use of two types of medications. Remind patient to bring all medications and the peak flow meter to every appointment for review.	Teach or review and demonstrate. Use of a daily self-management plan. Review and adjust as needed.
Ask relevant questions from previous visit and also ask:	Self-evaluation of progress in asthma control using symptoms and peak flow as a guide.	Use of an action plan. Review and adjust as needed.
What medications are you taking? 'How and when are you taking them?'		Peak flow monitoring and daily diary recording.
'What problems have you had using your medications?' 'Please, show me how you use your inhaled medications?'		Correct inhaler and spacer/holding chamber technique.

written material better than the more sophisticated. Studies also show that there is no significant difference between videos and written materials in patient perception of healthiness and retention of information (54).

In order to assure consistency and continuity it is important that health professionals from both the secondary and the primary care team develop strategies for shared care, both in regard to diagnosis, treatment and education. According to this a patient-kept record may be a simple and effective tool.

Non-pharmacological treatment

THE ENVIRONMENT IS OF MAJOR IMPORTANCE

The airways constitute one of the bodies largest exposure areas to the environment. The airways have an elaborate defence system including cough, surface lining with mucous production and an active immunological system. In asthma stimuli result in an exaggerated response with inflammation of the mucosa, cough and altered mucus. Both sensitization to airborne allergens and asthmatic inflammation, as well as the occurrence of symptoms and attacks, are strongly related to environmental exposure. Asthma is often associated with inflammation of nasal mucosa and the conjunctiva. This emphasizes the importance of exposure to airborne triggers.

The environmental agents or triggers causing asthma symptoms have been divided into inducers, agents which cause allergic inflammation (environmental allergens and sensitizers), and inciters which mainly elicits symptoms in hyper-reactive subjects (i.e. cold air, exercise, airway irritants etc.).

PRIMARY PREVENTION

Avoidance of environmental tobacco smoke (ETS)

It has been demonstrated that smoking during pregnancy reduces lung function measured in the neonatal period (55). Furthermore, parental smoking during early childhood increases the risk of developing asthma (25). Avoidance of tobacco smoke exposure during infancy is probably the most important preventive measure that can be undertaken. Moreover, it is extremely cost-effective. In adults, smoking has been shown to increase sensitization (56).

Allergy avoidance

Avoidance of allergens and sensitizers has been attempted to prevent the development of asthmatic disease in the first place. Such actions have been proved to be valuable in the work environment to prevent occupational asthma (57). In contrast, there are conflicting data regarding the efficacy of allergy avoidance in the home environment, aimed at preventing later development of allergic sensitization or development of asthma. Prospective studies have shown that the risk of sensitization to indoor allergens increases in proportion to specific allergen exposure (e.g. cat and house dust mites (14)). Others have found that exposure to animal allergens during the first year of life, prevents atopic rhinitis and allergic asthma (58). Moreover, one study has shown that farmer's children are less often sensitized to aero allergens then other children in rural Switzerland (59). However, very early exposure to aero allergens may well be a risk factor. The existence of a particularly vulnerable period around the age of 3 months has been hypothesized. It has been demonstrated that children born in the pollen season are more prone to development of allergic sensitization toward pollen allergens, especially in seasons with high pollen counts (60). These conflicting data point towards the existence of important unknown confounding factors making strategies for primary prevention based upon scientific evidence difficult.

SECONDARY PREVENTION

In already established asthma, action should be taken to avoid exposure to specific allergens and known triggers. A prolonged exposure to an allergen in a sensitized person is associated with a high risk of persistent and worsening disease (61,62). It is also known that repeated exposure to low levels allergen doses, which for the patient are unnoticeable, can lead to asthma development (63). On the other hand, early intervention and removal from exposure give good possibilities of remission (64). Protection can be divided into source control and exposure control. An example of source control is exclusion of indoor animal dust exposure, and examples of exposure control are an increase in house ventilation and use of mattress covers for avoidance of house dust mite exposure (65). In all cases action should be taken to detect specific allergens. However, the general improvement of the environment and reduction of environmental irritants should be regarded as the major task. It is important to enforce research to identify harmful agents.

SPECIAL CONSIDERATION

House dust mite

Presence of house dust mites (HDM) is highly dependent on indoor humidity. Because of dry winters HDM allergy is of less importance in the northern part of Scandinavia. In contrast, in the southern part, HDM represents an increasing indoor allergen problem. Presumed explanations have been mild winters in combination with insulated houses and little natural ventilation.

Good ventilation, to reduce the indoor air humidity ($<45^{\circ}$ relative humidity) in winter months, is important. This may, however, not always be possible. Mite allergen tight bed covers encapsulate mites and reduce exposure from the bed.

Other measures, like the use of pesticides and other chemicals to combat mites, are of unknown value and these may themselves worsen asthma.

Allergy towards pets

Cat and dog allergens are ubiquitous and impossible to fully avoid. It is known that after removal of the animal and careful cleaning of the dwelling, allergens in large quantities may persist for months. The half life of these allergens are not known.

This motivates the introduction of an 'allergy clean' certificate for a home. It should be possible for those with severe allergy to choose furniture and dwellings which are guaranteed to be free from animal allergens and that the construction of the dwelling makes it possible to decrease the risk of mite replication.

Air cleaners

Many air cleaners are presently on the market which are proposed to be effective in reducing the amount of allergens in the air. However, most of the systems are small with insufficient capacity to make any impact on the air quality, even in very small rooms. Many patients ask for community funding for such equipment. At this time there is no evidence to support the use of this equipment among allergic individuals.

Vacuum cleaners

Conventional vacuum cleaners disperse allergen particles in large amounts. Vacuum cleaners with 'allergen filters' or central vacuum systems can avoid acute challenge. Many devices exist on the market and there is no direct correlation between efficacy and price. Consequently it is wise to consult a local specialist before investing in such equipment.

Air ionizers

Air ionizers have no proven effect and cannot presently be recommended.

Specific allergen vaccination

Specific allergen vaccination has been used since the beginning of this century. The effect on seasonal allergic rhinoconjunctivitis is well documented (66,67,68). A recent study indicates a possible preventive effect upon asthma development by specific allergen vaccination in pollen allergic children with allergic rhinoconjunctivitis (69). In allergic asthma, usually somewhat higher maintenance doses are needed to achieve an appreciable effect (70). This leads to longer treatment periods and a high risk of side effects, especially in those individuals with decreased lung function. Specific allergen vaccination is not recommended in individuals with $FEV_1 < 70\%$ and in those with unstable asthma.

A clinically significant effect on asthma has been documented for allergen vaccination with pollens, cat, dog and house dust mite allergen. With the standardized allergens present today, the risk with allergen vaccination is low when following recommended procedures (71). Initiation of specific allergen vaccination should only be carried out by trained physicians.

Monitoring—follow-up

ACTIVE QUESTIONING, EXAMINATION AND MANAGEMENT

It is important to detect under-treatment with active questioning for asthmatic symptoms in specific situations, for example physical exercise or early morning symptoms. Furthermore, the physical examination should be active, and include listening to lung sounds during forced expiration. Sometimes rhonchi and wheezing become audible in that situation.

