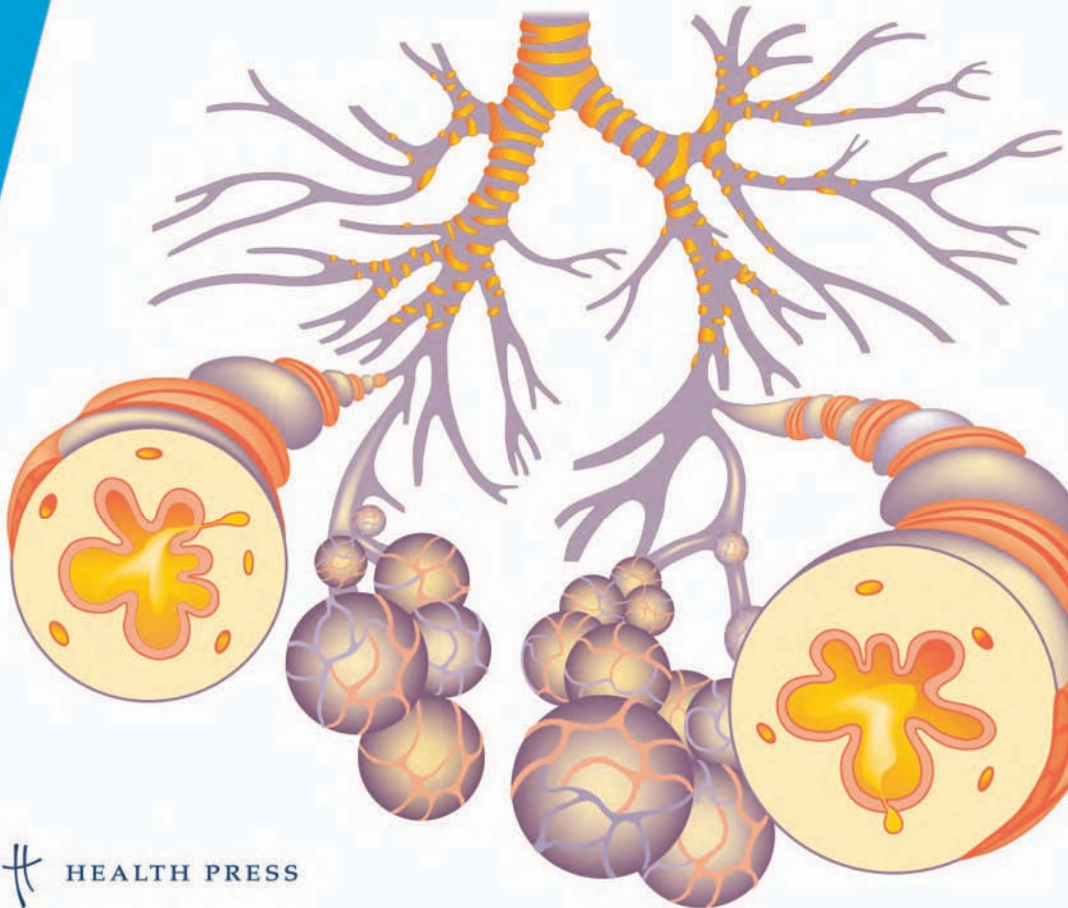


Fast Facts



Fast Facts: Asthma

Stephen T Holgate and Jo Douglass
Third edition





Fast Facts: Asthma

Third edition



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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com

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Glossary

AMP: adenosine 5'-monophosphate

ASA: acetylsalicylic acid (aspirin)

Atopy: a condition characterized by excessive production of immunoglobulin (Ig)E in response to allergens

Basophil: a type of white blood cell, distinguishable on staining

B lymphocyte: a type of white blood cell that produces antibodies

COPD: chronic obstructive pulmonary disease

CysLTs: cysteinyl leukotrienes, a powerful class of bronchoconstricting mediators

Cytokine: a peptide secreted by cells involved in inflammation and the immune response; cytokines can control the activity and growth of the cell that secreted them, or nearby cells

Daily variability: variability in daily peak expiratory flow (PEF), calculated as a percentage of the mean daily PEF value

DPI: dry-powder inhaler

Eosinophil: a type of white blood cell involved in allergic responses, distinguishable on staining

