Asthma is a chronic inflammatory disorder characterised by increased bronchial tree reactivity and reversible airway narrowing, resulting in eosinophil inflammation, oedema, mucus plugs and wheezing.

**Epidemiology:** prevalence 4-10%, 1 in 10 adults and 1 in 12 children, 1500 deaths per year

**Risk factors:**
- Personal/family history of atopy
- Smoking or passive smoking
- Inner city environment, social deprivation
- Obesity
- Prematurity, low birth weight, viral infections before age 2, early exposure to broad spec Abx

**Causes/triggers** include:
- Allergens e.g. animal hair, house dust mite faeces, perfumes/chemicals
- Cold air and exertion
- Pollution/smoke
- URTI, usually viral infections
- Drugs: NSAIDs, aspirin, beta blockers

**Symptoms**
- Wheeze, SOB, cough and chest tightness
- Variable with clear triggers +/- early morning waking (diurnal variation)
- Relieved by salbutamol

**Signs**
- Fast, laboured breathing, anxiety/distress, may not be able to complete full sentences
- Purpled lips, nasal flaring, accessory muscle use, recession in children
- Cyanosis = SEVERE ASThma
- ↑ HR, ↑ RR, ↓ O2 sat, tremor
- Generalised polyphonic wheeze, bronchial breath sounds, prolonged expiration
- Hyperinflated "barrel chest", Harrison's sulcus in chronic disease

**Diagnosis**
- In children: croup, inhaled foreign body, bronchiolitis, postnasal drip, CF, TB, bronchiectasis
- In adults: COPD, fibrosis, TB, cancer, recurrent PE, angina/IHD, HF, GORD

**Investigations**
- Peak expiratory flow rate: reduced
- Spirometry: obstructive i.e. normal TLC, ↓ FEV1, ↓ FEV1/FVC and prolonged expiration
- CXR: to exclude other lung pathologies and heart failure
- Bloods: ↑ eosinophils on WCC
- ABC: good indicator of severity, be wary of NORMAL CO2 in tachypnoeic patients, should be low

**Severity of acute asthma (British Thoracic Society)**
- Moderate: PEF >50%
- Severe: PEF 33-50%, RR >25, HR >110, can’t complete full sentences
- Life-threatening: PEF <33%, O2 <92%/<8kPa, normal PaCO2, silent chest, cyanosis, ↓ GCS
- Near fatal: raised PaCO2 (type 2 respiratory failure due to increased airway resistance)

**Management of acute severe asthma**
- give high flow O2 to increase sats to 94-98%
- high dose O2-driven nebulised salbutamol (reserve IV for those who cannot inhale reliably)
- adequate doses of oral steroid e.g. prednisolone 40-50mg daily for at least three days
- add nebulised ipratropium bromide 0.5mg 4-6hrly if poor response/severe/life-threatening
- consider single dose IV magnesium sulphate if still poor response/life-threatening features
- refer to ICU if: poor response, ↓ PEF, hypoxia, hypercapnoea, acidosis, ↓ GCS, resp. arrest
- adrenaline and antihistamines may also help
- in children: admit if fail to respond to 10 puffs salbutamol +↑ nebulised salbutamol/single IV dose with oral prednisolone → ipratropium → IV aminophylline → ICU admission

**Drugs used to treat Asthma**

1. **Short-acting beta-2 agonists: salbutamol, terbutaline**
   - Act on smooth muscle beta 2 receptors to relax bronchospasm
   - Last 4-6 hours
   - The only “reliever” inhaler used as required in all kinds of asthma, also used before exercise
   - Can also be given orally/IV in more severe asthma
   - **Cautions:** hyperthyroidism, CV disease, arrhythmias including long QT, hypertension, diabetes
   - **Contraindications:** no absolute contraindications as you need to stop the bronchospasm!
   - **Side effects:** fine tremor, anxiety/tension, headache, muscle cramps, palpitations/tachycardia, myocardial ischaemia, sleep/behavioural disturbance, hypokalaemia in high doses