Careful clinical observation is even more important for the small child. It is important to register the child's behaviour during daily activity. Observation of the child during play and physical activity gives the trained physician a good idea of the present condition of the child.

Management plans are important in all cases of asthma. For children they should be made in co-operation with the parents in order to prevent the child from being hampered in his/her daily physical activities.

The monitoring and management of asthma should take into account the long and short perspective. In the short run it is important to achieve sufficient disease control in order to help the patient live a normal or 'close to normal' life. In the longer perspective it is important to avoid the development of chronicity and also try to avoid the development of irreversible changes of lung function.

OBJECTIVE MEASUREMENTS OF DISEASE CONTROL

A normal lung function should be achieved throughout the day. During the initial phase of the disease the subject should be instructed to record PEF morning and evening, as well as on demand. This should be done in order to establish the diagnosis and to assess the disease severity. Moreover, the patient learns during this phase to relate symptoms to disease severity. Moreover, in the initial registration period, it is often wise to let the patient measure PEF before and after β_2-agonist inhalation. A consistent diurnal variation[2] after inhalation of β_2-agonist of more than 10%, indicates insufficient disease control. Home monitoring of PEF for a week before a visit to the doctor, preferably combined with a reversibility test when the

[2](Highest PEF − Lowest PEF) × 100/Highest PEF

patient attends, is recommended in the outpatient clinic. An increase in the patient's PEF-value of more than 10% 15–20 min after inhalation of β_2-agonist suggests that the patient has a bronchoconstriction and indicates less than optimal treatment.

Early in the evaluation phase it is important to establish the individual optimal PEF value, which later will serve as a 'reference value'. The patient should know his/her optimal 'normal' PEF range and be taught how to act when the PEF value falls below that interval. Children are usually able to measure PEF from 5–6 years of age.

A spirometry should be done on a regular basis when the patient comes to visit the doctor. Spirometry with flow–volume loops provides additional information of peripheral airway functions ($MMEF_{25/75}$, FEF_{50}). While a spirometry is often normal when the patient sees the doctor later on during the day, regular PEF registration detects the disease variability and thus give a better view over the degree of disease control. A spirometry, especially the post-bronchodilator value, if performed at regular intervals, may reveal a tendency of long-term deterioration in lung function.

It should be mentioned that not all subjects benefit from PEF registration and, especially in children, a low grade relationship has been demonstrated between PEF-monitoring and disease activity (72). Both children and parents have difficulties in correctly perceiving and assessing degrees of airway obstruction (73). Thus the physician should, after an initial evaluation phase, decide whether useful information is obtained from continuous PEF registration. In most situations it is sufficient to only use PEF measurements on demand when the disease situation changes or asthma medication is changed, and during asthma deteriorations.

BRONCHIAL HYPER-RESPONSIVENESS (BHR)

Monitoring of bronchial hyper-responsiveness with methacholine (PD_{20}) was found to be superior to conventional assessment of severity by symptoms and lung function. When BHR was included as a monitoring tool, superior disease control was achieved, including better symptom control, improved lung function, fewer exacerbations and morphological evidence of decreased airway remodelling (74).

INFLAMMATORY MARKERS

Clinical disease control is dependent on the control of the underlying inflammation in the bronchial mucosa. Thus, parameters that reflect the degree of underlying inflammation would be of importance. The measurement of blood eosinophil count and serum concentration of eosinophil cationic protein (ECP) have been proposed for follow-up of asthmatic inflammation. Activated eosinophils play an important role in the late asthmatic response and in the asthmatic airway inflammation (75). ECP is a toxic protein secreted by activated eosinophils (76). Correlation has been demonstrated between the severity of asthma and ECP levels in bronchoalveolar lavage (75,77). Measurement of ECP may be of importance in certain clinical settings, such as monitoring of effects of anti-inflammatory therapy, as well as an indicator of under-treatment or poor drug compliance (78,79). However, individual variation is large and whether or not it may be valuable in all asthmatics, needs to be evaluated. In the future, measurement of eosinophil protein X (EPX) or eosinophil peroxidase (EPO) may offer advantages (80). EPX can be measured in urine, for obvious reasons an advantage in paediatric practice (80). Urinary measurement of ECP is not possible.

Eosinophilic airway inflammation can be readily studied from induced sputum, which has been shown to be similar to lower respiratory secretions expectorated spontaneously (81), and to give comparable results to more invasive bronchoscopic methods (82). The presence of eosinophils in sputum is a more sensitive marker of asthmatic airway inflammation than the blood eosinophils or serum ECP (83,84). In asthmatic children treated with inhaled budesonide for 6 months, significant clinical improvement was accompanied by a decrease in sputum ECP, whereas serum ECP did not change (85).

ASTHMA SYMPTOMS CONTROL

A disturbed night's sleep, due to asthma symptoms, profoundly affects the performance during the day. Possible restrictions in daily activities are important to detect. Is the patient able to use public transport, visit a restaurant or go to a movie? Is he/she able to perform physical exercise and, importantly, is the asthma disease interfering with relationships with family or friends.

The physician should identify factors and situations that limit the patients possibility of living a normal social life. Moreover, the physician should help the patient to identify these situations and then assist in learning to manage them. This may lead to adjustment of maintenance therapy and constructions of as needed medication schedules to be used in these situations. Some situations may even be avoided. The important thing is that the patient has professional guidance in learning how to manage these problems. It is often a delicate balance between the acceptance/sacrifice asked from the environment and what is being demanded by the patient.

LONG-TERM FOLLOW-UP

The long-term goal should be to avoid persistence of the disease and occurrence of irreversible airway damage (86). A spirometry when the patient is in an optimal condition should be achieved early in the course. Thereafter, it is recommended that the patient should be followed with spirometry regularly during the years. While daily PEF-measurement is excellent for monitoring short-term asthma control, a spirometry measuring lung volumes and FEV_1, preferably with a flow–volume curve, is recommended for long-term follow-up. In early detected asthma, a provocation test for bronchial responsiveness (87) or an exercise test is often valuable (88). Changes in the degree of bronchial

responsiveness (BHR) or response to exercise gives valuable information of the long-term disease control. This is especially important in children where exercise control reflects function in daily activities (89). However it should be noted that in patients with long-standing disease, the reactivity may not change much over time, despite adequate anti-inflammatory therapy (90).

Pharmacological treatment strategies basic considerations

DISEASE MANIFESTATIONS

Asthma should be considered as a heterogeneous disorder, and as such needs to be individually characterized in order to select the correct treatment strategy.

The different compartments of the respiratory tract may influence the disease presentation and severity. Concomitant rhinitis should be treated with the same accuracy as asthma disease itself. A blocked nose forces the patient to breathe more through the mouth, thereby exposing the lower airways to unfiltered, unconditioned air.

