UNIT NO. 4

ASTHMA CONTROL IN ADULTS

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ABSTRACT

Compared with that in previous decades, bronchial asthma today is generally better controlled. However, there are still patients who have daytime and nocturnal symptoms, and asthma exacerbations. This suboptimal asthma control is often accepted as inevitable. The challenge into the future will be for patients and providers to work on the understanding that total control is possible, at least for the great majority. The unsatisfactory asthma treatment that used to be based on severity classification of disease has been resolved in the 2006 GINA Guidelines. It introduced new concept of 'asthma control'.

INTRODUCTION

Bronchial asthma is a pulmonary disease characterized by (1) reversible airway obstruction, (2) airway inflammation, and (3) increased airway responsiveness to various stimuli. Inflammation is central to the disease process. Symptom progression and control depends on the successful management of inflammation.[1]

Compared with that in previous decades, bronchial asthma today is generally better controlled, thanks to the widespread use of inhaled corticosteroids (ICS) since the early 1970s. However, there are still patients who have daytime and nocturnal symptoms, and asthma exacerbations.[2,3,4] Patients and providers alike often accept suboptimal asthma control as inevitable. The challenge into the future will be for patients and providers to work on the understanding that total control is possible, at least for the great majority.

Asthma treatment used to be based on severity classification of disease. This is not satisfactory because except for the initial treatment being based on the severity classification, subsequent treatment cannot be based on severity classification. This has been resolved. In the revised GINA Guidelines of 2006, the new concept of "control of asthma" has been introduced. This is based on the aggregate score of day time symptoms, limitation of daily activities, nocturnal symptoms, need for reliever treatment, no exacerbations, and normal or near-normal lung function test results.[5]

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CONTROL AND SEVERITY

What exactly do the terms asthma 'control' and asthma 'severity' mean? Asthma control reflects fluctuation in symptoms and lung function (or lack of them) over time; asthma severity reflects both asthma control and the need for medication. Thus, 'severity' is a property of the disease which reflects the degree of patho-physiological abnormality, whereas 'control' refers to the reduction of the clinical manifestations of disease achieved by treatment - thereby reflecting the adequacy of treatment.[2] Figures 1A and 1B, taken from the 2007 NHLBI Expert Panel Report 3 (EPR 3), show respectively the classification by asthma severity and the classification by asthma control.[1]

ULTIMATE GOAL AND DESIRED ENDPOINTS

The ultimate goal of asthma management is to achieve and maintain continuous disease control.[6] Table 1 shows the desired endpoints as described in the MOH 2008 guidelines.

Doctors and patients need to be convinced of the benefits of long term preventive treatment of asthma (MOH, 2008):
- Improved quality of life
- Reduced frequency and severity of asthma exacerbations
- Reduced risk of emergency room visits
- Reduced risk of hospital admissions
- Prevent loss of productivity from days missed work/school
- Reduce total cost of asthma treatment in the longer term
- Reduce risk of death from asthma.

Factors that predict poor adherence to treatment and hence sub-optimal control are shown in Table 2.[7,3]

Table 2. Predictors of Poor Adherence to Asthma Treatment

Factors that are difficult or impossible to alter
- Psychological problems
- Cognitive impairment
- Asymptomatic disease (good control)
- Disease duration
- Cost of treatment

Patient issues
- Missed appointments

Doctor or joint issues
- Inadequate follow-up or discharge planning
- Side effects of drugs or worries about such effects
- Lack of belief in treatment
- Lack of insight in to illness
- Poor patient-provider relationship
- Barriers to care and treatment
- Complexity of treatment

Source: Osterberg and Blaschke, 2005; Rees, 2006

ASSESSING ASTHMA CONTROL

Figure 1a. Classification of asthma severity (from national heart, lung and blood institute. Expert panel report 3 [epr 3]. Guidelines for the diagnosis and management of asthma)

Source: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm. Accessed on July 2, 2008.)

Figure 1b. Classification of asthma control (from national heart, lung and blood institute. Expert panel report 3 [epr 3]. Guidelines for the diagnosis and management of asthma)

Source: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm. Accessed on July 2, 2008.)

