The disease management approach to controlling asthma

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Abstract. Asthma has become an important public health issue worldwide and certain groups, such as children, are at particular risk of the disease. Often asthma remains under-diagnosed and under-treated. Despite these worrying trends, the disease management approach to asthma control can help most asthma patients achieve a normal way of life. The increased prevalence and greater diagnostic awareness of asthma have placed increased demands on healthcare resources, but effective asthma control can minimize the personal, social and economic burdens of asthma. Early diagnosis and immediate anti-inflammatory treatment is the first step in gaining control of symptoms. A stepwise approach is then used to classify asthma severity and treatment, with the number and frequency of medications increasing (step up) as asthma severity increases and decreasing (step down) when asthma is under control. This stepwise approach to asthma management necessitates regular review of treatment once asthma is under control. However, effective asthma management is dependent on successful patient education, adherence to prescribed medication and good doctor–patient partnerships. Current treatment guidelines recommend the use of a written asthma management plan that should be agreed between the doctor and patient. These plans should cover all aspects of asthma treatment, including prevention steps for long-term control and action steps to stop attacks once a worsening in asthma has been recognized. This comprehensive approach to asthma management increases the likelihood of achieving asthma control, which in turn reduces the need for emergency visits to the hospital or clinic and reduces the limitations on physical activity previously imposed by the condition.

INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways that involves many cells and cellular elements. In susceptible individuals, this inflammation causes recurrent episodes of coughing, wheezing, tightening of the chest and difficulty in breathing. Difficulty in breathing is caused by variable airflow obstruction when airways are exposed to various stimuli or triggers.

An increase in the understanding of the pathophysiology of asthma has influenced the development of new pharmacotherapies. The use of pharmacotherapy in asthma helps prevent and control asthma symptoms, reducing the frequency and severity of asthma exacerbations and reversing airway obstruction. Asthma is not always progressive and early diagnosis and treatment with prescribed medication may help reduce or prevent progression (1). Asthma is also a variable disorder that changes in severity over short periods of time; the frequency of acute attacks also varies with time. These changing characteristics make asthma management a challenge for both the doctor and patient.

Given the highly variable nature of the disorder, it is important that patients have a good understanding of their condition and are able to recognize a worsening of asthma symptoms. Disease management programmes enable both the patient and physician to make therapeutic, behavioural and environmental adjustments when the early signs of an asthma exacerbation appear. Patient co-operation and adherence to prescribed medication and management programmes are essential in asthma management since daily monitoring and frequent treatment adjustments help optimize control in persistent asthma. Recent improvements in patient education and an increase in the level of patient involvement in their treatment programme should help achieve good asthma control with better doctor–patient partnerships and a more appropriate use of asthma medications.

THE BURDEN OF ASTHMA

Asthma is a major public health concern affecting over 100 million people worldwide (2,3). The prevalence of
the prevalence of asthma in Scotland concluded that the prevalence of asthma in the general population is increasing and certain subgroups (e.g. children and young people) are at particular risk (3,5). A recent report on the prevalence of asthma in Scotland concluded that the prevalence of asthma in adults has increased by more than twofold in the last 20 years and this is seen largely in association with trends in atopy. Greater diagnostic awareness was not thought to account for the trend in atopic asthma (6). Changes in factors such as the severity of the disease, rather than prevalence, may account for the increased mortality, morbidity and number of hospital admissions (7). Poorly controlled asthma is frequently due to inappropriate or insufficient medication and the costs of these inadequacies have considerable social and economic impact (4).

The cost of asthma comprises both direct and indirect costs. The direct costs include all medical expenditure, including primary care and emergency room visits, and inpatient treatment. Of these costs, inpatient hospital expenditure and emergency care are consistently disproportionately high. Indirect costs are an estimate of lost productivity due to asthma or time taken off work to care for a family member with asthma. A number of recent reports estimate that indirect costs of asthma range from 39% to 49% of the total cost of the disease (8,9). In one study, indirect costs were reported to be twice as high as direct costs at all levels of asthma severity and a minority of severe asthmatics incurred 41% of total asthma costs (10). Therefore, reducing the indirect costs associated with asthma management will have a significant impact on the total cost of the disease.