Many patients with allergic rhinitis, without asthma symptoms, are known to have concomitant bronchial hyper-responsiveness. This hyper-responsiveness increases during allergen season and some patients are only hyper-reactive during the season. It has also been shown that provocation with methacholine in the nose produces an increased lower airway resistance in susceptible rhinitis patients (91). If the hyper-responsiveness is associated with lower airway symptoms, there is need for treatment. It is not known whether treatment of asymptomatic hyper-reactivity decreases the risk of later asthma development.

Asthma inflammation involves all parts of the lower airways. The more severe the disease, the more involved is the entire respiratory tract, including the peripheral airways. Severely obstructed patients not only have airflow limitations, they also develop complete occlusion of parts of the peripheral airways, leading to a decreased forced vital capacity (FVC) and increased residual volume (RV) with an increased amount of unventilated areas.

This type of obstruction is usually not completely reversed by acute bronchodilatation, and inhaled corticosteroids may likewise be insufficient to reach all affected airways. In such cases, a short course with systemic steroids is warranted, as a complement to starting treatment with inhaled corticosteroids.

DRUG DEPOSITION—COMPLIANCE

Both the peripheral and the central airways are important in asthma pathophysiology.

The severity of asthma is associated with the degree of airway inflammation. Inflammation does not only vary in intensity, but also in distribution within the entire bronchial system. Consequently, to achieve maximum control, it is important to also assure sufficient drug deposition in the peripheral airways.

The inhalation device should ideally deliver a dose with heterogeneous particle distribution with a size range in adults between 2 and 6 μm, to reach all airways. In children with smaller diameters of the airways, this ideal diameter is probably lower.

Moreover, the inhalation flow should not be too high, since it has been shown that the higher the flow the more of the drug is likely to be delivered in the central airways. Extremely slow inhalation flow (at 3 l min^{-1}) facilitates peripheral deposition in normal, but also in obstructive, inividuals (92).

The patient must, in addition to being motivated to take the medication, have a proper inhalation technique (technical compliance). Poor compliance is probably the most common reason for insufficient treatment response and should always be considered before changing treatment strategy. Therefore check of inhalation technique should be routine in almost every asthma visit.

AGE — DISEASE DURATION

Anti-inflammatory treatment, preferably with inhaled corticosteroids, is the treatment of choice in all asthma patients with newly detected disease. Early intervention not only improves asthma symptoms and lung function, but also to a certain degree restores bronchial hyper-responsiveness, may normalize the airway structure and, in children, ensures normal growth of lung function (93,94).

There are also indications, that early intervention in a longer follow-up perspective, reduces the total amount of steroids needed for control of the disease.

The addition of a long-acting β_2-agonist or leukotriene antagonist should be considered when optimal disease control is not achieved with medium to high doses of corticosteroids.

In contrast to patients with newly detected disease, disease with a longer duration (usually more than 3 years) is less likely to be fully controlled by inhaled corticosteroids alone (95,37). In these patients, it may be adviseable to add long acting β_2-agonists or leukotriene antagonists earlier, if they are already on a low to medium dose of corticosteroid therapy.

TREATMENT STRATEGY

The philosophy of asthma treatment has profoundly changed in recent years. At the moment the three widely accepted principles of asthma therapy are: 1. anti-inflammatory management is introduced at an early stage of the disease; 2. anti-inflammatory medication is supplemented with bronchodilators; 3. physician-centred management is replaced by patient-orientated management plans.

Approximately 60% of asthma patients are symptom-free most of the time and have very mild or mild symptoms, which may increase in certain situations (e.g. during respiratory infections, irritant or allergen exposure). Approximately 20% of patients have moderate symptoms

most of the time, 15% severe and only a small minority, about 5%, have very severe symptoms with frequent life-threatening exacerbations (96).

The same patient may have mild symptoms on one occasion and extremely severe symptoms on another. Asthma is a disease with marked fluctuation of activity, which is caused by various trigger factors, or variation may take place spontaneously. Symptomatic asthma should always be treated pharmacologically, although other prophylactic treatments play a central role.

In practice, the clinician deals with a newly diagnosed patient, who has mainly been without long-term treatment (early management of asthma), or a patient with a history of asthma for some time, and who has already been using drugs (chronic management of asthma).

EARLY MANAGEMENT OF ASTHMA

The initial symptoms of asthma — mucus production, occasional cough and wheezing — are clinical markers of the inflammatory reaction of the bronchial mucosa. Measurable disturbances of lung function indicate that the process has been going on for some time. This emphasizes the importance of early detection of symptoms and abnormalities of lung function. Early diagnosis and treatment improve outcome of asthma and overall need for medical help.

ANTI-INFLAMMATORY MEDICATION

When the diagnosis of asthma has been objectively established and symptoms or signs of asthma are present more than twice weekly, long-term treatment is started with inhaled corticosteroid, which is the drug of choice.

The anti-inflammatory treatment is introduced as first-line treatment to gain control of the disease as fast as possible. Initially, a quite large dose of inhaled steroid is used, which is then step-wise reduced, according to the clinical response, to the smallest dose able to control the symptoms. The dosage is individually chosen with consideration of disease activity, therapeutic benefits and side-effects. Most of the steroid-treated patients become symptom-free. However, it is not known how long steroid treatment should be continued after the remission, or what kind of dosage schedules should be recommended. If symptoms are fully controlled we recommend the continuation of regular anti-inflammatory treatment, the dose of which can vary, for 1–2 years after the diagnosis, before intermittent use is tried. For anyone initiating treatment with inhaled corticosteroids, it is their responsibility to ensure that the treatment is effective and that subsequent dose adjustment and titration takes place. In patients who do not respond fully to inhaled corticosteroids or go on developing a chronic persistent asthma, long-term management with combination therapy is preferred (described in more in detail the section 'long-term management' below).

In patients with severe obstruction and evidence of small airway occlusion, a short course of systemic steroids is recommended (see above).

If the initial symptoms are severe, treatment is started with oral corticosteroids (prednisone, prednisolone, methylprednisolone). For example, 20–40 mg prednisolone is given every morning for 10–14 days. For short courses of oral steroids, there is no need to taper off the dosage. High-dose inhaled steroid is introduced simultaneously. The treatment is continued with the inhaled steroid.

The topically active corticosteroids used in Scandinavia today are safe and effective in long-term clinical use in low and moderate doses. In daily dosages above 1000 μg in adults and 400 μg in children, an influence on biochemical parameters appears. However, due to large individual differences in steroid sensitivity, these limits are not absolute and stress the importance of individual assessments. In children, a short-term effect on growth, even on low steroid doses has been observed, although the long-term relevance is not known (97). The disease itself is a major stress causing metabolic changes, which normalize when the bronchial inflammation is tackled by therapy but long-term experience is lacking.

Leukotriene antagonists offer a new approach in asthma treatment. Full dose response curves for clinical outcome parameters, such as lung function, symptom control and exacerbation rate, still need evaluation. The optimum dose may differ considerably between individuals.