Table 1. Levels of asthma control

Characteristic	Controlled (All of the following)	Partly controlled (Any measure present in any week)	Uncontrolled
Day time symptoms	None (twice or less/week)	More than twice/ week	
Limitation of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	Three or more features of partly controlled asthma present
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/ week	
Lung function (PEFR or FEV1)*	Normal	Less than 80% predicted or personal best (if known)	
Exacerbations	None	One or more / year#	Once in a week @

Source: MOH 2008. * = Lung function is not a reliable test for children 5 years and younger # = any exacerbation should prompt review of maintenance treatment to ensure that it is adequate. @ = by definition, an exacerbation in any week makes that an uncontrolled asthma week.

Beyond the initial assessment, measurement of the control of asthma or the lack of it uses one of the psychometric measures of asthma control – ACT, ACQ, or ATAC. [8,9,1]; peak expiratory flow monitoring; and minimally invasive tests and measurements. The latter include airway hyperesponsiveness, sputum eosinophils, and exhaled nitric oxide, which require more evaluation to determine if they will be useful for routine clinical management.[10]

Psychometric measures of asthma control

The ACT can be used to identify patients with varying degrees of asthma control. See Figure 2. Patients respond to five questions in which they rate their degree of asthma control over the preceding 4 weeks on five questions:

1. How much of the time did your asthma keep you from getting as much done at work or home?
2. How often have you had shortness of breath?
3. How often did your asthma symptoms wake you up at night, or earlier than usual in the morning?
4. How often have you used your rescue inhaler?
5. How would you rate your asthma control?

The ACT has been shown to have excellent internal consistency (r = 0.84) in Western populations. In addition, ACT scores also correlate well with physicians' ratings of control (r = 0.45), and only weakly with FEV1 (forced expiratory volume in 1 second) (r = 0.19).[8,11] The validity of ACT has also been tested in 305 Chinese patients from 10 teaching hospitals across China and also gave good results. The internal consistency reliability was 0.854. The correlation coefficient between ACT and the specialists' rating was 0.729.[12]

The value of the ACT is that it can supplement physician assessment of asthma control and provide information in a separate domain from objective pulmonary function testing. This combined approach to the assessment of control can increase the ability of physicians to prescribe effective regimens of management.[11]

Based on a 5-point scoring system in the ACT, a maximum score of 25 will indicate 'total control' of asthma. 'Well controlled' asthma is defined as a score of 20-24, and a score of less than 20 will imply 'poor control'. The ACT will also enhance doctor-patient dialogue by standardizing the language and expectations of the goals of asthma management, consistent with those of GINA. A practical application and management plan based on ACT assessment is provided below (See figure 3).[6]

Figure 3. Management of asthma to achieve control
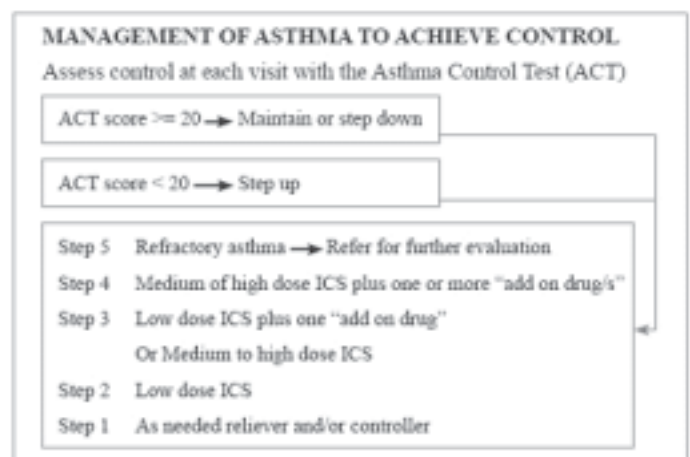
Use of Peak Flow Monitoring

Consider long term daily PEF monitoring for patients who:
κ   Have a moderate or severe persistent asthma
κ   Have a history of severe exacerbations
κ   Poorly perceive airflow obstruction and worsening asthma
κ   Prefer this method of monitoring

If PEF monitoring is performed, the patient's personal best measurement is the reference value to be used. Long-term daily PEF monitoring can help:
κ   Detect early changes in disease states that require treatment
κ   Evaluate responses to therapy changes
κ   Afford a quantitative impairment measure

PEF monitoring during exacerbation will help determine the

severity of exacerbations and guide therapy. Consider home PEF monitoring during asthma exacerbations in patients who have:

κ A history of severe exacerbations
κ Moderate to severe persistent asthma
κ Difficulty in perceiving signs of worsening asthma.

