Respiratory Diseases in Children

General principles:

1. Cough is a very common symptom – however, while 15-30% of children experience episodes unrelated to respiratory tract infection, it is important to be able to recognise serious cough
2. Cough may be stimulated by airway secretions, inflammatory mediators, aspirated foreign material, irritates (e.g. smoke) or tussive agents (e.g. capsaicin, citric acid)
3. Cough is good as it enhances mucociliary clearance, but can be troublesome and can even indicate serious illness
4. History should include age of onset, mode of onset, character, duration, severity, severity, frequency, pattern, aggravating factors and alleviating factors

Acute coughs:

1. Common cold – acute, highly infectious viral disease characterised by nasal stuffiness, sneezing, coryza (nasal inflammation and discharge), throat irritation and little or no fever
   a. Aetiology – viral (rhinovirus, parainfluenza virus, RSV, coronavirus); rarely M. pneumoniae, Coccidioides inmmittis, Histoplasma capsulatum, B. pertussis, C. psittaci, Coxiella burnetii
   b. Clinical features – prodromal cold symptoms, progressing to cold symptoms (har, har) and resolving after 7-14 days. Infants may have a fever, irritability or vomiting/diarrhoea.
   c. Complications include acute otitis media, otitis media with effusion, tonsillitis, sinusitis and lower respiratory tract infection
   d. Management – supportive, no specific therapy for the vast majority of cases
2. Viral croup affects children 6 months to 3 years of age (rarely >6 years), typically with extrathoracic subglottic swelling and oedema that results in increased airway resistance and decreased airflow
   a. Aetiology – parainfluenza 1>3>2, RSV, adenovirus, influenza type A; sometimes rhinovirus, enterovirus, herpes simplex, reovirus; rarely measles, varicella and M. pneumoniae.
   b. Clinical features – rhinorrhoea (this always sounds excruciatingly painful to me), sore throat and fever; progressing to barking cough, hoarseness and inspiratory strider ± fever
   c. Complications – severe airways obstruction, idiopathic pulmonary oedema (rare), recurrent croup (at least 2 episodes, ~50% of cases; mainly boys with personal/family history of atopy)
   d. Management – usually no specific treatment unless hypoxic or progressive obstruction; consider oral dose of high-dose steroid (e.g. dexamethasone 0.1mg/kg), adrenaline
3. Viral bronchitis usually follows an upper respiratory tract infection, lasting 7-10 days.
   a. Aetiology – adenovirus, influenza, parainfluenza, C. pneumoniae, B. pertussis, RSV, Coxackievirus, herpes simplex, H. influenzae, various others
   b. Clinical features – cough (initially dry then productive), fever, fatigue and aching, haemoptysis, chest burning, dyspnoea (sometimes), rales, rhonchi, wheezing
   c. Complications – bronchopneumonia, acute respiratory failure, bronchiectasis, chronic cough
   d. Management – supportive, antibiotics if bacterial aetiology suspected
4. Others – pertussis, foreign body, acute wheezing illnesses (asthma, bronchiolitis, pneumonia)

Recurrent coughs – episodes lasting up to three weeks, then resolving completely

a) Viral respiratory tract infection – while children often have 6-10 viral respiratory tract infections a year, cough usually indicates that an infection that has spread beyond the upper respiratory tract,
   a. The cough may be loose and rattly in the early stages, but often becomes hard and dry – it usually lasts 1-3 weeks but may persist for up to 4-6 weeks (occasionally longer)
   b. Prolonged cough may be due to transient alteration in sensitivity of cough receptors by the viral infection, and passive tobacco smoke inhalation may also be a contributing factor
b) ‘Cough variant asthma’ was first described in 1979 as cough associated with prolonged expiratory time, wheeze, hyperinflation and decreased FEV.
   a. The cough is characteristically dry, persistent and nocturnal, especially occurring in the early morning; often exacerbated by cold or following exercise (cool air irritating epithelium)
   b. While cough may be a major symptom of asthma, be careful about diagnosing asthma on cough alone unless there is also other signs/symptoms or personal or family history of atopy

Subacute persistent cough – cough lasting three weeks to three months

1. Post-viral cough – see above
2. Whooping cough is a highly infectious respiratory infection that produces a paroxysmal spasmodic cough, ending in a prolonged high-pitched inspiratory whoop or crow (not the flying kind)
   a. Aetiology – Bordetella pertussis; milder illness with B. parapertussis and B. bronchiseptica
   b. Clinical features – paroxysmal staccato cough with post-tussive inspiratory gasp or emesis, mild fever, rhinorrhoea, anorexia, may have episodic apnoea
Respiratory

c. Complications – lots including death, pneumonia, hypoxic encephalopathy, coma, otitis media, TB activation, epistaxis, hernia, re-induction of coughing (several months)
d. Management – supportive; isolation for 4 weeks (or 1 week after antibiotics started); may need respiratory monitoring, mechanical ventilation and/or nutritional support