Several studies have shown significant protection against various forms of challenge tests including exercise (98,99) and most studies show an effect compared to placebo. More comparisons with other established therapies, especially to inhaled corticosteroids, are needed. Patients with concomitant rhinitis and impaired smell, may benefit from these treatments, especially those patients with known non-steroidal anti-inflammatory drugs (NSAID) intolerance (100).

Leukotriene antagonists interfere with asthma pathogenesis in a way different from corticosteroids and β_2-agonists. The inability of corticosteroids to suppress leukotriene production indicates that leukotriene antagonists may have a complementary action to inhaled corticosteroids in the control of asthma. Further knowledge is needed to establish whether leukotriene antagonists may influence airway remodelling and long-term outcome. Leukotriene antagonists has been found to have additional effects to inhaled corticosteroids, and beneficial effects from leukotriene antagonists as add-on therapy to inhaled steroids, indicates that this may be advantageous (101,102).

Long-term studies are needed to evaluate whether leukotriene antagonist treatment, as a single anti-inflammatory treatment, have impact on long-term lung function and bronchial hyper-responsiveness.

CHROMONES

In some adults with mild symptoms, nedocromil or cromoglycate may be symptomatically effective (whereas the effect on the bronchial inflammation is weak). However, there are no means to predict the efficacy of cromoglycate

or nedocromil. If there is no effect within 2 months, they should be abandoned.

MONITORING THE NEED FOR ANTI-INFLAMMATORY THERAPY

At present, in general practice, the need for therapy is judged by clinical evaluation (symptom history, lung auscultation) and lung function measurements (PEF and spirometry). Measurement of lung volumes, bronchial responsiveness and exercise tests can give additional information. Biochemical markers of the inflammatory process, indicating cell activity and measured in serum and sputum (e.g. eosinophilic cationic protein, ECP), may be of value (see monitoring, page 33).

Patients should as soon as possible be able to take responsibility for continuous treatment and management of the disease. This is done through a self-management plan based upon recognition of asthma symptoms and self-monitoring of lung function by method, such as PEF or FEV_1.

STEROID RESISTANCE

The lack of clinical response to steroids does not exclude the diagnosis. A genuine steroid resistance exists, and there are subgroups in which the cellular response does not follow the usual pattern. In these patients the effects of steroids may be altered.

However, before a patient is regarded as steroid resistant, factors like non-compliance, poor inhalation technique, strong persistent trigger factors and allergens should be considered. In addition, a re-evaluation of the diagnosis should be made.

BRONCHODILATORS; β_2-AGONISTS, ANTICHOLINERGICS AND THEOPHYLLINES

Short-acting β_2-agonists are used as rescue medication and are essential drugs for acute or sub-acute symptoms. Regular use is, however, not indicated in maintenance treatment of newly detected asthma. They are used 'as needed', which has two major advantages. Firstly, they help to recognize optimum disease control, because the use is minimal, when control has been achieved. Secondly, increased use of β_2-agonists is usually an early sign of worsening asthma.

Long-acting β_2-agonists are not usually employed in newly detected asthma. Their use is indicated, if disease control is not achieved with moderate doses of inhaled corticosteroids, the patient needs short-acting β_2-agonist several times a day or has nocturnal symptoms (103).

Regular treatment with long-acting β_2-agonists twice daily has been shown to induce a certain degree of tolerance. Usually the bronchodilator response is maintained, whereas the protective effect towards direct and indirect stimuli is reduced. Tolerance develops rapidly within a few days. However, the loss of protection is partial and protection does not disappear or deteriorate further over time. In clinical studies, no convincing anti-inflammatory effects have been described when patients have received regular treatment [for review see (104)].

The addition of long-acting β_2-agonists to a moderate dose of inhaled corticosteroids improves lung function, symptom control and reduces asthma exacerbations in patients with chronic asthma (103,105).

Inhaled anticholinergics may be used instead of β_2-agonist in patients who are sensitive to side-effects (muscle tremor, palpitation) of β_2-agonists. The bronchodilation effect of inhaled anticholinergics is caused by blocking of the efferent parasympatic nerves on the post-ganglionic level, thereby reducing the vagal tone in the airways (106). Ipratropium bromide has proven to be a first line drug in the treatment of patients with COPD (107). However, the bronchodilation seen in asthma, especially in those of a young age is modest and inferior to that seen with β_2-agonists (108,109). Ipratropium bromide has a slower onset than β_2-agonists and has no effect on the early or late allergic reaction. Ipratropium bromide delivered by nebulizer has synergistic effect to β_2-agonist therapy in asthmatics with acute exacerbation (110).

Theophylline has been considered as a bronchodilator agent, but recently non-bronchodilator effects have been detected. Examples of potential positive effects are increased mucociliary clearance (119) improved diaphragmatic muscle function (111), stimulation of the respiratory drive (112,113), and decreased vascular resistance in the lungs (114). Theophylline has also been proposed to have some anti-inflammatory potential (115,116), but the clinical importance needs to be determined.

Theophylline has the disadvantage of a narrow therapeutic index and a wide spectrum of side effects. The most common toxic side effects are due to neurological and cardiovascular actions with nausea and vomiting, seizures, tachyarrythmias and muscle cramps. Another disadvantage is the hazard of metabolism of other drugs with common metabolic pathways in the liver (117). Important examples are, Verapamil, Cimetidine, Disulphirame, Phenytoin and several antibiotics as Erythromycin, Ciprophloxacine, Rifampicine and Isoniazid. In addition theophylline metabolism is influenced by diet and smoking.

Theophylline may be helpful in patients whose disease is not fully controlled with moderate doses of inhaled steroids, who use a short-acting β_2-agonist several times a day and have nocturnal symptoms (118). Theophylline may be an alternative to long-acting β_2-agonists, but the latter seems more effective.

Despite the disadvantages, theophylline is still frequently used in clinical practice. Recent data also demonstrates that theophylline has some pharmacological properties supporting a continuous use of the drug in some defined clinical settings (119).

ANTIBIOTICS, ANTITUSSIVES, EXPECTORANTS

The bronchial inflammation is not usually caused by microbes, and antibiotics are indicated only if signs of

bacterial complication is suspected (CRP, fever etc.). In adults and children asthma often manifests and worsens in association with a viral respiratory tract infection. Viral infections may trigger inflammation leading to asthma and are therefore not treatable with antibiotics. Asthmatic airways excreting excess mucus are associated with cough. When the asthmatic inflammatory reaction is treated, antitussives and expectorants are not needed.

LONG-TERM MANAGEMENT OF ASTHMA

There are a wide variety of clinical stages in an asthmatic population, for example a patient with 50 years of symptom history and a patient who has wheezed for a week. The two patients need totally different treatment strategies, but anti-inflammatory medication is essential for both.

It is essential to diagnose other diseases of the lungs including concomitant irreversible airways obstruction.

There are patients who seem to have severe and chronic asthma from the very beginning (usually non-allergic asthma manifested in association with a respiratory infection), as well as patients with mild disease for decades. All asthma patients, who have had abnormal lung function at some time of their disease, should be monitored and offered special evaluation when needed.