FEV₁: forced expiratory volume in 1 second, a measure of lung function

FVC: forced vital capacity, a measure of lung function

GINA: Global Initiative for Asthma, an international scientific initiative created to provide and encourage the use of

scientific reports on asthma and asthma research

IFN γ : interferon- γ , a cytokine that has the capacity to inhibit the development of the allergic pathways, under normal conditions

IgE: immunoglobulin class E, a class of antibody secreted by B lymphocytes on exposure to allergen; binding of IgE to certain cells involved in the immune response results in the release of inflammatory mediators

IL: interleukin, a cytokine that controls a specific aspect of hemopoiesis or the immune response

LABA: long-acting β_2 -agonist

Leukocyte: white blood cell

Mast cell: a large cell containing chemical mediators that are released in inflammatory and allergic responses

MDI: metered-dose inhaler

NSAID: non-steroidal anti-inflammatory drug

PaCO₂: partial pressure of carbon dioxide in arterial blood

PaO₂: partial pressure of oxygen in arterial blood

PEF: peak expiratory flow, a measure of lung function

pMDI: pressurized metered-dose inhaler

SABA: short-acting β_2 -agonist

SpO₂: oxygen saturation measured by pulse oximeter

T lymphocyte: a type of white blood cell that is mainly responsible for cell-mediated immunity

Th lymphocyte: T helper lymphocyte; a type of T lymphocyte that is activated on exposure to allergen and releases cytokines

Trigger: a stimulus that increases asthma symptoms and/or airflow limitation

Introduction

Asthma remains a major cause of morbidity and mortality throughout the world. This involves not only the burden of disease to individuals through loss of life and hospital admissions, but also in lost productivity as asthma remains a leading cause of absences from work and school. Whilst asthma mortality in developed nations appears to be stable or declining, international studies still report a very high burden of illness in those with asthma despite the availability of very effective asthma treatments.

It has long been recognized that asthma is a disorder of widespread airway obstruction, reversible either spontaneously or with treatment. It is also clear that underlying airway inflammation is a predominant cause of airway dysfunction in asthma, leading to increased responsiveness to a variety of stimuli. Recent research has identified some of the fundamental immunologic and cellular differences of the asthmatic airway, leading to greater understanding of the chronic inflammation associated with accelerated loss of lung function, which is characteristic of asthma.

Asthma most commonly begins in early childhood, but may occur in any age group and persist through life. Recent large epidemiological studies have identified several groups of very young children who wheeze, not all of whom will have asthma. However, once asthma is established, its severity, like all chronic inflammatory diseases, may vary from mild and intermittent to severe and persistent. Thus, its impact on the quality of life of an individual can vary greatly. However, if asthma is correctly diagnosed and properly treated, most patients can lead a normal life, although many will need to take medications regularly.

Because of the chronic nature of asthma, its underlying airway abnormalities and the burden of disease, national and international guidelines for asthma management have been developed that focus on:

- accurate asthma diagnosis
- objective assessment of airway inflammation and its severity
- prevention of asthma with drug treatment
- patient education

- management strategies
- monitoring.

This fully updated third edition of *Fast Facts: Asthma* draws its treatment recommendations from the Global Initiative for Asthma (GINA) guidelines, produced by the World Health Organization and the US National Heart Lung and Blood Institute and based on best available evidence. Key to these guidelines is the prescription of asthma treatments, which is determined by the level of asthma symptoms requiring control. In this book we have attempted to distill the essential features of the latest GINA treatment guidelines into a palatable and easily accessible form without losing information.

By the time guidelines for any disease are written and published they are, almost by definition, out of date on account of the continued research into the disease and its management. Asthma is no exception. It is our intention that this book provides the basis for good asthma management. However, guidelines are guidelines, and should not be taken as rules. The individual patient must be assessed in his or her own right, with individual circumstances taken into account. The principles raised in this book should nevertheless provide a framework to improve the lives of the many patients with this disease.

Asthma is a chronic inflammatory condition of the airways. It is characterized by recurrent episodes of airflow limitation which, depending on the severity of the attack, produce symptoms such as breathlessness, wheezing, chest tightness and cough. Acute exacerbations can be rapid or gradual in onset, and may be severe and potentially life-threatening.