There is a large variation in the total cost of asthma among countries, but a cross-comparison between countries shows that hospitalization and emergency care are consistently high and the cost of medication is a key element of the healthcare costs. Cost comparisons between industrialized countries, such as the USA, and more agricultural areas, such as South Africa, show that the total costs for asthma as a single condition currently account for 1–2% of total healthcare expenditure (4). The social impact of asthma varies from country to country and across cultures. When asthma is poorly controlled, it affects patients’ social functioning and limits their involvement in various activities. All levels of asthma severity have a social impact and reduce the patient’s quality of life. Asthma management programmes are, therefore, designed to redress the negative social impact and have a positive impact on quality of life. Patients with chronic cough and wheezing may develop social stigma, whereas lost days at work due to asthma may result in a gradual loss of steady employment, which may lead to marginal jobs or unemployment (4).

Occupational asthma is another contributor to the social burden of the disease (4,11). A number of occupations involve exposure to allergens and agents that can sensitize the airways and cause asthma. The incidence of occupational asthma is expected to increase with the introduction of new materials in the workplace, despite better regulation of occupational hazards. Once a worker has become sensitized to an agent, it is essential that they have no future contact with the sensitizing agent; this may require redeployment.

Asthma is a leading cause of hospital admissions for children in the USA, with a total of 1.9 million days of inpatient treatment. Childhood asthma is also estimated to result in 7.3 million days confined to bed and 10.1 million missed school days per year (12). Days absent from school is only one measure of the social impact of asthma and other factors, such as associated pain and number of days with asthma symptoms, are also used to obtain a fuller impression of how asthma affects children. It is recognized that missed education may have long-term consequences on academic performance, social functioning and self-esteem (4). Poorly controlled asthma in children affects all immediate family members, particularly parents who take time off work to care for a child at home.

DIAGNOSIS OF ASTHMA

Diagnosing asthma is still a challenge and for some patients correct diagnosis may take years (13). Failure to diagnose asthma may lead to the prescription of inappropriate and ineffective treatments, such as antibiotics or cough medication, thus delaying the start of effective asthma therapy. Some patient populations are particularly difficult to diagnose and these include: small children, the elderly, smokers, people with seasonal asthma and those with cough-variant asthma. Asthma also remains under-diagnosed because some people do not seek medical advice.

Initial assessment and diagnosis of asthma is the first step in gaining early control of symptoms. In order to diagnose asthma, the presence of episodic airflow obstruction, which is at least partly reversible, must be confirmed. The patient’s medical and family history also helps assess the patient’s allergic status and should reveal predisposing factors for developing asthma. Pulmonary function tests are needed to ensure a correct diagnosis of asthma (14). Other diseases of the airways need to be excluded and these include chronic obstructive pulmonary disease, bronchiectasis, interstitial pulmonary fibrosis, recurrent respiratory infections, laryngeal dysfunction, cystic fibrosis and localized obstruction of the airways. Asthma should, however, always be sus-
The diagnosis of asthma in children is more difficult than in adults (14) because they may only have asthma symptoms along with viral illness, exercise or as coughing at night. The presence of night-time coughing that awakens the child in the early hours of the morning is almost always asthma (4). Asthma should also be considered if a child has a cold with a cough that lasts for more than 10 days. Current guidelines recommend that recurrent wheezing in infants, with or without atopy, should be treated as asthma (14). 

**CLASSIFICATION OF DISEASE SEVERITY**

The severity of asthma can be highly variable in any patient and the need for regular reviews is now recognized in the current guidelines (5,14). Clinical assessment and self-assessment are the primary methods of monitoring asthma and they are instrumental in establishing whether the goals of treatment are being met.

Assessing the severity of a patient's asthma helps the clinician in selecting the correct level and frequency of treatment. Asthma was previously classified as mild, moderate or severe (4) and this classification was widely accepted within the asthma community. However, in the more recent revisions (5,14) these classifications were revised to mild intermittent, mild persistent, moderate persistent and severe persistent to reflect the clinical manifestations of asthma (Table I). Classifying asthma in this way is not intended to restrict the type of therapy received by an individual patient. It is intended as a guide to the level of therapy that may be required by a patient in order to gain symptomatic control, with a subsequent increase or decrease in therapy as required. Patients diagnosed with any level of asthma may have mild, moderate or severe exacerbations, and these exacerbations need defined management (14).

The underlying pathophysiology of asthma is defined by chronic inflammation of the airways (15). Death resulting from asthma is usually accompanied by massive cellular infiltration (eosinophils, mast cells and mononuclear cells) in both the large and small airways (16) but extensive inflammatory changes in the airways are not restricted to severe asthma and are frequently seen even in mild clinical disease (17-20). These findings are consistent with the view that daily anti-inflammatory medication should be initiated early in treatment to reduce the risk of irreversible airway remodelling (1,21-23).