Pharmacological treatment depends on the severity of symptoms and functional abnormality. A patient who has recovered from newly detected asthma, is free of symptoms and has normal lung function does not necessarily need any medication, while a patient with severe daily symptoms may need oral and inhaled steroids, β_2-agonists, and theophylline. In very severe cases experimental treatments such as cyclosporin or methotrexate may be tried in specialist clinics.

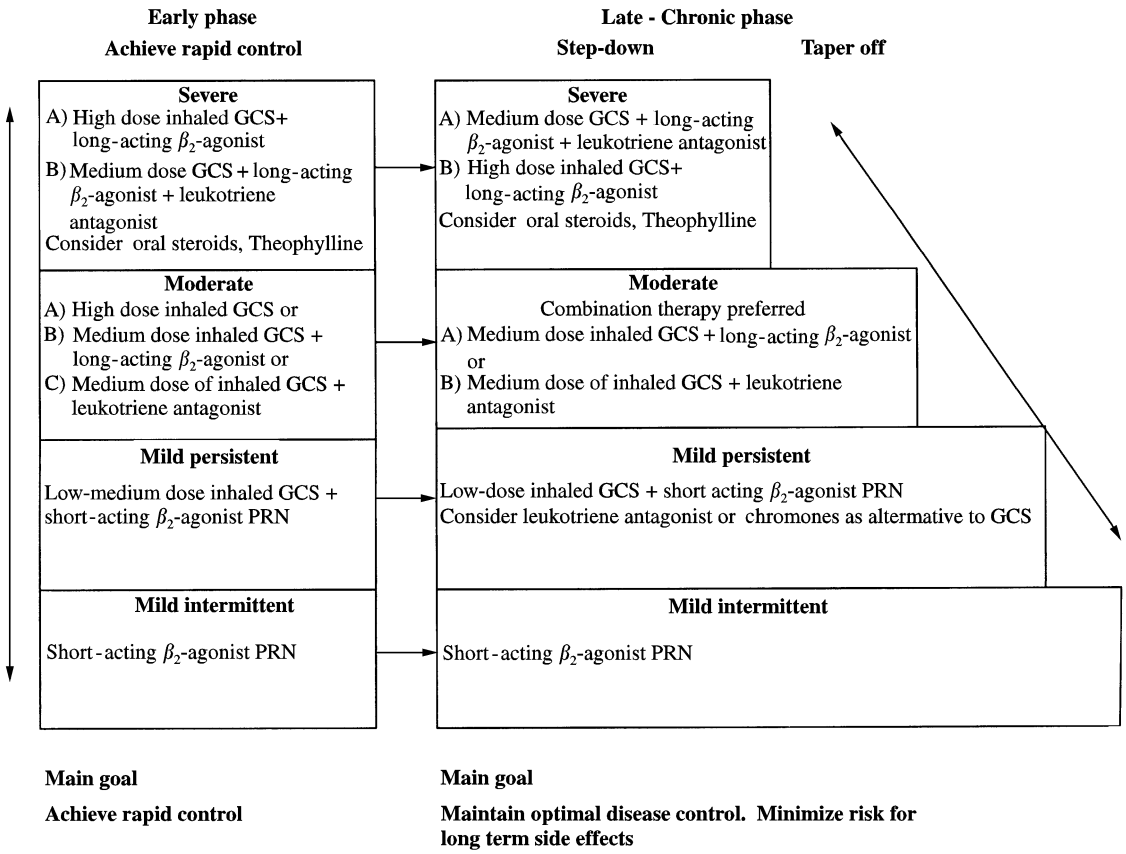

FIG 1. Classification of disease severity is according to the global initiative for asthma (GINA) guidelines (120). During the early phase of the disease, the primary goal should be to achieve rapid control of the clinical disease as well as over the underlying inflammation. This may have positive effects on the long-term prognosis and facilitate good patient compliance. Later in the phase, during step-down/tapering off, the primary goal should be to maintain optimal disease control with minimal risk for long-term side effects. Corticosteroids in medium to high dose + short acting β_2-agonist PRN is recommended in early disease management, while in the chronic phase, combination therapy with long-acting β_2-agonist or leukotriene antagonist as add-on therapy to inhaled corticosteroids is preferred. When optimal control is not reached with a medium dose of inhaled corticosteroids, it is important to consider other reasons for insufficient response. This could be a persistent environmental trigger factors or bad technical or medical compliance. A steroid reversible test should always be done when optimal inflammatory control is difficult to achieve or questioned.

A step-wise approach to therapy is recommended, the first step always aiming to achieve good control of the disease. Reduction of therapy, a step-down, is considered, when the good result has been sustained for months. Increase of therapy, a step-up, is indicated, when control cannot be achieved with the current medication. This usually means increase of the dose of inhaled steroid, giving a burst of oral steroid and/or introduction of new drugs, long-acting β_2-agonists, leukotriene-antagonist, theophylline, ipratropium etc. If asthma is not controlled by a daily dose of inhaled steroid equivalent to 1 mg beclomethasone diproprionate, other mechanisms should be considered. Other therapies and referral to a specialist must be considered.

The use of nebulized therapy for chronic use is seldom necessary. Usually, for those with co-ordination problems, excellent results are achieved by the use of powder inhalators or pMDI and a volume spacer. Nebulized therapy should be reserved for those with severe asthma with frequent exacerbations insufficiently controlled by high dose inhaled steroids.

MANAGEMENT OF EXACERBATIONS

If the patient uses an inhaled steroid, the current dose is immediately doubled during an exacerbation caused by respiratory infection, allergen exposure or unidentified reason. If doubling the dose of inhaled steroid does not help in 24 h, a short course of oral steroid, for example 20–40 mg prednisolone once daily, is used. Symptoms are further controlled by the regular use of bronchodilators. Under these circumstances temporary treatment with long-acting β_2-agonists should be considered. Tapering of the oral steroid dose is usually not necessary when the course does not exceed 2 weeks.

Despite the fact that nebulizers are no more effective than ordinary pMDI or powder inhalers, they are frequently used in some areas partly due to local traditions. Nebulizers may be of use in some patients who have difficulties with other inhaled therapies.

It is essential to communicate time aspects and principles of treatment to the patient. In the early stage of disease the goal is to achieve rapid symptom control which takes 8 weeks with moderate or high dose corticosteroid. The step-down is a slow process during the next year whereafter intermittent therapy may be possible.

PHARMACOLOGICAL TREATMENT STRATEGIES IN CHILDREN

The treatment strategy for children is basically the same as for adults, with a few exceptions, as add-on therapy strategies are less well documented. Respiratory allergy is a much more common aetiology in children of 2 years and older than in adults above 50 years of age. Environmental control and allergy avoidance has a central role in asthma management.

Moreover it is often possible to detect the disease in young adults and children early in the course of the disease. Early anti-inflammatory treatment is mandatory in order to rapidly achieve full disease control and to avoid occurrence of irreversible changes in the airways. Careful attention should be directed to achieve full anti-inflammatory control, before stabilizing treatment is considered with leukotriene antagonist, long-acting β_2-agonist therapy or theophylline.

