Asthma

- Asthma is a chronic inflammatory disorder of the airways, in which many cells and cellular elements play a role.
- Chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night and in the early morning.
- These episodes are usually associated with widespread but variable airflow obstruction within the lung that is often reversible, either spontaneously or with treatment.
- The prevalence of asthma increased steadily over the latter part of last century. As asthma affects all age groups, it is one of the most common and important long-term respiratory conditions in terms of global years lived with disability.
- The development and course of asthma and the response to treatment are influenced by genetic determinants, while the rapid rise in prevalence implies that environmental factors are critically important in the development and expression of the disease.
- The potential role of indoor and outdoor allergens, microbial exposure, diet, vitamins, breastfeeding, tobacco smoke, air d obesity have been explored but no clear consensus hasemerged.

Pathophysiology

- Airway hyper-reactivity, the tendency for airways to narrow excessively in response to triggers that have little or no effect in normal individuals – is integral to the diagnosis of asthma and appears to be related, although not exclusively, to airway inflammation .
- Other factors likely to be important in the behavior of airway smooth muscle include the degree of airway narrowing and neurogenic mechanisms.
- The relationship between Atopy (the propensity to produce IgE) and asthma is well established and in many individuals there is a clear relationship between sensitization and allergen exposure, as demonstrated by skin-prick reactivity or elevated serum-specific IgE.
- Common examples of allergens include house dust mites, pets such as cats and dogs, pests such as cockroaches, andfungi.
- In exercise-induced asthma, hyperventilation results in water loss from the pericellular lining fluid of the respiratory mucosa, which, in turn, triggers mediator release. Heat loss from the respiratory mucosa may also be important.
- In persistent asthma, a chronic and complex inflammatory response ensues, characterized by an influx of numerous inflammatory cells, the transformation and participation of airway structural cells, and the secretion of an array of cytokines, chemokines and growth factors.
- Examination of the inflammatory cell profile in induced sputum samples demonstrates that, although asthma is predominantly characterized by airway esnophilia, neutrophilic inflammation predominates in some patients while in others scant inflammation is observed: so-called ‘paucigranulocytic’ asthma.
- With increasing severity and chronicity of the disease, remodelling of the airway may occur, leading to fibrosis of the airway wall, fixe wing of the airway and a reduced response to bronchodilator medication.

Clinical features

- Typical symptoms include:
- recurrent episodes of wheezing, chest tightness, breathlessness and cough.
- Asthma is commonly mistaken for a cold or a persistent chest infection (e.g. longer than 10 days).
- Classical precipitants include exercise, particularly in cold weather, exposure to airborne allergens or pollutants, and viral upper respiratory tract infections.
- Wheeze apart, there is often very little to find on examination. An inspection for nasal polyps and eczema should be performed.
- Patients with mild intermittent asthma are usually asymptomatic between exacerbations. Individuals with persistent asthma report ongoing wheeze but these are variable, with symptoms fluctuating of one day, or from day to day or month to month.
- Asthma characteristically displays a diurnal pattern, with symptoms and lung function being worse in the early morning.
- Particularly when poorly controlled, symptoms such as cough and wheeze disturb sleep.
- Cough may be the dominant symptom in some patients, and the lack of wheeze or breathlessness may lead to a delay in reaching the diagnosis of so-called '**cough-variant asthma**'.
- Some patients with asthma have a similar inflammatory response in the upper airway. Careful enquiry should be made as to a history of sinusitis, sinus headache, a blocked or runny nose and loss of sense of smell.
- Although the a etiology of asthma is often elusive, an attempt should be made to identify any agents that may contribute to the appearance or aggravation of the condition.
- Particular enquiry should be made about potential allergens, such as exposure to a pet cat, guinea pig, rabbit or horse, pest infestation, exposure to moulds following water damage to a home or building, and any potential occupational agents.
- In some circumstances, the appearance of asthma is triggered by medications. Beta-blockers, even when administered topically as eye drops, may induce bronchospasm, as may aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).
- Other medications implicated include the oral contraceptive pill an cholinergic agents.
- An important minority of patients develop a pa vere form of asthma and this appears to be more common in women.

Diagnosis

- The diagnosis of asthma is predominantly clinical and is based on the combination of the history, lung function and 'other' tests, which allows high, intermediate or low probability of asthma to emerge.
- The approach may vary from patient to patient and may need to be re-evaluated following the introduction of treatment.
- Supportive evidence is provided by the demonstration of variable airflow obstruction, preferably by using spirometery to measure FEV1 and FVC.
- Forced expiratory volume (FEV) measures how much air a person can exhale during a forced breath.
- The amount of air exhaled may be measured during the first (FEV1), second (FEV2), and/or third seconds (FEV3) of the forced breath. Forced vital capacity (FVC) is the total amount of air exhaled during the FEV test.