2. **Inhaled corticosteroids: beclometasone, budesonide, ciclesonide, fluticasone, mometasone**
   - Prevent changes of asthma by reducing inflammation and secretions
   - Use is indicated if patients require salbutamol >3 days per week or >3 times per day, if they are woken by symptoms >1 night per week, and if they have severe acute exacerbations
   - Allievation of symptoms usually occurs 3-7 days after initiation so patients must stick with it
   - **Cautions:** history of paradoxical bronchospasm, pregnancy, breastfeeding
   - **Contraindications:** no absolute contraindications but benefits must outweigh risks
   - **Side effects:** headache, abdominal pain, thirst, hyperkinesia in young children, tremor, suicidal behaviour, hypersensitivity, Churg-Strauss syndrome

3. **Long-acting beta-2 agonists: salmeterol, formoterol**
   - Same action on smooth muscle beta 2 receptors, last 12 hours
   - Relieved by salbutamol

4. **Leukotriene receptor antagonists: montelukast, zafirlukast**
   - Block cysteinyl leukotrienes to reduce inflammation and bronchoconstriction
   - **Cautions:** pregnancy, breast-feeding, warfarin (potentiated), theophylline (1 plasma level)
   - **Side effects:** headache, abdominal pain, thirst, hypertension in young children, tremor, suicidal behaviour, hypersensitivity, Churg-Strauss syndrome

5. **Sodium cromoglicate**
   - mode of action poorly understood, less effective than corticosteroids, causes bronchospasm

6. **Xanthines: theophylline, aminophylline, caffeine (used in neonatal apnoea)**
   - Antagonise adenosine receptors to induce smooth muscle relaxation and bronchodilation
   - Theophylline is metabolised in the liver by CYP450 so many factors influence plasma levels:
     - Increased by heat failure, cirrhosis, viral infections, elderly, enzyme inhibitors
     - Decreased by smokers, chronic alcoholism, enzyme inducers
   - Aminophylline is a mixture of theophylline with ethylendediamine to increase its solubility for IV use in severe acute asthma → very slow IV infusion over at least 20 minutes
   - **Cautions:** cardiac disease, ↑BP, hypothyroidism, peptic ulcers, epilepsy, elderly, fever, hepatic impairment, pregnancy, breastfeeding, risk of hypokalaemia, enzyme inhibiting drugs
   - **Side effects:** tachycardia, palpitations. GI upset, headache, antihistamines, convulsions if IV infusion given too quickly, narrow therapeutic window and extremely toxic in overdose

**Treatment Strategies**

1. short-acting beta-2 agonist (salbutamol) as required
2. add inhaled corticosteroid (beclometasone) 200-800µg per day
3. add inhaled long-acting beta-2 agonist (salmeterol) two doses 12 hours apart
4. gradually increase steroid to 2000µg per day +↑ add fourth drug e.g. LRA, X, oral beta-2 agonist
5. start daily oral corticosteroid at lowest dose maintaining adequate control (keep inhaled steroid) review treatment every three months, consider stepwise reduction if adequate control achieved
6. refer to ICU
7. non-pharmaceutical strategies: weight loss, smoking cessation, avoidance of triggers, antihistamines, allergen-specific immunotherapy, relaxation therapy, breathing techniques

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COPD

- COPD is characterised by progressive, fixed airway obstruction with bronchitis (inflammation of airways) and emphysema (dilatation of terminal bronchioles)
- **Causes:**
  - Smoking in 80-90% of cases
  - Occupational exposures e.g. coal dust, gold dust, textiles, isocyanates, welding
  - Air pollution e.g. urban environments, indoor cooking fires in developing countries
  - Chronic severe bronchial hyperreactivity e.g. asthma
  - Genetics: α1-antitrypsin deficiency causes 2% emphysema (panacinar), autoimmune

- **Symptoms:**
  - Age >50 (usually over 50) with >10PY smoking history or occupational exposures
  - Progressive SOBOE, chronic productive cough, wheeze and recurrent infections
  - May complain of PND/orthopnoea or ankle oedema
  - Little variability, salbutamol has limited effect, leads to functional capacity and fatigue

- **Signs**
  - Cachexia, cyanosis, CO2 retention tremor
  - Cor pulmonale causes raised JVP, hepatomegaly, peripheral oedema and heart failure
  - Pursed lips, nasal flaring, accessory muscle use, recession, increased AP diameter of chest/hyperinflation, Hoover’s sign (paradoxical lower rib movement on inspiration)
  - Reduced chest expansion
  - Hyperresonance to percussion +/- bibasal dullness
  - Reduced air entry, wheeze, prolonged expiration +/- bibasal coarse crackles