On the other hand, it is likewise important to avoid unnecessary long treatment with high dose corticosteroid. It is necessary to continuously re-evaluate the actual treatment in order to reach the lowest effective dose that can control the disease. If the disease, after 1 year of treatment, is difficult to control on a daily inhaled steroid dose equivalent to more than 500 μg beclomethasone diproprionate daily, combination therapy with other anti-inflammatory regimes such as chromones or leukotriene antagonist should be considered. Before doing so, it is important to rule out other possible causes of insufficient treatment response, such as improper compliance and strong environmental trigger factors. If the disease is difficult to control despite increased anti-inflammatory treatment, addition of long acting β_2-agonist or theophylline is recommended.

Acute severe asthma

ACUTE SEVERE ASTHMA IN CHILDREN AND ADULTS

Assessment of clinical severity should be based upon clinical signs as breathlessness, respiratory rate, heart frequency and mental status. As objective laboratory measurements PEF and blood-gas analyses are used (see Table 6).

A short and concise clinical history should be obtained. This includes usual daily medication intake and medication taken during the last 24 h. Known allergy, smoking history and concomitant diseases are important to register. A possible cause of the actual episode needs to be identified. It is extremely important to rule out concomitant factors that could endanger the outcome and initial handling of the patient, such as pneumothorax, pneumonia, cardiac insufficiency etc.

The patient is often frightened and agitated and it is of utmost importance to secure a calm and confident atmosphere around the treatment. Oxygen should be given immediately and β_2-agonist combined with ipratropium bromide should be given by nebulizer driven by oxygen.

Steroids should always be given early in the course. In most situations orally delivered prednisolone is sufficient. However, in very severe asthma, the first dose is preferably given by injection, in order to secure delivery. A steroid with low mineral corticosteroid effect should be used.

Repeated blood gas analyses is important early in the course. Special attention should be given to a tendency to respiratory acidosis, which in contrast to the COPD patient may have a very rapid onset and development. Usually, a slight respiratory acidosis is rapidly corrected as soon as the ventilation improves. In rare circumstances, metabolic

TABLE 6. Severity of asthma exacerbations*

	Mild	Moderate	Severe	Respiratory arrest imminent
Breathless	Walking	Talking Infant-softer and shorter cry; difficulty feeding	At rest Infant-stops feeding	
	Can lie down	Prefers sitting	Hunched forward	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Often $>30\,min^{-1}$	
	Guide to rates of breathing associated with respiratory distress in awake children:			
	Age	Normal rate		
	<2 months	<60/min		
	2–12 months	<50/min		
	1–5 years	<40/min		
	6–8 years	<30 min		
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical thoraco-abdominal movement
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Absence of wheeze
Pulse/min	<100	100–120	>120	Bradycardia
	Guide to limits of normal pulse rate in children:			
			Normal rate	
	Infants	2–12 months	<160/min	
	Pre-school	1–2 years	<120/min	
	School age	2–8 years	<110 min	
Pulsus paradoxus	Absent < 10 mm Hg	May be present 10–25 mm Hg	Often present > 25 mm Hg (adult) 20–40 mm Hg (child)	Absence suggests respiratory muscle fatigue
PEF after initial bronchodilator % predicted or % personal best	Over 80%	Approx. 60-80%	<60% predicted or personal best (< 100 L/min adults) or response lasts < 2 hrs	
PaO_2 (on air) and/or $PaCO_2$	Normal Test not usually necessary < 45 mm Hg (6.0 kPa)	>60 mm Hg (8.0 kPa) < 45 mm Hg (6.0 kPa)	< 60 mm Hg (8.0 kPa) Possible cyanosis > 45 mm Hg (6.0 kPa) Possible respiratory failure (see text)	
SaO_2 % (on air)	> 95%	91–95%	< 90%	
	Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents.			

*The presence of several parameters, but not necessarily all, indicate the general classification of the exacerbation

correction with buffer infusion may be indicated. One of the reasons for metabolic correction is to improve renal haemodynamics and to restore β-receptor function.

Very severe cases should always be monitored closely in units prepared to assist ventilation mechanically whenever needed.

The following signs should immediately result in transferral to intensive observation:

1. impairment of speech;
2. impairment of mental alertness;
3. silent chest;
4. $PaO_2 < 8$ kPa at admission;
5. hypercapnia $PaCO_2 > 6$ kPa;
6. progression of disease severity.

The combination of the initial hyperventilation with administration of β_2-agonist may lead to significant depletion of potassium in blood. However, the intracellular potassium concentration is usually within the normal range, and therefore this extra cellular depletion needs no correction. However, special attention should be directed to those patients who has been on long-term regular treatment with loop diuretics. These patients may from the start have depletion of intracellular as well as extracellular potassium, and may have simultaneous depletion of magnesium. In these cases, it may be advisable to correct both potassium and magnesium levels.

In addition, steroids with marked mineral corticosteroid effect can further contribute to the electrolyte disturbances and should therefore be avoided.

In most circumstances, it is possible to manage the patient with frequent high dose bronchodilator inhalation. Systemic β_2-agonist administration may be considered in those with severe obstruction.

Theophylline is seldom necessary and usually gives no additional effects when sufficient β_2-agonist and anticholinergic treatment is given. Theophylline also has the disadvantage of a narrow therapeutic window. From clinical experience we know that a limited number of patients benefit from the addition of theophylline. Therefore theophylline should be given on an individual basis, but cannot be generally recommended.

Sedatives, including anti-histamines with sedative actions, should be avoided and only given when the possibility of immediate ventilator support is at hand.

Physiotherapy has no place in the initial management plan.

CLASSIFICATION OF SEVERITY IN CHILDREN

Clinical assessment

Registration of clinical observations is important, from the initial evaluation to later examinations, in order to follow the effect of treatment and progression of the illness. Important clinical observations include respiratory rate and pattern; heart rate, respiratory chest recessions, auscultatory sounds, skin colour and, in children, the general condition and spontaneous activity. The respiratory rate may vary, especially in early infancy. As a general rule the respiratory rate should be below 40 per min during the first year of life and in older children below 20 per min. The respiratory pattern is usually changed during acute asthma to be marked by a prolonged expiratory phase. The heart rate is often high due to increased ventilatory work load and the child's anxiety. In spite of the positive chronotropic effect of many asthma drugs, the heart rate often decreases when the asthma attack is treated and the dyspnoea recedes. The respiratory chest recessions during acute asthma (jugular, intercostal and subcostal) is a good measure of severity. By lung auscultation, presence of prolonged expiratory phase, diminution of the respiratory sounds over parts of or over the entire lung, or sounds such as rhonchi and rales, should be observed. Diminished respiratory sounds in the absence of extraneous respiratory sounds such as rhonchi and rales may signify very severe bronchopulmonary obstruction due to low airflow, and should not be misinterpreted as a sign of improvement. Rhonchi may become audible after the use of a bronchodilating drug. A clinical classification, developed by Kjell Aas, of the bronchopulmonary obstruction during acute asthma, based mainly upon lung auscultation, is given in Table 7 (121).