Use of Spirometry

This can be used:

κ At the time of initial assessment
κ After treatment is initiated and symptoms and peak flow measurements have stabilized, to document attainment or (near) "normal" airway function
κ During period of progressive or prolonged loss of asthma control
κ At least every 1-2 years to assess the maintenance of airway function

FROM ASSESSMENT TO STEPWISE PHARMACOTHERAPY

Asthma medications can be classified as either controller medications or rescue medications. Since the underlying pathophysiology of asthma involves ongoing inflammation, controller medications are used daily to down-regulate inflammation and to maintain asthma control. Controller medications for asthma include orally inhaled corticosteroids (alone or in combination with long-acting *beta*2-agonists), leukotriene modifiers, mast cell stabilizers, theophylline, omalizumab, and systemic corticosteroids.[11]

While rescue medications such as salbutamol are recommended as primary treatment for intermittent asthma, they should be used only sporadically to reverse bronchoconstriction and decrease asthma symptoms. In treating patients with persistent asthma, rescue medications are only used as adjuvant treatment with controller medications. Rescue medications used for asthma include primarily short-acting *beta*2-agonists, although rapid-acting inhaled anticholinergics, short-acting theophylline, and short-acting oral *beta*2-agonists can also be used in select circumstances.[11]

Figure 2 from the 2008 MOH guidelines shows the steps 1-5 for achieving control mapped to the ACT results. Each step has treatment options, which are alternatives for controlling asthma. Steps 1-5 provide steps of increasing lack of control. In the management scheme described in Figure 2, the dose of daily asthma medication is adjusted according to the ACT scores evaluated at each clinic visit. Patients who do not achieve good asthma control despite Step 4 levels of

Figure 2. Asthma Control Test

Source: MOH 2008 with permission from QualityMetric

treatment have refractory asthma and should be reviewed by a specialist. Thus, management at Step 5 should be supervised directly by specialists.

The 5 steps asthma treatment plan in the 2008 MOH guideline corresponds broadly to the 2005 British Thoracic Society (BTS) & Scottish Intercollegiate Network guidelines treatment plan which also has 5 steps.[6,13] The treatment modalities in each of the steps is summarized below.

Step 1 – Mild intermittent asthma – as needed inhaled SABA (short acting beta2 agonist) and or low dose ICS

Step 2 – Mild persistent asthma – regular controller therapy needed – start low dose ICS (inhaled steroids) at dose equivalent to beclomethasone 200-400 ug/day. Alternatives: leukotriene modifier or theophylline.

Step 3 – Additional therapy – Low dose ICS + one "add on drug" e.g. LABA or medium dose ICS. Alternative: Low dose ICS + either leukotriene modifier, theophylline.

Step 4 – Persistent poor control – Medium dose ICS + one or more "add on drugs" e.g., LABA. Alternative: Medium dose ICS + either leukotriene modifier, theophylline

Step 5 – Refractory asthma – patients whose asthma is still not controlled should be referred to a specialist for assessment and consideration of further options including high dose ICS + LABA, frequent or regular oral corticosteroids, and omalizumab.

Note that the NHLBI 2007 guidelines uses a 6-step plan. Compared to the 2008 MOH guidelines' 5-step plan, the difference lies in steps 5 and 6. See Figure 4.

Corticosteroids

Inhaled corticosteroids (ICS) are generally considered to be the most effective class of asthma controller therapy. ICS reduce asthma symptoms, improve quality of life and lung function, and decrease airway hyper-responsiveness and bronchoconstriction. Their net effect is to reduce the frequency and severity of asthma exacerbations and decrease asthma morbidity and mortality. The dosage of ICS can be individually adjusted based on an ongoing assessment of asthma control.

Treatment with low doses of ICS is not generally associated with significant suppression of the hypothalamic-pituitary-adrenal (HPA) axis, although at higher doses mild changes can be seen in susceptible individuals. ICS can be

