



SEVERE ASTHMA
*understanding the professional
guidelines*

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This guide includes information on what the European Respiratory Society (ERS) and the American Thoracic Society (ATS) have said about severe asthma.

It is based on a longer version, written for professionals, to explain what severe asthma is, how to diagnose it and suggestions for treating the condition.

You can view the full guideline on the ERS website: www.ers-education.org/guidelines.

This version is written for patients and the public to help explain what to expect if you have severe asthma. This guide does not include background information on asthma or severe asthma, but this can be accessed on the European Lung Foundation website: www.europeanlung.org

WHAT IS SEVERE ASTHMA?

Severe asthma was identified as a condition in the early 2000s. The ERS/ATS guideline defines severe asthma as asthma that requires two types of controller medication, instead of the usual one, or asthma that remains uncontrollable despite this high level of medication.

Recent research has indicated that severe asthma is not one single condition. Instead, the term is used as an umbrella term for many different types of the condition. Healthcare professionals term these different types of any condition as a 'phenotype'.

To define these different types, researchers look at how the condition is different in different people. To do this, they assess biological characteristics of the condition, such as a person's genetic characteristics and the cells and tissues found in the airways, along with medical characteristics that can be measured by a healthcare professional or reported by a patient, such as lung function and symptoms.

These assessments need to be carried out in big population studies to help experts understand the different types of severe asthma that exist. Once these types are defined, it will be easier for experts to match the appropriate treatment to each person.



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HOW SHOULD SEVERE ASTHMA BE DIAGNOSED?

Healthcare professionals should follow three steps to diagnose severe asthma:

1. Determining if a person has asthma

To diagnose asthma, a healthcare professional should assess a person's symptoms, including feelings of chest tightness, wheezing, breathlessness and waking up often in the night. They will also look at any triggers, such as environmental (e.g. dust, pollen, or perfume) or occupational (e.g. chemicals or dust in the workplace) factors, that may be worsening the symptoms.

The ERS/ATS guideline includes a suggestion that a high-resolution CT (computerised tomography) scan be used to exclude any other conditions that may mimic asthma if a person has symptoms that are not typical, i.e. asthma that does not cause the usual symptom of wheezing. If a person has asthma, the scan may show changes in the structure of the bronchi such as thicker walls of the airways.

2. Determining why asthma may be difficult to treat

Some people have asthma that is difficult to control. If this is the case, healthcare professionals should look at a number of factors, such as the treatment of allergies or other co-existing conditions, inhaler techniques or lifestyle factors (e.g. diet, exercise, smoking), to try to help a person gain control of their symptoms. If all other factors have been addressed and the person still has asthma symptoms, a diagnosis of severe asthma should be given.

3. Determining the type of severe asthma

Different types of severe asthma may respond differently to current treatments. It is important to try and determine which type of severe asthma a person has. There are currently no widespread definitions; however there appear to be three general patterns:

- Severe asthma that started in childhood with symptoms triggered by a person's allergies. This is known as the early-onset allergic type.
- Severe asthma that started in adulthood and is linked with obesity. This is known as later-onset obese type.



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- Severe asthma that started in adult life and is characterised by increased levels of eosinophils (a type of white blood cell). This is known as the later-onset eosinophilic type.

As these three groups are not an exhaustive list of the different types of severe asthma, current research efforts are focused on providing clearer definitions so that treatment can be more personalised and tailored in the future.

HOW SHOULD SEVERE ASTHMA BE TREATED?

Using established medications

There are several medications licensed to treat mild or moderate asthma but not all of them are effective for severe asthma. The ERS/ATS guideline discusses these established therapies and their effectiveness in treating severe asthma and their recommendations are summarised below. A healthcare professional should discuss each of these treatment options with a patient, including the positives and negatives, to help identify the best treatment approach.

- ***Corticosteroids***

Corticosteroids are a group of medicines that are used to treat asthma. Severe asthma is defined as asthma that does not respond to the usual dose of corticosteroids. This does not mean that the treatment does not work at all, but rather that corticosteroids are less effective for people with severe asthma and higher doses may be required.

- ***Inhaled and oral corticosteroid therapy***

When corticosteroids are inhaled, they go directly into the lungs to reduce inflammation and swelling. When used regularly by people with mild-to-moderate asthma, they help to prevent asthma attacks. It is likely that higher doses of inhaled corticosteroids are needed to help treat severe asthma.

Another report suggests that the usual dose of inhaled corticosteroids can be quadrupled to effectively treat exacerbations (worsening of symptoms) in mild-to-moderate asthma; however, this is not practical in people with severe asthma, who are already on a high dose.



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Oral corticosteroids are more powerful than inhaled corticosteroids. They are, therefore, often added to the usual maintenance therapy of inhaled corticosteroids to treat exacerbations of severe asthma. The timing for starting this treatment is not yet clear and it is not yet known whether it is better to maintain small doses of treatment all the time or take several higher doses at regular bursts to control an exacerbation.

As oral corticosteroids travel to all parts of the body, there can be some side-effects from taking high doses, such as an increased risk of fracturing bones, restricted growth in children and weight gain. Therefore, it is important to have regular visits to a healthcare professional who should monitor weight, blood pressure, blood glucose, eye and bone density, and growth in children.

- ***Short- and long-acting β -adrenergic bronchodilators***

Short- and long-acting β -adrenergic bronchodilators help treat asthma by relaxing the muscles in the airways, which makes them wider. Adding a long-acting β -agonist (LABA) in combination with inhaled corticosteroids may improve control in severe asthma. Short- and long-acting β -adrenergic bronchodilators can be delivered by nebulisers as well as inhalers.

