Background information

Asthma

Asthma is a complex disease affecting the lungs that can be managed but cannot be cured. Asthma can be controlled well in most people most of the time, although some people may have more persistent problems. Asthma attacks (exacerbations) occur when symptoms worsen, and those affected can require hospitalisation. There are different types of asthma; more than half of patients have Type 2 asthma, an important distinction because the causes of inflammation that result in Type 2 asthma symptoms have been clearly identified.

Epidemiology

There are 334 million people with asthma across the globe today. The number of asthma patients could grow by a third within ten years due to better diagnosis and changes in diet, housing, pollution and exposure to nature. A quarter of a million people die from asthma each year worldwide, or one person every two minutes. The annual costs of healthcare and lost productivity on account of asthma are €33.9 billion in the EU. Of this, direct costs for drugs, inpatient and outpatient care were €19.5 billion, and indirect costs €14.4 billion. A small fraction of people with asthma are estimated to have severe disease yet they absorb over 50% of the treatments costs and account for nearly 40% of asthma deaths. It is estimated that 10% of asthma patients have severe disease that is not controlled by medication. Costs for uncontrolled patients can be more than double those for controlled patients.

Causes of asthma and triggers

Asthma results from inflammation of the bronchioli (which carry air in and out of the lungs), leading to restricted airflow. In asthma patients, the inflamed bronchioli are more sensitive to particles in the air. When an asthma attack occurs, mucus production is increased, muscles of the bronchioli become tight and the lining of the air passages swells, reducing airflow and producing the characteristic wheezing sound associated with asthma.
A number of factors can increase the chance of developing asthma, including:

- A family history of asthma or other related allergic conditions, such as food allergy or hay fever
- Having another allergic condition
- Childhood bronchiolitis
- Childhood exposure to tobacco smoke, particularly if exposure occurs during pregnancy
- Being born prematurely, especially if ventilator support was required
- Having a low birth weight as a result of restricted growth within the womb

**Triggers**

Triggers can be anything that irritates the lungs. When asthma patients encounter triggers, the airways narrow and the muscles tighten around them. An increase in the production of sticky mucus (phlegm) also occurs. Common triggers include:

- Respiratory tract infections, particularly viral infections affecting the upper airways, such as colds and flu
- Allergens, including pollen, dust mites, animal fur or feathers
- Airborne irritants, including cigarette smoke, chemical fumes and atmospheric pollution
- Medicines, particularly non-steroidal anti-inflammatory drugs (NSAIDs) and beta blockers
- Emotions, including stress or laughing
- Foods containing sulphites, e.g. concentrated fruit juice, jam, prawns and many processed or precooked meals
- Weather conditions, including sudden changes in temperature, cold air and poor air quality
- Indoor conditions, including mould or damp, house dust mites and chemicals in carpets and flooring materials
- Exercise
- Food allergies, including allergies to nuts or other food items
Symptoms and diagnosis
Asthma symptoms can range from mild to moderate or severe. The main symptoms of asthma are wheezing, shortness of breath, a tight chest and coughing. Most people will only experience occasional symptoms, but symptoms are harder to control in those with severe asthma, and they may have problems almost all the time.

There are a number of ways to diagnose asthma, including lung function tests (spirometry, peak expiratory flow test), airway responsiveness, inflammation tests, and allergy tests.

Severe asthma
Severe asthma can be defined as asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy. Asthma control is ranked by doctors according to lung function, symptoms and the need for reliever medication, as controlled, partly controlled and uncontrolled.

Researchers believe severe asthma is linked to a variety of factors: genetic inheritance, the age of asthma onset, the duration of disease, exacerbations, sinus disease and inflammatory characteristics. Many patients have difficulty breathing most of the time, as well as frequent, life-threatening attacks needing hospital admissions. Severe asthma is a complex, unpredictable disease. Work and social life become limited and every-day activities such as climbing stairs or leaving the house can be a challenge.