Figure 4. Choice of Medications in Adults & Teenagers More Than 12 Years
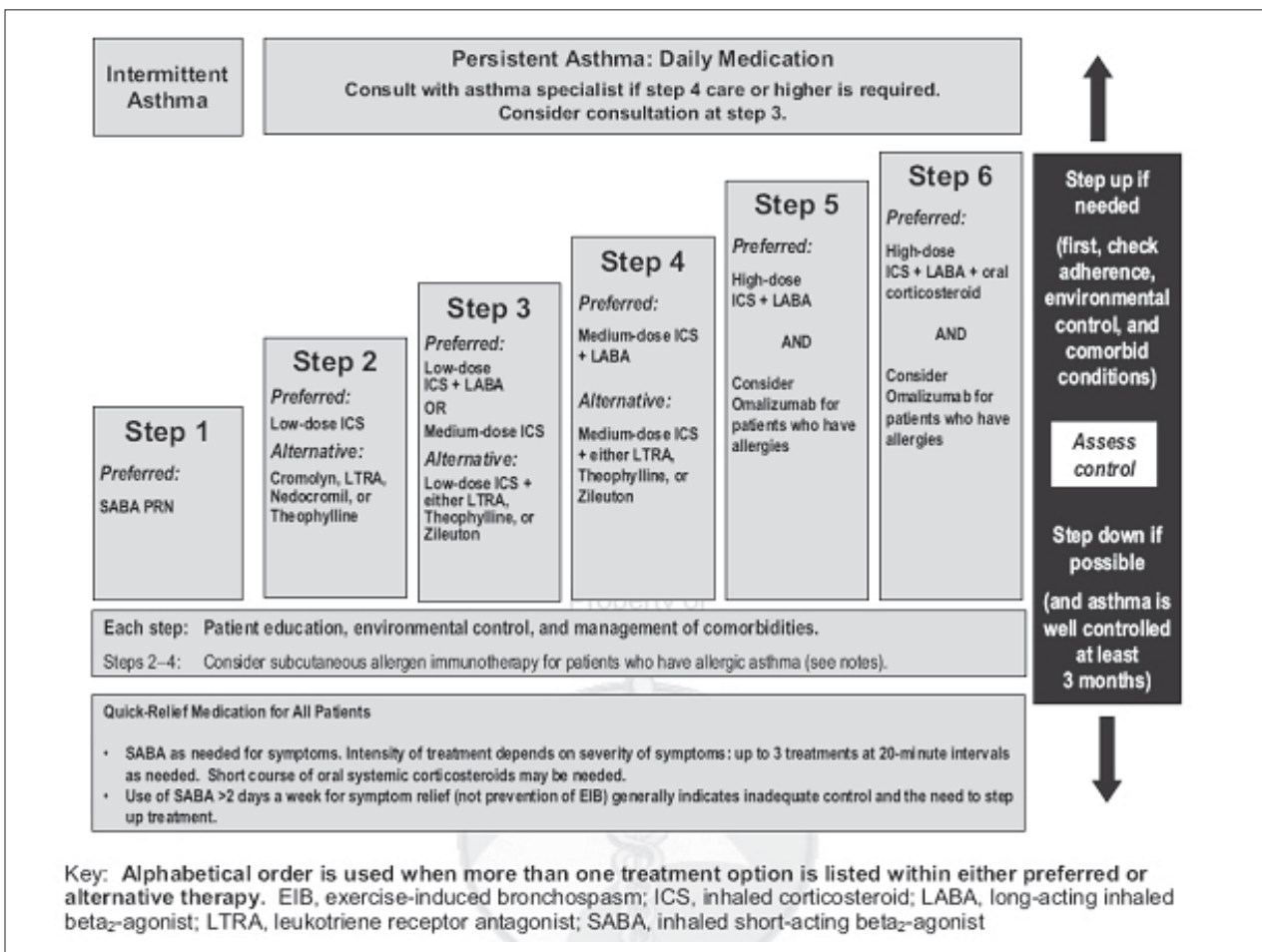
Source: National Heart, Lung and Blood Institute, 2007

associated with local mucosal effects, including topical candidiasis, hoarseness, and mucosal dryness. Inhaled corticosteroids can also be associated with ocular events, including cataracts and glaucoma, although these effects are uncommon.

In patients whose asthma is under poor control, systemic corticosteroids are often necessary to decrease symptoms and improve control. Systemic corticosteroids can be associated with significant adverse systemic effects, and are therefore reserved for the most difficult or poorly controlled patients. Oral corticosteroids such as prednisone are generally preferred to parenteral corticosteroids.

Leukotriene modifiers

There are two types of leukotriene-modifying medications that can be used in the management of asthma: (1) cysteinyl leukotriene (CysLT) receptor antagonists such as montelukast and zafirlukast; and (2) the 5-OH-lipoxygenase inhibitor, zileuton. Leukotriene modifiers decrease the inflammatory effect of the CysLTs, and have been shown to have a beneficial effect on lung function.[11] They are often used for patients with mild persistent asthma; however, they are generally observed to be less effective than the ICS.[14] Leukotriene modifiers may also be used as adjuvant medications to ICS in select patients to improve their asthma control.