- **Differential diagnosis**
  - Asthma, bronchiectasis, lung cancer, TB, obliterator bronchiolitis, heart failure

- **Assessing Severity of COPD**

  **Spirometric classification (GOLD 2008)**
  - All patients must have post-bronchodilator FEV1/FVC <70% predicted (obstructive disease)
  - The rest of the classification concerns post-bronchodilator FEV1 as % predicted
  - Stage 1/mild >80%
  - Stage 2/mild to moderate 50-79%
  - Stage 3/severe 30-49%
  - Stage 4/very severe <30% (or <50% with signs of respiratory failure)

  **Symptomatology and functional impact (MRC dyspnoea scale)**
  - 1 = not troubled except when exercising
  - 2 = SOB when hurrying or walking up a hill
  - 3 = slower than peers on level ground/has to stop for breath when walking at own pace
  - 4 = stops for breath after 100m/a few minutes on flat ground
  - 5 = too SOB to leave the house, SOB when dressing/undressing

  **BODE prognostic index:** BMI + airflow obstruction + dyspnoea + exercise capacity

- **Drugs used to treat COPD**

  1) **Non-pharmaceutical management**
     - Smoking cessation: nurse-led clinics, nicotine replacement, can have varenicline/bupropion
     - Weight loss
     - Improve exercise tolerance: pulmonary rehab with physiotherapists, gentle aerobic exercise

  2) **Short-acting beta-2 agonists:** salbutamol, terbutaline

  3) **Long-acting beta-2 agonists:** salmeterol, formoterol

  4) **Antimuscarinic bronchodilators:** ipratropium, tiotropium
     - Block muscarinic ACh receptors to ↓cGMP and reduce airway smooth muscle contractility

  5) **Inhaled corticosteroids:** beclometasone, fluticasone, budesonide
     - Oral corticosteroids e.g. prednisolone may be required in advanced disease

  6) **Xanthines:** theophylline (oral)
     - Offered only if inhaled bronchodilators fail or cannot be taken

  7) **Mucolytic drugs:** carbocisteine, erdosteine, mecysteine
     - Facilitate expectoration by reducing sputum viscosity, used for chronic productive cough
     - Facilitate expectoration, pregnancy, lactation, hepatic or renal impairment
     - Side effects: GI upset, ulceration and bleeding, hypersensitivity

  8) **Long-term oxygen therapy**
     - This is indicated in those with very severe disease (FEV1 <30%) or FEV1 30-49% with:
       - O2 sats ≤92% on room air
       - Cachexia
       - Polycythaemia
       - Signs of cor pulmonale: raised JVP, peripheral oedema
       - Should breathe supplemental oxygen for 15 hours per day (DON’T SMOK!!)
     - Target O2 sats of 88-92% to avoid abolishing hypoxic drive and causing respiratory depression

- **Treatment strategies for COPD**

  1) **Short acting “reliever” bronchodilators:** salbutamol (Ventolin) or ipratropium (Atrovent)

  2) **Infective exacerbations of COPD**
     - Common organisms include S. pneumoniae, H. influenzae, Moraxella, S. aureus, Pseudomonas
     - Other triggers include viral infections e.g. influenza, adenovirus; and pollutants
     - **Treatment:** lots of reliever drugs, paracetamol, appropriate steroid provision, oral prednisolone, antibiotics
     - **Prevention:** flu and pneumococcal vaccines, treatment level, “rescue” corticosteroids and antibiotics

- **Assessing Severity of COPD**
  - FEV1 ≥50%
  - FEV1 ≥80%
  - FEV1/FVC <70% predicted, poor response to bronchodilators
  - CXR: may show hyperinflation, also useful for excluding other pathologies
  - Bloods: anaemia of chronic disease, polycythaemia secondary to chronic hypoxia
  - Others: pulse oximetry to assess for LTOT, sputum culture, ECG/echo, α1-antitrypsin

- **Infective exacerbations of COPD**
  - Symptoms: ↑↑SOB, cough with purulent sputum, fever, distress and worsening RHF
  - Frequency of exacerbations tends to increase with severity of disease
  - Other triggers include viral infections e.g. influenza, adenovirus; and pollutants
  - **Treatment:** lots of reliever drugs, paracetamol, appropriate steroid provision, oral prednisolone, antibiotics
  - **Prevention:** flu and pneumococcal vaccines, treatment level, “rescue” corticosteroids and antibiotics

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