Most people with severe asthma are treated with a ‘one-size-fits-all’ approach, which often doesn’t control their daily symptoms or improve outcomes. Patients cycle through different medicines or add on new treatments to find one that relieves their symptoms, but they do not address the root cause. Not only do many patients with severe asthma not respond to conventional treatments, many develop adverse effects from their sustained or repeated use. These adverse events include diabetes, obesity, osteoporosis and depression.

Type 2 asthma
Asthma is a heterogeneous disease. The various forms of asthma result from specific molecular pathways in the immune system and the effects that these have on different types of inflammation in the tissues of the lungs.

Among patients with severe asthma, the majority have Type 2. This category derives its name from increased levels of type 2 inflammatory signals. Type 2 inflammation results from the action of a specific group of molecular messengers (cytokines) produced by the immune system, IL-13, IL-5 and IL-4. An important mediator of Type 2 asthma is IL-13, a protein messenger released by cells that causes inflammation. By targeting the IL-13 pathway, we have the potential to block the development of a wide range of symptoms that are most important to severe asthma patients and that they experience nearly every day. Blocking IL-13 activity has a broad impact on key mechanisms (such as mucus production, airway...
inflammation, narrowing and hyper-responsiveness) and the day-to-day symptoms. This could include improvement in breathing, relief from daily symptoms, reduced limitations on daily activities, less time spent awake at night, less use of rescue medication and reduced need for medical attention and intervention.

**Treatment**

Likely patient response to treatment is untested in the majority of cases, so conventional treatment is administered in a stepwise approach, following successive treatment failure. Asthma treatment starts with reliever therapy, followed by the addition of preventer medications, as required. In poorly controlled asthma, other treatments may be added to the patient’s medication regimen. Treatment doses are reviewed and altered to achieve the best control using the lowest dose.12

**Reliever medication** is taken via an inhaler to relieve asthma symptoms quickly. Most often, these inhalers contain a short-acting beta agonist (SABA) which works by relaxing the muscles surrounding the narrowed airways.13

**Preventer inhalers** work over time to reduce the amount of inflammation and sensitivity of the airways, and reduce the chances of asthma attacks occurring. They must be used regularly (typically twice or occasionally once daily) and indefinitely to keep asthma under control. Most often, preventer inhalers contain inhaled corticosteroids.13

**Add-on therapies** are introduced if a patient’s asthma does not respond to initial treatment. The dose of preventer medication may be increased, or an inhaler containing a long-acting reliever (long-acting bronchodilator/long-acting beta2-agonist, or LABA) may be prescribed.13

Additional treatments include leukotriene receptor antagonists, theophyllines, oral steroids and injectable monoclonal antibodies. Bronchial thermoplasty may also be used. Bronchial thermoplasty works by destroying some of the muscles surrounding the airways in the lungs, which can reduce their ability to narrow the airways.13

**The role of personalised treatment approaches in asthma**

Identifying and targeting treatments to specific types of a disease or patient group is called Personalised Healthcare. Already widely applied in cancer treatment, Personalised Healthcare could provide severe asthma patients with the confidence that their medicine is right for them. The way asthma is treated will change dramatically with several new treatments becoming available in the next decade. Treatments are needed that target the critical underlying mechanism responsible for different types of asthma. This in turn may eliminate the cost of trying different medicines to find one that works, and may reduce the side effects and the burden for the patient from the use of multiple therapies to relieve symptoms.
Presence of Type 2 messenger molecules cannot be detected with commercially-available tests, but IL-13 activity produces a protein called periostin that can be detected in the blood as a reliable biomarker for Type 2 asthma. Periostin is the most promising biomarker for Type 2 asthma. By knowing that a patient has Type 2 asthma, physicians could confidently prescribe a Type 2-specific treatment.

References


19. Woodruff et al. T-helper Type 2-driven inflammation defines major subphenotypes of asthma. Am J Respir Crit Care Med. 2009 Sep 1;180(5):388-95.