- This identifies the obstructive defect, defines its severity, and provides a baseline for bronchodilator reversibility .
- A trial of glucocorticoids (e.g. 30 mg daily for 2 weeks) may be useful in establishing the diagnosis, by demonstrating an improvement in either FEV1 or PEF.
- The peak expiratory flow (PEF, also known as a peak flow or peak flow r al rate that a person can exhale during a short maximal expiratory effort after a full inspiration
- It is not uncommon for patients whose symptoms are suggestive of asthma to have normal lung function. In these circumstances, the demonstration of airway hyper reactivity (AHR) by challenge tests may be useful to confirm the diagnosis. AHR has a high negative predictive value but positive results may be seen in other conditions, such as COPD, bronchiectasis and cystic fibrosis.
- The use of exercise tests is useful when symptoms are predominantly related to exercise. The diagnosis may be supported by the presence of Atopy demonstrated by skin-prick tests or measurement of total and allergen-specific IgE.
- Chest X-ray appearances are oft bar collapse may be seen if mucus occludes a large bronchus .

Management

- Setting goals
- Asthma is a chronic condition but may be controlled with appropriate treatment in the majority of patients.
    - The goal of treatment should be to obtain and maintain complete control (Box 17.20) but aims may be modified according to the circumstances and the patient.
- Unfortunately, surveys consistently demonstrate that the majority of individuals with asthma report suboptimal control.
- Whenever possible, patients should be encouraged to take responsibility for managing their own disease. A full explanation of the nature of the condition, the relationship between symptoms and inflammation, the importance of key symptoms such as nocturnal waking, the different types of medication and, if se of PEF to guide management decisions should be given.

Avoidance of aggravating factors

- This is particularly important in the management of occupational asthma but may also be relevant in atopic patients, when removing or reducing exposure to relevant antigens, such as a pet, may affect improvement.
- House dust mite exposure may be minimized by replacing carpets with floorboards and using mite impermeable bedding. So far, improvements in asthma control following such measures have been difficult to demonstrate.
- Many patients are sensitized to several ubiquitous aeroallergens, making avoidance strategies largely impractical. Measures to reduce fungal exposure may be applicable in specific circumstances and medications known to precipitate or aggravate asthma should be avoided.
- Smoking cessation is particularly important, as smoking not only encourages sensitization but also induces a relative glucocorticoid resistance in the airway.

The stepwise approach to the management of asthma

Step 1: Occasional use of inhaled short-acting β2-adrenoreceptor agonist bronchodilators

- A variety of different inhaled devices are available and the choice of device should be guided by patient preference and competence in its use.
- The metered-dose inhaler remains the most widely prescribed.

- For patients with **mild intermittent asthma** (symptoms less than once a week for 3 months and fewer than two nocturnal episodes per month), it is usually sufficient to prescribe an inhaled short-acting β2-agonist, such as salbutamol or terbutaline, to be used as required.
- However, many patients (and their physicians) under-estimate the severity of asthma. A history of a sever exacerbation should lead to a step-up in treatment.

Step 2: Introduction of regular preventer therapy

- Regular anti-inflammatory therapy (preferably inhaled glucocorticoids (ICS), such as beclometasone, budesonide (BUD) and others ,should be started in addition to inhaled β2-agonists taken on an as-required basis for any patient who:

✓ has experienced an exacerbation of asthma in the last 2 years
✓ uses inhaled β2-agonists three times a week or more
✓ reports symptoms three times a week or more
✓ is awakened by asthma one night per week.

- Alternative but much less effective preventive include chromones, leukotriene receptor antagonists and theophyllines.

Step 3: Add-on therapy

- If a patient remains poorly controlled despite regular use of an inhaled glucocorticoid, a thorough review should be undertaken of adherence, inhaler technique and ongoing exposure to modifiable aggravating factors.
- A further increase in the dose of inhaled glucocorticoid may benefit some patients but, in general, add-on therapy should be considered .
- The addition of a long-acting β2-agonist (LABA) to an inhaled glucocorticoid provides more effective asthma control compared with increasing the dose of inhaled glucocorticoid alone.
- Oral leukotriene receptor antagonists (e.g. montelukast 10 mg daily) are generally less effective than LABAs as add-on therapy but may facilitate a reduction in the dose of inhaled glucocorticoid and control exacerbations.

Step 4: Poor control on moderate dose of inhaled glucocorticoid and add-on therapy: addition of a fourth drug

- In adults, the dose of inhaled glucocorticoid may be increased.
- A nasal glucocorticoid preparation should be used in patients with prominent upper airway symptoms.
- Leukotriene receptor antagonists, long-acting antimuscarinic agents, theophyllines or a slow-release β2-agonist may be considered.
- If the trial of add-on therapy is ineffective, it should be discontinued.

