Asthma is a chronic inflammatory respiratory disease characterized by reversible obstruction of the airways. Identification and avoidance of triggers is clearly a fundamental aspect of asthma management. However since this is often difficult or impossible, most patients rely on medication for symptom control and prevention.\(^1\)

The specific medical treatment recommended to patients with asthma depends on the severity and frequency of symptoms. Treatments for asthma are broadly classified as relievers (rapid-acting agents for a quick reverse of bronchoconstriction and quick relief of symptoms), controllers (medications taken on a regular basis to keep asthma under clinical control, primarily through their anti-inflammatory effects) and emergency treatment for when attacks become particularly severe and fail to respond to usual measures. In recent years, relief and control medications have been combined in one inhaler device and use of these treatments is now widespread.

### Asthma management guidelines

All current asthma guidelines recommend a stepwise approach to therapy based on how well controlled asthma symptoms are. For example, the Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention recommends a five-step therapeutic approach that starts with reliever treatment alone at step one and works its way up through combination therapy with inhaled corticosteroids and long-acting beta-two (\(\beta_2\)) agonists, with a wide range of alternatives and additional combinations at steps three and four, ending with additional oral glucocorticosteroids at step five.\(^2\)

### Relief medication

Wheezing and shortness of breath associated with asthma can generally be relieved with fast-acting bronchodilators (agents that help to reverse constriction of the bronchioles). These are typically provided in pocket-sized, metered-dose inhalers.

In young children with asthma who may have difficulty with the coordination necessary to use inhalers, or those with a poor ability to hold their breath for ten seconds after inhaler use (generally the elderly), an asthma spacer is used. The spacer is a plastic cylinder that mixes the medication with air in a simple tube and allows for the active agent to be split into smaller and larger particles – the former being inhaled for good lung deposition and the latter being retained within the spacer.

A nebulizer that provides a larger, continuous dose can also be used. Nebulizers work by vaporizing a dose of medication in a saline solution into a steady stream of foggy vapour, which the patient inhales continuously until the full dosage is administered.

**Reliever medications include:**
- Rapid-acting, inhaled \(\beta_2\)-agonists, such as salbutamol, terbutaline, reprotrol and fenoterol. Tremors and tachycardia (rapid beating of the heart), the major side effects, have been greatly reduced by inhaled delivery, which allows the drug to target the lungs directly.\(^3\)
- Anticholinergic medications, such as ipratropium bromide may be used as an alternative. They have no cardiac side effects and thus can be used in patients with heart disease,\(^3\) however, they take up to an hour to achieve their full effect and are not as powerful as the \(\beta_2\)-adrenergic agonists
- Xanthines like theophylline may be considered for relief of asthma symptoms, but they may provide no additive bronchodilator effect over rapid-acting \(\beta_2\)-agonists\(^4\)
Controller medication

Current treatment guidelines recommend controller medications, such as inhaled corticosteroids, as the most effective anti-inflammatory medication for the treatment of persistent asthma as they reduce asthma symptoms, improve lung function, reduce the frequency and severity of exacerbations and improve quality of life. If symptoms persist, additional controller drugs may be added until the asthma is controlled.

Inhaled corticosteroids are the most widely used of the controller medications (e.g. ciclesonide, beclomethasone, budesonide) and are normally delivered via inhaler devices. Long-term use of corticosteroids can have many side effects including a redistribution of fat, increased appetite, blood glucose problems and weight gain. Patients on high doses of corticosteroids may experience adrenal suppression, decreased bone mineral density and easy bruising. Local adverse effects from inhaled corticosteroids include oropharyngeal candidiasis (an oral infection) and dysphonia (hoarseness of the throat). Risk of these side effects may be minimized by rinsing the mouth with water after inhaler use, as well as by using a spacer which increases the amount of drug reaching the lungs directly. There are also some new formulations and devices that reduce mouth/throat deposition.

Patients’ concerns about corticosteroid side effects may lead them to discontinue treatment as soon as they control their symptoms, which can result in further asthma symptoms and exacerbations. Asthma management guidelines advise that the minimum effective dose of corticosteroid should be used for maintenance of asthma control to minimize the risk of side effects.