Asthma in children over the age of 5 years is classified in the same way as for adults. For infants and children under 5 years of age, objective measurements of lung function are difficult to obtain due to a lack of appropriate methods and evaluation therefore relies on the infant's medical history, symptoms, physical examination and an assessment of quality of life.

**MANAGING A VARIABLE DISEASE**

The successful management of persistent asthma involves both routine clinical assessment and regular self-monitoring by the patient. This ongoing evaluation helps to determine whether the goals of therapy are being achieved. These goals are the same for every asthma patient and aim to: minimize or eliminate symptoms; reduce the frequency of exacerbations; reduce the need for emergency department visits and hospitalization; minimize the need for acute rescue therapy such as inhaled β₂-agonists; normalize pulmonary function; establish a normal lifestyle without limitations on activities, including exercise; and minimize or eliminate adverse effects from medication.

<table>
<thead>
<tr>
<th>Table I. Classification of asthma severity (5)</th>
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<td><strong>Clinical features before treatment</strong></td>
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<td><strong>Step 4</strong></td>
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<tr>
<td><strong>Severe persistent</strong></td>
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<td><strong>Step 3</strong></td>
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<td><strong>Moderate persistent</strong></td>
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<td><strong>Step 2</strong></td>
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<tr>
<td><strong>Mild persistent</strong></td>
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<td><strong>Step 1</strong></td>
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PEF: peak expiratory flow.

NB: The presence of one of the features of severity is sufficient to place a patient in that category.
Given the variable nature of the condition, asthma treatment needs to be tailored to individual patients. This means that a patient's treatment plan takes into account disease severity, current symptom patterns (within the previous 12 months) and the present age of the patient (14). Asthma severity is often underestimated and preventative therapy under-prescribed (724); this may result in poor asthma control and lead to an increase in rate or severity of exacerbations. It is now well accepted that appropriate treatment can prevent a substantial proportion of hospital admissions. In one study, approximately 74% of admissions were considered to be preventable (25). Prescribing even low doses of inhaled corticosteroids may reduce asthma mortality (26,27).

Managing asthma in patients susceptible to seasonal variations and/or exposure to irritants can be difficult. For these patients, it is essential that they monitor symptoms carefully and undergo clinical assessment as needed. In addition to recognizing a worsening in their condition, patients need to know what action to take and what relief they can reasonably expect from short-acting bronchodilators (28). Appropriate patient intervention can only be achieved if patients are willing to make decisions about their own asthma care and this can only be achieved if they are informed about their condition (28). Some patients are unwilling to accept that there is underlying airway inflammation present even when the severity of the disease is reduced, and that this may require long-term maintenance therapy. This non-acceptance leads to poor adherence to daily anti-inflammatory medication (29).

Current guidelines advocate a stepwise approach to long-term asthma treatment that places a patient at a certain level or step (mild intermittent, mild persistent, moderate persistent or severe persistent) based on current symptoms and recommends therapy accordingly (Table 2). This stepwise approach to asthma management involves routine treatment assessment and a step up or down the treatment ladder until the optimal treatment is attained. Stepping up can involve either a change in therapy or an increase in medication so that asthma control is achieved. A step down in treatment is recommended when symptoms have been well controlled for at least 3 months. Stepping down is an important part of asthma therapy and ensures that patients are not overtreated. Within the guidelines, there are two approaches to gaining asthma control. A clinician may prescribe:

1. a high level of therapy (e.g. add a short course of prednisolone or a higher dose of inhaled corticosteroids that corresponds with the patient's level of asthma therapy) to establish prompt asthma control and then reduce the medication to a level that maintains symptom control;
2. alternatively, a patient can start treatment at the step most appropriate to the level of asthma severity and treatment can then be 'stepped up' more gradually until control is achieved.

The first approach should be favoured, because the second approach may lead to a significant delay in controlling asthma symptoms and the frequent use of rescue medication. This step up/step down approach to asthma can only achieve optimal disease management if the doctor and patient are willing to reassess the need for medication regularly. Since many patients are under-diagnosed, they are most likely to receive a level of therapy that fails to control asthma symptoms and this can result in an over-reliance on relievers (14). This situation is not optimal and newer therapeutic approaches, such as combination treatments, which reduce the need for rescue medication by controlling the acute and chronic aspects of asthma, are being introduced.