Autopsy studies of patients who have died from asthma show hyperinflated lungs, with both large and small airways blocked by plugs containing a mixture of mucus, serum proteins, inflammatory cells and cell debris. Microscopic examination reveals extensive inflammatory infiltration of the airways (Figure 1.1), with edema due to vasodilatation

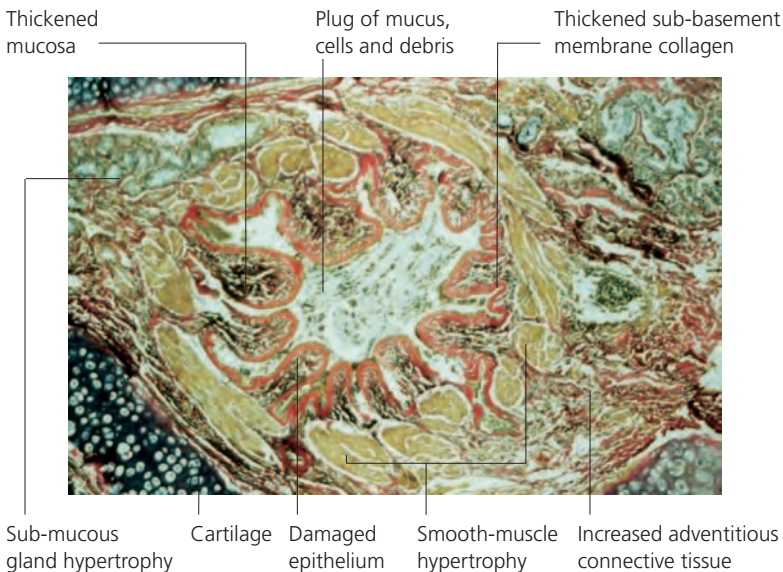


Figure 1.1 Pathological features associated with death from asthma. Airways are blocked by plugs of mucus and inflammatory exudate. There is also vasodilatation and edema, vascular remodeling, smooth muscle hypertrophy and thickening of the basement membrane.

and blood vessel engorgement, and epithelial disruption. Biopsy studies have shown increased numbers of leukocytes, particularly eosinophils, mast cells and T lymphocytes, in the airways, and increases in the markers of lymphocyte activation. Structural changes resulting from chronic inflammation include bronchial smooth muscle hypertrophy and hyperplasia, new vessel formation, interstitial collagen deposition resulting in basement membrane thickening, and airway wall remodeling.

Disease mechanisms

In many cases, asthma is an allergic disorder mediated in part by immunoglobulin (Ig)E-dependent mechanisms. Exposure to allergen results in allergen uptake and its presentation by dendritic cells to T helper (Th) lymphocytes (Figure 1.2).

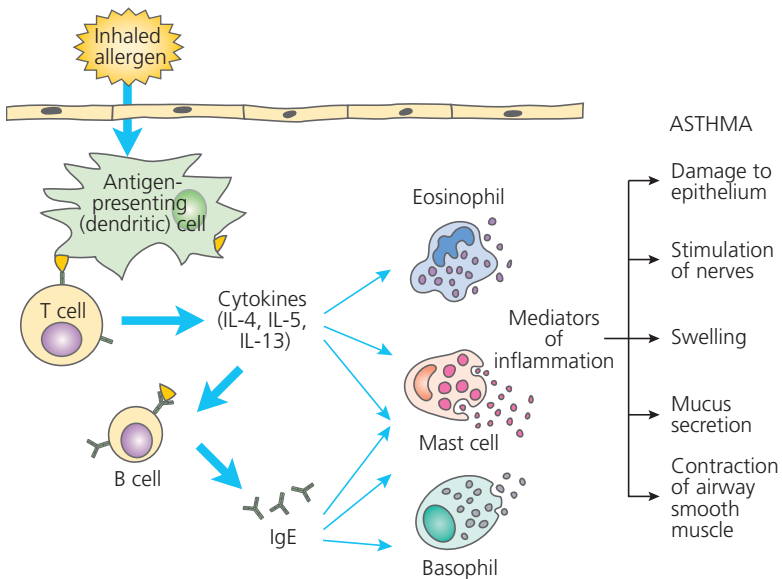
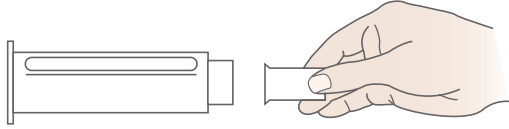
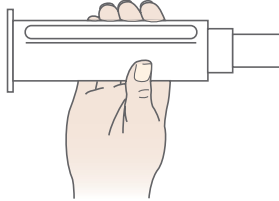