LABORATORY AND TECHNICAL ASSESSMENT OF ACUTE ASTHMA

Blood gases, pH and base excess are used routinely in emergency rooms and hospital wards. PCO_2 may be low early during the acute exacerbation (hyperventilation) with a normal PO_2 in arterial or arterialized blood samples. Increasing PCO_2 towards or beyond the normal level (5·4 kPa) may imply an increasing obstruction. In respiratory failure PO_2 decreases while PCO_2 increases. With PCO_2 levels above 8 kPa in a patient without other chronic respiratory disorders, ventilator treatment should be considered.

Arterial oxygen saturation (SaO_2) measured by pulse oximetry is a useful and simple way of observing the acutely ill asthmatic (122). SaO_2 levels below 91% are regarded as representing a severe condition in small children and infants, levels of 91–93% indicate moderate asthma and levels above 94% mild acute asthma. Whilst SaO_2 has been shown to be effective in surveillance, it is not sufficiently sensitive to be used as a single criterion for admission to hospital (123,124). Monitoring of transcutaneous arterial blood gases is valuable in small children and infants with acute asthma to detect deterioration (125) and to monitor the effect of treatment (126).

Measurement of lung function is of value in the assessment of acute asthma (PEFR, FEV_1) (124). In severe asthma forced expiratory manoeuvres may aggravate the dyspnoea. Furthermore, these techniques are not suitable in pre-school children.

Registration of tidal breathing pattern, by tidal flow–time curves and tidal flow–volume curves in adults (127)

TABLE 7. Clinical assessment of bronchopulmonary obstruction during acute asthma in children

Score	Description
P0	Normal; no signs of bronchopulmonary obstruction.
P1	No dyspnoea. Slightly faint respiratory sounds.
P2	No dyspnoea. Moderate rhonchi. Slightly prolonged expiration. The expiration may be audible.
P3	No dyspnoea at rest. Abundant rhonchi. Slight use of auxiliary respiratory muscles. Low grade jugular recessions may be present.
P4	Slight dyspnoea at rest. Abundant rhonchi. Obvious use of auxiliary respiratory muscles. Jugular and intercostal chest recessions. No cyanosis.
P5	Severe dyspnoea at rest. Abundant rhonchi. Wheezy expiration audible without stethoscope. Jugular, intercostal and subcostal chest recessions. Slight cyanosis may be present.
P6	Alarming obstruction, often both inspiratory and expiratory. Faint respiratory sounds. Chest recessions. Use of auxiliary respiratory muscles and high respiratory rate. Cyanosis may be present but not mandatory.

and in infants and small children (128,129), is a sensitive tool in monitoring bronchopulmonary obstruction (130,131).

ACUTE SEVERE ASTHMA IN CHILDREN

Treatment in the home

All children with the diagnosis of asthma need individualized written instructions for treatment during acute exacerbations. It is important to ascertain that the parents (or the patient in case of school children and adolescents) understand the instructions. It is usual to recommend that the doctor/hospital should be contacted if the treatment according to written instructions is without effect, if the medication has a shorter duration than 3 h, if the child is getting fatigued, or the dyspnoea lasts more than 3 days. A practical guideline for the practitioner is that if an adequate dose of inhaled nebulized β_2-agonist is insufficient, the patient should be admitted to hospital.

During acute asthma, the effect of oral drugs is uncertain. Inhaled β_2-agonists, salbutamol or terbutaline (dosage, see Table 7) may be given every third hour at home. If more frequent inhalations are needed, the patient ought to be admitted to hospital. In case of severe dyspnoea, the administration of systemic steroids should be considered before transportation to hospital, either orally (prednisolone or betamethasone) or as an intravenous injection (hydrocortisone acetate).

Treatment of acute asthma in hospital

A plan for the management strategy of acute childhood asthma in hospital is outlined. The management strategy (Table 8) is based upon the classification of the acutely ill asthmatic child according to the criteria given in Table 7. The dosage of drugs is shown in Table 9.

Ventilator treatment

Ventilator support may be required, based upon clinical assessment. Is the patient fatigued? $PCO_2 < 8$ kPa or $PCO_2 > 7$ kPa may necessitate ventilator support.

Laboratory examinations during acute asthma:

The following samples are taken when anticipated to have consequences for treatment: Leukocytes, CRP, serum theophylline levels, blood-gases and chest X-ray (important in case of suspected pneumothorax); Surveillance: SaO_2, transcutaneous PO_2, PCO_2, electrocardiogram, blood-pressure monitoring and electrolytes (β_2-agonist may contribute to hypokalemia).

Special considerations

PREGNANCY

The severity of asthma during the period of pregnancy is difficult to predict in individual cases. Approximately a third of patients will improve, a third will be unchanged and a third will get worse. Patient compliance is a major target for therapeutic intervention. It is important to inform the pregnant mother properly. Generally the disease itself is a larger threat for the foetus health than any part of the treatment (132,133,134). Inhaled corticosteroids with inhaled β_2-agonist therapy should be the cornerstone of therapy. Oral theophylline may also be used and neither of these drugs have been shown to increase the risk of foetal malformations. Acute exacerbations should be treated quickly in order to decrease the risk of foetal asphyxia. Nebulized β_2-agonist therapy and anticholinergics, oxygen and systemic steroids should be used when needed.

TABLE 8. Treatment of acute asthma

Asthma classification	Management strategy
P1-P3: *Mild*	You have ample time to investigate the case history and perform a thorough clinical examination of the child. Give inhaled β_2-agonists. Then wait for 10 min and give another dose of nebulized salbutamol or terbutaline if needed. If necessary, take required samples for laboratory investigation. If the treatment has a satisfactory effect (P0-P1 after treatment): the patient may be discharged from hospital with home medication up to every third hour. The parents are instructed to contact the hospital if the condition aggravates.
P4-P6: *Moderate to severe*	Do a rapid medical history and clinical investigation. Observe: pneumonia; atelectasis, pneumothorax. Commence inhalation therapy while preparing and setting up an intravenous cannula. Inhalation therapy is given as nebulized β_2-agonists. Give oxygen therapy by face mask if needed. If the response to inhalation therapy is non-satisfactory administer systemic steroid treatment, repeat β_2-agonist inhalation and consider nebulized adrenaline or nebulized racemic adrenaline. Especially in infants and young children nebulized adrenaline or racemic adrenaline can be useful. Theophylline can be considered. If the child improves, continue surveillance. If the child still has considerable dyspnoea, set up intravenous infusion of fluids. If the initial therapy does not improve the patient's condition: prepare transfer to an intensive care unit as soon as the patient is stabilized clinically (heart condition and respiration).

Starting specific allergen vaccination during pregnancy is not recommended. However, if the treatment has been initiated and titrated before the pregnancy occurred, it is generally safe to continue (135), but the maintenance dose should be modified.