Beta2-agonists

Short-acting beta2-agonists (SABA) such as salbutamol are important medications in the treatment of the acute symptoms of asthma. They can be used on an infrequent basis to manage the symptoms of intermittent asthma, and as rescue medications in patients with persistent asthma. They are not appropriate for frequent use, and should not be used as controller medications for asthma symptoms as they do not have any effect on the underlying inflammation that is characteristic of the disease. The increasingly frequent use of SABA is an important indicator that the patient's asthma control is worsening, and that medical attention is necessary.

Long-acting beta2-agonists (LABA), including salmeterol and formoterol, are used as adjuvant therapy in patients who are difficult to bring under adequate control. LABAs do not decrease inflammation, however, and should not be used for asthma treatment without a controller anti-inflammatory medication. LABAs combined with ICS have been shown to decrease asthma symptoms, improve pulmonary function, and reduce asthma exacerbations. This approach can result in improved asthma control with lower doses of ICS than with ICS alone. Since there have been studies indicating an increased statistical risk of asthma-related deaths associated with the use of salmeterol, LABAs should only be used in conjunction with ICS, with consideration given to advancing doses of ICS before adding a LABA for asthma control.[15,11]

Theophylline

Theophylline is used infrequently in current management strategies, although in certain circumstances it may have some benefit. While theophylline acts primarily as a bronchodilator, it also appears to possess some weak anti-inflammatory properties. Current evidence suggests that theophylline has little benefit as a first-line controller medication, while it may have a role in patients who do not respond to ICS alone.[11]

Omalizumab

Omalizumab is a recombinant, humanized, monoclonal anti-E antibody that binds to IgE at the same Fc site as the high-affinity IgE receptor. Its primary mechanism of action is binding free IgE in the circulation, forming biologically inert, small complexes that do not activate complement and are cleared by the reticuloendothelial system.[16,17] The place of omalizumab in the step asthma pharmacological treatment is in step 4 as a means to avoid higher doses of ICS (evidence category D), and in steps 5 and 6 of the NHLBI 2007 guidelines (evidence category B)[17] which corresponds to the step 5 of the 2008 MOH guidelines.

Patients requiring more attention

It is useful to identify patients requiring more attention. They are patients with more severe disease, and those who have non-adherence problems. See Table 2. The following need some comment.

Recently hospitalised

Self management is particularly recommended for adults recently admitted to hospital or recently attending emergency departments because of asthma. This group is not only over-represented in mortality and morbidity statistics, but are also more likely to be re-admitted to hospital than any other group of asthmatics,[18] and therefore have the most to gain from optimal asthma management.[19]

Mood problems

Asthma is a common cause of anxiety and depression, particularly where sub-optimal therapy leads to chronic disability. If concurrent psychiatric illness is present, death rate from asthma rises.[6]

Asthma in pregnancy

During pregnancy, one-third of women experience worsening of asthma, one-third, an improvement, and one-third remain the same. Poorly controlled asthma may contribute to adverse fetal outcomes. The risk of an asthma exacerbation is high immediately postpartum. Poor control is associated with pre-eclampsia, and uterine haemorrhage, as well as greater rates of caesarean section, pre-term delivery, intrauterine growth retardation, low birth weight, and congenital malformation. Inhaled therapies remain the cornerstone of treatment and most are safe in pregnancy.[20]

THE FOUR KEY ELEMENTS OF ASTHMA CONTROL EDUCATION

In each step of the asthma pharmacological treatment plan, education for asthma control is required. A successful asthma control education plan for each patient consists of attention to each of the following elements:

ĸ   Education-motivation
ĸ   Self assessment and management
ĸ   Environment management.
ĸ   Understanding pharmaceutical management.

Education-motivation

Common barriers to effective asthma treatment are: [6]

ĸ   Failure to agree to a set of common goals with patient
ĸ   Patient resistance/objection to inhalational therapy
ĸ   Poor inhalational technique
ĸ   Inconvenient dosing schedules
ĸ   Underestimation of worsening symptoms
ĸ   Steroid phobia
ĸ   Concern about potential adverse effects during pregnancy
ĸ   Worry about excessive costs

The only effective way to deal with these problems is by more intensive patient education. Strong motivation and repeated, sustained education is necessary to overcome every one of these barriers.