Figure 1.2 Role of immunoglobulin E (IgE) in airway inflammation and asthma symptoms. Exposure to allergen leads to activation of T lymphocytes, cytokine expression (interleukins [ILs]) and release of IgE from B lymphocytes. IgE binds to cells involved in inflammation, which then release inflammatory mediators.

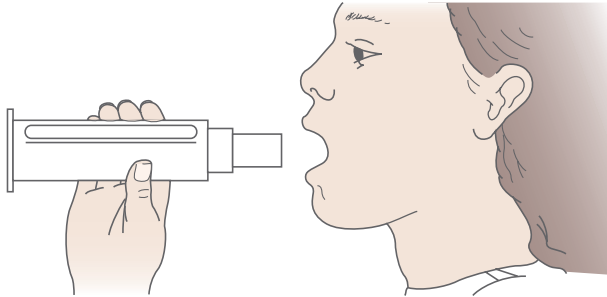
Put the disposable mouthpiece on the peak flow meter.



Stand up and hold the peak flow meter horizontally. Make sure that the end of the marker is at the end of the scale and that your hand is not restricting marker movement.



Breathe in as deeply as you can.



Then close your lips tightly around the mouthpiece and breathe out quickly. Note the results and repeat the procedure twice. Use the highest reading.

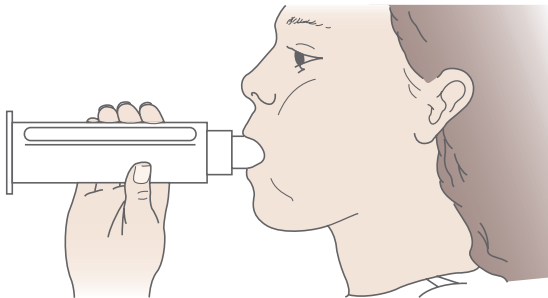


Figure 3.1 Use of a peak flow meter.

should measure PEF immediately on waking before taking any bronchodilator medication and last thing at night after taking bronchodilator. Variability in daily PEF can then be calculated as a percentage of the mean daily value:

$$\text{Daily variability (\%)} = \frac{\text{PEF}_{\text{evening}} - \text{PEF}_{\text{morning}}}{\frac{1}{2} (\text{PEF}_{\text{evening}} + \text{PEF}_{\text{morning}})} \times 100$$

Daily variability of more than 20% indicates asthma.

Measurement of bronchial responsiveness

Measurement of bronchial responsiveness can be useful in the diagnosis of asthma, although there is some overlap between the range of values found in patients with asthma and in those with rhinitis or other causes of lower airway obstruction, such as chronic obstructive pulmonary disease (COPD). The most usual tests are performed in a lung function laboratory and involve the patient inhaling incremental doses of a bronchoconstricting substance, such as histamine, methacholine, hypertonic saline, adenosine 5'-monophosphate (AMP) or mannitol. Spirometry is then used to follow the changes in airway caliber. Airway responsiveness is usually defined as that dose (D) or concentration (C) of agonist that reduces the FEV₁ by 20% of the starting volume (i.e. PD₂₀ or PC₂₀). A standardized exercise test is also useful, especially for children with suspected asthma.

Skin-prick tests

Skin-prick tests with allergens or detection of allergen-specific immunoglobulin (Ig)E in the circulation are the most common diagnostic tests for allergy. For the diagnosis of asthma, the results should always be interpreted in relation to the patient's history and the relationship between asthma symptoms and allergen exposure, because up to 40% of the population may exhibit atopy but only a proportion of these individuals will have asthma. Nevertheless, the identification of allergens that may be contributing to persistent asthma and exacerbations is important in order to provide advice on allergen avoidance or other treatment strategies.