PETS

Hypersensitivity to cat and/or dog allergens is commonly found in individuals with allergic asthma (136,137). It is often difficult to convince the patients to get rid of their animals, even in a situation with evident clinical hypersensitivity. It is even more difficult to recommend removal of the pet in a situation where allergy is not yet present but highly suspected in the future. Most atopic individuals with animal allergy develop their hypersensitivity within the first 12 months. However, it may also appear at a later stage after 2–6 years (138). A risk factor for development of pet allergy in infants is atopic disposition, especially on the maternal side (139). Increase of cord blood IgE may identify individuals at greater risk (140). A large exposure to a wide variety of known allergens in early infancy may predispose to allergy later in life (141). Other important risk factors are passive smoking increasing the risk of overall sensitisation (142,143,16). Pet allergens are commonly found in significant concentrations in most public places and in homes without pets (144). Thus it is virtually impossible to avoid pet allergen exposure. Today, there are no data indicating that avoidance of pets in the home provides protection from being sensitized to pet allergen. On the contrary, some studies indicate that early and regular exposure to pets and farm animals protects against sensitization (59,60).

EXERCISE-INDUCED ASTHMA

Exercise-induced asthma is a clinical manifestation of bronchial hyper-responsiveness. Liability to experience wheezing and obstruction in association with exercise varies from one patient to another and also in the same patient according to asthma severity. Consequently treatment with anti-inflammatory medications should always be considered. Traditionally patients have been advised to inhale short-acting β_2-agonists or cromoglycate just before exercise, and a combination of the drugs has an additive effect. Leukotriene antagonist treatment may serve as an alternative. Pre-treatment with short-acting β_2-agonist before exercise is difficult to achieve in children. Therefore, especially in active children, drugs with longer protective action, i.e. covering the whole day, are recommended. The combination of inhaled corticosteroids with a long-acting β_2-agonist, or a leukotriene antagonist should be considered.

PHYSICAL ACTIVITY

Although physical exercise may trigger asthma attacks, regular physical training, through improved fitness, may

TABLE 9. Treatment of acute severe asthma in children

Drug	Dosage
Racemic adrenaline nebulizing solution 20-25 mg/ml	< 1/2 years old: 2–2.5mg (0.1ml) in 5 ml NaCl (isotonic) > 1/2 years old: 4–4.5mg (0.2ml) in 5 ml NaCl (isotonic)
Salbutamol nebulizing solution 5 mg ml^{-1}	0.5–1.5 mg (0.1–0.3ml) / 10 kg body weight in 5 ml NaCl (isotonic)
Ipratropium bromide nebulizing solution 0.25 mg ml^{-1}	0.05 mg (0.2 ml = 4 drops) in 2–5 ml NaCl (isotonic). May be combined with salbutamol inhalation
Theophyllamine for intravenous use	*Saturating dose* should be infused over 15 min: 6 mg/kg body weight, maximum 300 mg (in case of regular theophylline use, half of the ordinary dose should be given if the patient uses theophylline regularly or has received theophylline during the last 6–8 h. *Maintenance dose:* < 8 years: 0.9 mg kg^{-1} body weight per hour > 8 years: 0.5–0.7 mg kg^{-1} per hour To be given in glucose 50 mg ml^{-1} with added Na^{+} 2 mg kg^{-1} body weight over 24 h, and K^{+} 1 mg kg^{-1} body weight over 24 h.
Hydrocortisone (Solu-Cortef) or [Methylpredisolone (Solu-Medrol)] intravenously 20mg Solu-Medrol ≈ 100mg Solu-Cortef	Initial dose: 100 mg [20mg] after that: < 20 kg: 50 mg × 4 (10 mg × 4) > 20 kg: 100 mg × 4 (20 mg × 4)
Terbutaline 0.5mg ml^{-1} for intravenous infusion	5–10 μg kg^{-1} and hour Mixture of 5 mg (10 ml) terbutaline in 1000 ml isotonic infusion solution (1 ml = 5 μg, 10 drops = 2.5 μg).
Adrenaline subcutaneously 1 mg ml^{-1}	0.01 ml kg^{-1} (= 0.1 ml per 10 kg) as a single dose
Prednisolone tablets	1–2 mg kg^{-1} body weight per day in 4 days

increase the ability for physical performance (145,146,147). Asthmatics should be encouraged to take part in physical activity and exercise should be included in rehabilitation programmes for asthmatic individuals. Proper pre-treatment with β_2-agonists and/or cromoglycate together with a sufficient warming-up reduce exercise-induced obstruction (148). Often pre-treatment with a β_2-agonist does not sufficiently prevent exercise induced obstruction. It is then advisable to add anti-inflammatory treatment, preferably a low to medium dose of inhaled corticosteroids.

Exercise induced asthma is the most common feature seen in children with asthma and should primarily be regarded as an indicator of insufficient asthma control. It is difficult to instruct a child to take β_2-agonist prophylactically before exercise. They often forget and sometimes do not want to expose themselves by taking medication in front of their class mates. In children, therefore, long-term protection throughout the day is desirable. A combination of a low-medium dose of inhaled corticosteroid and long-acting β_2-agonist or leukotriene antagonist is recommended.

GASTROESOPHAGEAL REFLUX

The incidence of gastroesophageal reflux (GER) and oesophagitis is increased in asthmatics (149,150). The use of xanthines may enhance the reflux by relaxation of the lower oesophageal sphincter. Whether GER may trigger asthma exacerbation and especially night asthma symptoms is still debated. Simultaneous oesophagus pH and lung function measurement, preferably continuously, help establish the diagnosis (151). Oral β_2-agonists and xanthines should be avoided. Patients should avoid eating between meals and especially before bed time. Spicy food, coffee and alcohol should also be avoided. Present oesophagitis should be treated with a proton-pump blocker. Surgery should be considered in more severe cases.

RESPIRATORY INFECTIONS

Viral infections are common triggers of asthma exacerbation (152). However, viral infections may also contribute to the development of asthma (153). Asthma in later life has been associated with hospitalization due to RSV bronchiolitis in early childhood (154,155). Experimental studies have also shown that viral infections may cause inflammatory changes similar to those seen in asthma (154,156). Careful prospective studies are needed to evaluate whether early intervention is able to prevent the development of asthma. Nevertheless data strongly support viral infections as an important aetiological factor in some asthmatic subjects. The definite value of early anti-inflammatory intervention has not yet been proved. However, we suggest that, especially for those infants and small children with atopic disposition, in occurrences of viral induced bronchiolitis early treatment with anti-inflammatory medication, i.e. inhaled steroids, should be given. Careful follow-up during the following years is strongly recommended.

PSYCHOLOGICAL ASPECTS

To achieve optimal disease control it is important to secure full patient compliance (157). The patient should early be involved as a 'partner' in the treatment program. Full insight into the disease mechanism and the formation of an individual 'self-management' plan are corner stones in modern asthma therapy (158). Information should be given gradually, allowing the patient to digest the information properly. Some information may be given in a group, i.e. as an 'asthma school'. However, most patients will also need individual education. A trained nurse and/or physiotherapist is often essential partners in the process.

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