Other controller options include:

- Leukotriene modifiers (such as montelukast and zafirlukast)
- Mast cell stabilizers (sodium cromoglicate and nedocromil)
- Antimuscarinics / anticholinergics (ipratropium, oxtropium, and tiotropium), which have a mixed reliever and preventer effect. (These are rarely used in preventive treatment of asthma, except in patients who do not tolerate β₂-agonists)
- Methylxanthines (theophylline and aminophylline), which are sometimes considered if sufficient control cannot be achieved with inhaled corticosteroids and long-acting β₂-agonists alone
- Antihistamines are used to treat allergic symptoms that may underlie the chronic inflammation. In more severe cases, hyposensitization («allergy shots») may be recommended
- Omalizumab, a blocker of the antibody IgE which is found in elevated levels in allergic asthma. This can help patients with severe allergic asthma that does not respond to other drugs. However, it is expensive and must be injected
- Methotrexate is occasionally used in some difficult-to-treat patients
- If chronic acid indigestion contributes to a patient’s asthma, it should also be treated because it may prolong the respiratory problem

Combination therapy with inhaled corticosteroids and long acting β₂-agonists

For patients whose asthma is not sufficiently controlled by a low dose of corticosteroid alone, GINA recommends, among other things, long-acting β₂-agonists (such as formoterol or salmeterol) with doses of inhaled corticosteroid.

Long-acting β₂-agonists are similar in structure to rapid acting selective β₂-adrenergic agonists, but have a 12-hour effect, and are used to give a smoothed symptomatic relief (used morning and night).

Currently available long-acting β₂-agonists include salmeterol, formoterol, bambuterol, and sustained-release oral salbutamol. Combinations of inhaled corticosteroids and long-acting bronchodilators are becoming more widespread since it has been shown that these agents in combination improve symptom scores, improve lung function, decrease the need for rapid-acting inhaled β₂-agonists, reduce the number of attacks.
and achieve clinical control of asthma in more patients, more rapidly and at a lower dose of inhaled corticosteroids than inhaled corticosteroids given alone.\textsuperscript{3}

Fixed combination inhalers (those that deliver set amounts of each active ingredient with each inhalation) are more convenient for patients and may increase adherence by delivering both the inhaled corticosteroid and the long-acting $\beta_2$-agonist at the same time.\textsuperscript{3}

**Emergency treatment**

When an asthma attack is unresponsive to a patient’s usual medication, an individual with asthma may need emergency care. A healthcare professional will usually take a brief history and conduct relevant physical examinations in conjunction with administration of therapy. Respiratory examinations may also be conducted. Initial treatment options range from oxygen to achieve $O_2$ saturation to the use of systemic glucocorticosteroids if there is no immediate response. It is recommended that the patient is reassessed after one hour and based upon this, different treatment options may be implemented and the patient may be discharged, admitted to an acute care setting or admitted to intensive care.\textsuperscript{7}

**Delivery technology: the importance of device and formulation**

Inhaler devices differ in their efficiency of drug delivery to the lower respiratory tract, depending on the type of device, formulation of medication, velocity of the aerosol cloud or “plume” (where applicable) and ease with which the device can be used by the majority of patients.\textsuperscript{2} These factors have been shown to influence efficacy and tolerability. A recent study also suggested that the particle size of medication may affect asthma control, with extra-fine aerosols offering a potential advantage.\textsuperscript{8} Similarly, tolerability can be expected to be improved by technology that delivers the particles deeper into the lungs since the dose required will be lower.\textsuperscript{9}

**Beyond guidelines: asthma management in the real world**

Asthma management in Western Europe is not considered to be as good as it could, or should, be.\textsuperscript{5} The Asthma Insights and Reality in Europe (AIRE) study demonstrated a considerable difference between the way asthma is managed in practice and the recommendations set out in GINA and other guidelines.\textsuperscript{5,10} In practice, physician adherence to guidelines is too low and patient adherence to prescribed controller medication is poor.\textsuperscript{5}

Many individuals with asthma underestimate what can be achieved in terms of asthma control, continuing to over-rely on reliever medication, thereby increasing the risk of persistent airway inflammation. Increasing patient understanding of the disease and of the role of anti-inflammatory medication might help improve patient adherence to therapy, as might the use of combination inhalers, a greater role for asthma nurses and involving patients in treatment decisions.\textsuperscript{5}