Self assessment and management

Continuous self assessment of symptoms and a written action plan (WAP) for managing acute exacerbations are important aspects of self assessment and management. An example of a WAP template taken from the MOH 2008 CPG is shown in Figure 5. [6]

Management of environmental triggers

This is an important aspect of preventive care and attention to details is worth the efforts in tracking them down and eliminating them.

Indoor allergens – House dust mite (*Dermatophagoides pteronyssinus*) are allergens most commonly found in bedding and carpets. The most effective method is to wash blankets, bed-sheets, pillow cases and mattress pads at least weekly using

Figure 5. Written Asthma Plan

Symptoms	Medication
WHEN WELL	
ı No asthma symptoms	Regular Controller Treatment **EVERYDAY**:
	1.
	2.
	3.
ı Before exercise	Reliever _____ puffs ONLY when necessary
CAUTION	
If you	**STEP UP** TREATMENT
ı Wake at night due to asthmasymptoms	
ı Have day time asthma symptoms more than 2 times	1. _____ puffs _____ times/day for next 7-14 days. If improved go back to regular treatment.
ı Used reliever more then 2 times	
ı Have limited activity or exercise	
ı Have influenza like symptoms	2. Reliever _____ puffs 4-6 hourly x 3 days.
EXTRA CAUTION	
If **NO** improvement at anytime with the above treatment then add ...	Prednisolone 30 mg per day x 5-7 days. (**for Adults**)
	(Children should consult Dr. first)
DANGER	
GET HELP WHEN	**SEE YOUR DOCTOR**
ı Severe shortness of breath	**DO NOT WAIT**
ı Reliever medicine is not helping	**CALL 995 FOR AN AMBULANCE**
ı Can only speak in short sentence	Reliever ____ puffs at 10 minutes interval till you get to
ı Feeling frightened	the nearest Dr. or hospital.
	Prednisolone 30 mg immediately.
Affix Patient Stickers	Reinforced by:
	Date:

water at 65 degree C and install impervious covers over mattresses and pillows. Remove carpets and soft toys (wash them weekly if present). Avoid prolonged contact with upholstered furniture. Cockcroach allergen is reduced by cockcroach extermination followed by routine cleaning.[6]

Irritants – Doctors should advise all asthmatics (children and adult) not to smoke and to avoid environmental exposure to tobacco smoke where possible.[6]

Outdoor air pollution – Asthmatics should avoid exertion or exercise outdoors when levels of air pollution are high (PSI>100). Increased pollution levels is reported to precipitate symptoms of asthma, increase emergency room visits and hospitalization.[6]

Drugs and Chemicals
Many substances in industry may provoke asthma. Many drugs also exacerbate asthma, including anti-inflammatory drugs (NSAIDs) and salicylates. The concurrent use of beta-blockers may provoke wheezing, which is quite refractory to the action of usual doses of beta-2 agonists.[6]

Understanding pharmacological management of asthma

The goal of asthma treatment is to achieve and maintain clinical control. To a large extent this is done by the judicious use of the various medications available to us. Patients need to understand the difference between controllers and relievers and their correct use.

- **Controllers** are medications taken daily on a long-term basis to prevent exacerbations of asthma and control asthmatic symptoms. They have an anti-inflammatory effect. The most effective controller medications currently available are inhaled glucocorticosteroids.

- **Relievers** are medications taken as required to relieve symptoms of wheeze or breathlessness. They act quickly and reverse the bronchospasm occurring during an attack of asthma. The most effective relievers are rapid acting inhaled beta2-agonists such as salbutamol, but inhaled anticholinergics such as ipratropium may also be useful.

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LEARNING POINTS

- The desired endpoints in the control of asthma is to have no symptoms night or day.

- There is a need to change the mindset of provider and patient alike to desire total control of symptoms versus subjective control.

- The Asthma Control Tool is a useful everyday assessment tool for patients and providers alike.

- The 5 step approach described in the Singapore clinical practice guidelines on management of asthma (MOH, 2008) provides a pharmacotherapy plan for asthma control.

- The four key elements of education for asthma control are: education-motivation, self assessment and management, management of environmental triggers, and understanding of pharmacotherapy.

- Patients requiring more attention need to be identified and more efforts devoted to them where necessary to bring their asthma under control.