Step 5 :Continuous or frequent use of oral glucocorticoids

- At this stage, prednisolone therapy (usually administered as a single daily dose in the morning) should be prescribed in the lowest amount necessary to control symptoms.
- Patients who are on long-term glucocorticoid tablets (> 3 months) or are receiving more than three or four courses per year will be at risk of systemic side-effects.
- In patients who continue to experience symptoms and asthma exacerbation and demonstrate impaired lung function despite step 5 treatment;
- omalizumab, a monoclonal antibody directed against IgE, should be considered for those with a prominent atopic phenotype, and mepolizumab, a monoclonal antibody that blocks the binding of IL-5 to its receptor phils, should be considered in those with eosinophilic-mediated disease.
- The use of immunosuppressant, such as methotrexate, ciclosporin or oral gold, is less common nowadays, as the response is variable and the limited benefits may be easily offset by side-effects.

Step-down therapy

- Once asthma control is established, the dose of inhaled (or oral) glucocorticoid should be titrated to the lowest dose at which effective control of asthma is maintained.
- Decreasing the dose of glucocorticoid 25 –50% every 3 months is a reasonable strategy for most patients.

Exacerbations of asthma

- The course of asthma may be punctuated by exacerbations with increased symptoms, deterioration in lung function, and an increase in airway inflammation.
- Exacerbations are most commonly precipitated by viral infections but moulds , pollens (particularly following thunderstorms) and air pollution are also implicated.
- Most attacks are characterized by a gradual deterioration over several hours to days but some appear to occur with little or no warning: so-called brittle asthma.
- An important minority of patients appear to have a blunted perception of airway narrowing and fail to appreciate the early signs of deterioration.

Management of mild to moderate exacerbations

- Doubling the dose of inhaled glucocorticoids does not prevent an impending exacerbation.
- Short courses of ‘rescue’ glucocorticoids (prednisolone 30–60 mg daily) are therefore often required to regaincontrol.
- Tapering of the dose to withdraw treatment necessary, unless glucocorticoid has been given for more than 3 weeks.

Indications for ‘rescue’ courses include:

- symptoms and PEF progressively worsening day by day, with a fall of PEF below 60% of the patient’s personal best recording
- onset or worsening of sleep disturbance by asthma
- persistence of morning symptoms until midday
- progressively diminishing response to an inhaled bronchodilator
- symptoms that are sufficiently quire treatment with nebulised or injected bronchodilators.

Management of acute severe asthma

- Measurement of PEF is mandatory, unless the patient is too ill to cooperate.
- Arterial blood gas analysis is essential to determine the $PaCO_2$, a normal or elevated level being particularly dangerous.
- A chest X-ray is not immediately necessary, unless pneumothorax is suspected.

Treatment includes the following measures:

- Oxygen
  High concentrations (humidified if possible) should be administered to maintain the oxygen saturation above 92% in adults. Failure to achieve appropriate oxygenation is an indication for assisted ventilation.
- High doses of inhaled bronchodilators.
  - ✓ Short-acting β2-agonists are the agent of choice. In hospital, they are most conveniently given via a nebulizer driven by oxygen
  - ✓ Ipratropium bromide provides further bronchodilator therapy and should be added to salbutamol in acute severe or life-threatening attacks.

- Systemic glucocorticoids.
- ✓ These reduce the inflammatory response and hasten the resolution of an exacerbation. They should be administered to all patients with an acute severe attack. They can usually be administered orally as prednisolone but intravenous hydrocortisone may be used in patients who are vomiting or unable to swallow.

- There is no evidence base for the use of intravenous fluids but many patients are dehydrated due to high insensible water loss and will probably benefit. Potassium supplements may be necessary, as repeated doses of salbutamol can lower serum potassium.
- If patients fail to improve, a number of further options may be considered. Intravenous magnesium may provide additional bronchodilatation in patients whose presenting PEF is below 30% predicted.
- Some patients appear to benefit from the use of intravenous aminophylline but cardiac monitoring is recommended.
- PEF should be recorded every 15–30 minutes and then every 4–6 hours.
- Pulse oximetry should ensure that SaO_2 remains above 92%, but repeat arterial blood gases are necessary .
- lists the indications for ation and intermittent positive pressure ventilation (IPPV):

Prognosis

- The outcome from acute severe asthma is generally good but a considerable number of deaths occur in young people and many are preventable.
- Failure to recognize the severity of an attack, on the part of either the assessing physician or the patient, contributes to delay in delivering appropriate therapy and to under-treatment.
- Prior to discharge, patients should be stable on discharge medication (nebulised therapy should have been discontinued for at least 24 hours) and the PEF should have reached 75% of predicted or personal best.
- The acute attack should prompt a look for and avoidance of any trigger factors, the delivery of asthma education and the provision of a written self- management plan.

- The patient should be offered an appointment with a GP or asthma nurse within 2 working days of discharge and follow up at a specialist hospital clinic within a month.