### PHARMACOLOGICAL MANAGEMENT OF ASTHMA

Inhaled corticosteroids are the mainstay of treatment for patients with persistent asthma (30). As potent

<table>
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<th>Action</th>
<th>Therapy</th>
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<tr>
<td>Gain control</td>
<td>preferably - establish prompt control with a high level of therapy and then step down treatment</td>
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<tr>
<td></td>
<td>or - start treatment at the step most appropriate to the severity of asthma and step up if necessary</td>
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<tr>
<td>Step up</td>
<td>improvement should be achieved within 1 month - if asthma control is not achieved and sustained, review the patient's medication technique, compliance and avoidance of triggers. If they are satisfactory, step up medication</td>
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<tr>
<td>Step down</td>
<td>the goal is to decrease treatment to the least medication necessary to maintain control. If control is sustained for 3 months, follow a gradual stepwise reduction in medication</td>
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<tr>
<td>Review</td>
<td>Asthma treatment should be reviewed every 3–6 months once asthma is under control</td>
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anti-inflammatory agents they effectively reduce and control airway inflammation and inhibit almost every aspect of the inflammatory process in asthma. Inhaled corticosteroids are effective in the majority of patients, irrespective of age or asthma severity. In addition to controlling asthma symptoms and improving lung function, they also reduce the number of exacerbations and asthma mortality (26). Inhaled corticosteroids are prescribed for the long-term control of asthma symptoms and systemic corticosteroids may be used to gain rapid control of symptoms along with commencing long-term therapy with inhaled corticosteroids (14).

Relief from asthma symptoms is achieved by short-acting β2-agonists (e.g. salbutamol and terbutaline). The frequent use of these drugs is commonly used as an indication that anti-inflammatory treatment is inadequate. An over-reliance on relief medication is common in patients who do not adhere to their treatment programme and only use a short-acting β2-agonist when long-term therapy with a corticosteroid has been advised. One concern is that effective bronchodilation through regular short-acting β2-agonist therapy alone may mask worsening airway inflammation (31). This may lead to a delay in recognizing the onset or presence of a severe asthma attack.

Once a patient requires quick-relief medication every day, or more than 3–4 times a week, daily long-term medication is recommended if none is currently administered. In practice, this is an unnecessarily late stage to initiate anti-inflammatory therapy with inhaled steroids (21,32). A step up (increase of the dose of the inhaled corticosteroid) to more effective therapy is required for patients already taking the prescribed doses of daily medication and whose inhalation technique is correct.

Long-acting β2-agonists (e.g. formoterol and salmeterol) have become an important part of the therapeutic approach to managing asthma, giving relief for more than 12 hours. Formoterol, however, has the advantage over salmeterol of being a full agonist at β2-adrenoceptors, with a near maximal effect (33). Formoterol has a rapid onset of action similar to that of salbutamol, whereas salmeterol has a slow onset of action (33). Despite the introduction of the more selective β2-agonists, there is still concern about increased morbidity and a worsening in asthma control with the maintenance use of these agents. However, moderate long-term use of the short-acting β2-agonists, salbutamol and terbutaline, and the long-acting β2-agonists does not appear to be associated with a significant worsening of asthma control or an increased frequency of acute attacks (31).

Optimizing control in moderate and more severe asthma can be achieved by combining long-acting β2-agonists with inhaled corticosteroids, thereby treating both the chronic inflammation of asthma and its functional consequence—airflow limitations (34–36). A recent treatment advance is the clinical development of Symbicort®, which combines two such effective agents, budesonide (inhaled corticosteroid) and formoterol (long-acting β2-agonist with a rapid onset of action), in a single inhaler (37).

Recent studies suggest that the addition of a long-acting β2-agonist to low-to-medium doses of inhaled corticosteroid may be more effective than increasing the dose of the inhaled corticosteroid alone when a step up in treatment is required in persistent asthma (34–36). This finding can be explained, in part, by the fact that increasing the dose of inhaled corticosteroids according to the severity of the disease does not have a uniform effect on the different indices of asthma severity. For example, lung function measurements respond readily to low-dose inhaled corticosteroids, but their overall dose response is flat (38).

The concomitant use of formoterol and budesonide was studied in a 1-year clinical trial in patients who had persistent symptoms of asthma despite treatment with inhaled corticosteroids (36). In this study, the addition of formoterol to a low dose of budesonide reduced the rate of severe and mild exacerbations by 26% and 40%, respectively, compared with low-dose budesonide alone. Moreover, the addition of formoterol to low-dose budesonide was more effective than the higher dose of budesonide alone in improving clinical outcomes including lung function, symptom scores during the day and night, and the number of symptom-free days (36). The clinical benefits seen with the addition of formoterol to budesonide were irrespective of the dose of inhaled corticosteroid.