- ***Slow-release theophylline***

Theophylline also acts to relax the muscles in the airways. No studies have been conducted to test whether theophylline is effective in people with severe asthma. However, in patients with moderate asthma, it has been reported to improve asthma control when used alongside inhaled corticosteroids.

- ***Leukotriene pathway modifiers***

Leukotrienes are a group of molecules in the body known to cause airway constriction, increased mucus production, swelling and inflammation in the lungs. This treatment acts by blocking the actions of these molecules. It can improve lung function of some people with asthma when added to inhaled corticosteroids, but its use in severe asthma is not clear.



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- ***Long-acting muscarinic antagonists***

This treatment blocks the effects of a part of the body known as a muscarinic receptor. This is found within a cell and can cause the tightening of the smooth muscle in the lungs for people with asthma. Ipratropium bromide is a drug used to treat asthma. It is supplied as an aerosol and can relieve symptoms for people with severe asthma. Tiotropium bromide is a long-acting muscarinic antagonist that has been reported to improve lung function and symptoms for people with severe asthma who are on moderate-to-high doses of inhaled corticosteroids, with or without long-acting β -agonists.

Specific approaches for severe asthma

The ERS/ATS guideline gives advice on three different approaches that can be used specifically to treat severe asthma.

- ***Using clinical and biological characteristics to guide therapy***

Counting the number of eosinophils (a type of white blood cell) found in sputum can be used to give an indication of how severe asthma should be treated. The guideline suggests using this count as an indicator for treatment, but only when taken at a centre experienced in using the technique and when it is used alongside other clinical measurements such as lung function tests.

Nitric oxide is a gaseous molecule that is produced by the body when it has some types of inflammatory responses. Therefore, some people with asthma have higher levels of nitric oxide than people without asthma. Its role in severe asthma has not been proven; therefore, the guideline suggests that it generally should not be used to guide therapy because it is an expensive test and there is no good quality evidence to suggest it is effective in severe asthma.

- ***Therapeutic approaches***

The guideline gives five recommendations concerning specific therapies that should be suggested to treat severe asthma:



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1. Omalizumab is a drug that can reduce the way in which the body responds to the allergens which cause severe allergic asthma. The guideline suggests that people with severe allergic asthma try using omalizumab for a set period of time. If the person does not see the benefits of this treatment after 4 months, it is unlikely to be a beneficial therapy for them.
2. Methotrexate is a drug used to treat a number of overactive inflammatory conditions and certain cancers. The guideline suggests that it should not be used for people with severe asthma due to the potential side-effects and the need for monitoring treatment. If it is needed to try and reduce the dose of oral corticosteroids, it should be used by specialist centres and only in patients who require daily oral corticosteroids.
3. Macrolides are a type of antibiotic that can be particularly useful in treating lung and chest infections. The guideline suggests that clinicians not use macrolide antibiotics in adults and children with severe asthma, due to the potential for people to develop resistance to the drugs.
4. Antifungal medications are used to treat any type of fungal infection in the body. The guideline suggests that antifungal medication could be useful for adults with severe asthma who have allergic bronchopulmonary aspergillosis (ABPA). It should not be used for the treatment of severe asthma in adults and children without ABPA.
5. Bronchial thermoplasty is a procedure that is reported to reduce the amount of muscle that surrounds the airways in the lungs. The procedure involves a small piece of wire being passed down a bronchoscope and into the lungs until it touches the airways. Radio waves are used to heat up the wire and this heat causes the muscles surrounding the airways to break up, making it more difficult for the airways to tighten. Bronchial thermoplasty can be used to treat adults with severe asthma, but the guideline recommends that it only be performed as part of an independent systematic registry or a clinical study because it is a new type of therapy.



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- **Experimental molecular-based treatments**

A new form of therapy is emerging for severe asthma. It is known as molecular-based therapy, which targets specific molecules in the body. Rather than trying to reduce the symptoms of asthma, as current medication does, molecular-based treatments try to prevent them occurring in the first place by blocking the molecules responsible. The first molecular-based treatment approved for asthma is anti-IgE therapy, which blocks immunoglobulin E, a substance in the body that is an underlying cause of inflammation in allergic asthma. This therapy is available in the form of the Omalizumab drug mentioned above.

Other molecular-based treatments are currently being investigated and experts are optimistic that in the future these treatments will help improve outcomes for people with severe asthma.

FUTURE RESEARCH

The ERS/ATS guideline is the first high-quality guideline on the definition, evaluation and treatment of severe asthma. In 2014, the phenotyping of severe asthma is still in its early stages and current and future research should focus on better defining the different types to personalise approaches to therapy. Additional research will make it easier to tailor medicines to individuals based on their specific disease. When doctors are in a position to personalise severe asthma treatment, people with the condition can expect to see much better outcomes and improvements in their symptoms.

ABOUT ELF AND ERS

The European Lung Foundation (ELF) was founded by the European Respiratory Society (ERS) to bring together patients, the public and professionals. The ERS has been in guideline development for more than a decade; providing continent-wide advice to healthcare professionals on the appropriate care and treatment for people with lung condition.

ELF produces public versions of these guidelines to summarise the recommendations made to healthcare professionals in Europe, in a simple format for all to understand.

These documents do not contain detailed information on each condition and should be used in conjunction with other patient information and discussions with your doctor.



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