**THE CHALLENGE OF INCREASING PATIENT AWARENESS AND ADHERENCE**

Adherence to prescribed therapy is a major factor in the successful management of asthma. In spite of significant advances in developing asthma medications and the introduction of patient self-management plans, many people are unable to manage their asthma therapy optimally. Patient compliance with asthma treatment has been repeatedly estimated at approximately 50% (39,40). This failure to follow medication regimens may lead to treatment failure or apparent lack of drug efficacy. The terms 'compliance' and 'adherence' are often used interchangeably in healthcare management without clear definition. In asthma management, treatment compliance implies a willingness on the part of the patient to follow their doctor's instructions, but sometimes with little or no understanding of the disease or involvement in their own management strategy. Treatment adherence, on the other hand, involves a commitment to the treatment plan and therapy is the driving factor (41,42). This necessitates negotiation between the patient and
all members of their asthma-care team. In order for optimal adherence to be achieved, patients must be informed about their condition and be able to take appropriate therapeutic actions. Compliance is not enough to achieve optimal control of persistent asthma and all asthma care-team members should work towards adherence (42).

Compliance with, or adherence to, asthma management plans can be improved if patients have the opportunity to talk about their concerns, fears and expectations related to their asthma. Common factors associated with non-compliance are given in Table 3.

Patients with asthma need to be aware of what triggers their asthma and how these factors can be avoided. Taking medication correctly (especially the use of inhalers) is a key factor in controlling symptoms. Patients also need to be educated about a number of issues including: the different types of therapy (e.g. 'quick-relief' and 'long-term preventative' medication); self-monitoring; and recognizing and taking correct action in the event of worsening asthma. The current guidelines strongly recommend the use of written management plans for the patient/patient’s family (14).

In addition to these practical issues, there is the more difficult problem of changing the patient’s perception of his/her illness and medication. Children are particularly susceptible to peer pressure and opinion, and may have a very negative perception of their disease due to exercise intolerance which limits their ability in sporting activities. Children with asthma are also reported to feel self-pity, have low self-opinion and poor relationships with their peers (4).

It is often difficult for patients to accept that asthma is a disease requiring long-term treatment, particularly when their symptoms are mild. Educating asthma patients about the variable nature of their condition and the underlying pathology is the only effective way of achieving long-term commitment to therapy.

Other factors have also been identified which affect compliance and include: problems with inhaler devices; awkward medication regimens; and multipharmacotherapy, as well as fears about side-effects (4). In recent years, new designs of inhalers have been introduced which are easier to use for both children and adults. All patients need to be trained how to use inhalers correctly so that they receive the correct dose of medication. Devices which are preferred by the patient tend to increase treatment adherence. It is now well established that complicated treatment regimens are poorly adhered to in all fields of clinical medicine (42). Long-term treatment, multiple therapies and frequent dosing are also predictors of poor compliance (39). Until recently, these factors were all characteristics of asthma therapy which is associated with poor adherence to prescribed medication (39).

Issues of adherence can be addressed to some extent by patient education and counselling, but this approach requires huge investment in both time and money, and a willingness on the part of patients to become involved in their own care and treatment. The implementation of a simple treatment regimen which achieves reasonably well the goals of asthma therapy and makes the patient feel confident, is likely to be of great benefit in improving adherence. There will always be a minority of patients who are resistant to managed care, for whatever reason, and their asthma control will be suboptimal despite every effort on the part of the healthcare team.

OPTIMIZING ASTHMA CONTROL

Optimizing the control of asthma requires a comprehensive approach to asthma management (Table 4) (43). First, patients need to be correctly diagnosed early enough and assessed for severity. Second, individualized care plans need to be established from the very start of treatment. Once established, the treatment plan should be written down, discussed and reviewed with the

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<th>Table 3: Factors associated with non-compliance (5)</th>
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<tbody>
<tr>
<td>Medication-related factors</td>
</tr>
<tr>
<td>• Misunderstanding the need for both long-term preventative and reliever medication</td>
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<tr>
<td>• Impractical regimen (e.g. four-times daily or multiple medications)</td>
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<tr>
<td>• Difficulty with inhaler devices</td>
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<td>• Side-effects</td>
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<td>• Fear of side-effects</td>
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<tr>
<td>• Cost of medication</td>
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<td>• Dislike of medication</td>
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<td>• Distant pharmacies</td>
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patient so that the patient is able to implement agreed treatment strategies. Clinicians need to ensure that both patients and healthcare team members are well educated about asthma and motivated so that treatment plans can be followed correctly. Treatment plans should be simple and easy to follow. Finally, good cooperation between patient, doctor and the healthcare team should lead to better long-term optimal control of this variable disease, with improvement in the patient’s quality of life.

REFERENCES