3. Inhaled foreign body and/or segmental or lobar collapse – seen on CXR, requires specialist referral
4. Tuberculosis – should always be considered, especially if the child was born in an area of high endemic tuberculosis, or living with a person who recently came from one
5. M. pneumoniae – patchy consolidation on CXR, confirm with serology (complement-fixing Abs)
6. Psychogenic cough – socially disruptive cough not present at night, normal physical examination and no evidence of other respiratory conditions; typically forced and barking (‘goose honking’)

Chronic persistent cough – a loose cough (especially in the morning) lasting more than three months is suggestive of suppurative lung disease; often clearing after antibiotics then recurs.

1. Cystic fibrosis is an inherited autosomal recessive disorder characterised by chronic obstructive lung disease, pancreatic exocrine insufficiency and elevated sweat chloride concentration. It is the commonest cause of suppurative lung disease, often in children who were not picked up at birth.
   a. Aetiology – mutation in CF transmembrane conductance regulator (CFTR) gene resulting in defective chloride conductance and increased viscosity of mucus
   b. Clinical features –
   c. Complications – multiple respiratory, gastrointestinal, endocrine and reproductive issues; disease course is variable and median survival is approximately 30 years of age
   d. Management – high-calorie diet, vitamin supplements, chest physiotherapy, antibiotics, bronchodilator, mucolytics, antiinflammatories; pancreatic enzyme replacement

2. Bronchiectasis (see last year’s notes) secondary to:
   a. Ciliary dyskinesia – rare, but easily recognised with appropriate investigations
   b. Immunodeficiency – uncommon, usually common variable immunodeficiency
c. Insidious onset – starts with chronic suppurative bronchitis; preventable if identified and treated within 6-12 months of onset (may require 3 months of antibiotics/physiotherapy)

3. Others – smoking, chronic aspiration, missed foreign body, structural airway lesions or tuberculosis

Management:
1. The most important aspect is to make a precise diagnosis based on history, clinical features, CXR and investigations – this will direct your therapy and allow you to explain the cough to the parents
2. Symptomatic treatment often fails – expectorants have no pharmacological basis; opiates have some effect but use is seldom justifiable; lemon/honey or liquorice may soothe pharyngeal irritation
3. Medications:
   a. Anti-asthma therapy should only be used if there is wheeze or reversible airways obstruction
      i. Ipatropium bromide is sometimes used in post-viral cough but evidence is scanty
      ii. A therapeutic trial of a β₂-agonist may be acceptable if the only symptom is cough
      iii. Similarly sodium cromoglycate can be trialled if there is evidence of atopy
   b. A 1-2 month trial of low-dose inhaled steroid is indicated when symptoms are disruptive, other diagnoses have been excluded and when a trial of cromoglycate has failed

• Wheeze in Children

The three lower respiratory tract disorders that cause the greatest morbidity in children are bronchiolitis (the most common LRTI in those <12 months), pneumonia and asthma (less commonly in those <12 months). All of these present with wheeze – note that 20% of all children have at least 1 episode of LRTI with wheeze in their first year of life of which up to 70% are viral; 15% of these see a doctor and 2% are hospitalised.

Differentiating airways obstruction

<table>
<thead>
<tr>
<th>Intrathoracic</th>
<th>Extrathoracic</th>
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<tr>
<td>Expiratory wheeze</td>
<td>Inspiratory stridor</td>
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<tr>
<td>Prolonged expiration</td>
<td>Prolonged inspiration</td>
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<tr>
<td>Hyperinflation</td>
<td>Normal or low lung volume</td>
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Assessment of severity:

<table>
<thead>
<tr>
<th>Wheeze</th>
<th>Indrawing</th>
<th>Nasal flare/grunting</th>
<th>Feeding</th>
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<tbody>
<tr>
<td>End expiratory</td>
<td>Non/mild</td>
<td>Absent</td>
<td>Normal</td>
</tr>
<tr>
<td>Entire expiration</td>
<td>Moderate</td>
<td>Absent</td>
<td>Less than usual, may stop, quantity &gt; half normal</td>
</tr>
<tr>
<td>Inspiration and expiration</td>
<td>Severe</td>
<td>Present</td>
<td>Not interested, choking, quantity &lt; half normal</td>
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Respiratory

Bronchiolitis is an acute lower respiratory illness that causes obstruction of the small conducting airways of the lung. It is a seasonal disease that peaks during winter and early spring, and is usually seen in children under 2 years of age; 57% of those hospitalised are younger than 6 months. Mortality is 0.005% to 0.02% in otherwise healthy children; this increases to 1-3% amongst hospitalised children.

1. Aetiology:
   a. Respiratory syncytial virus is the most common cause (40-90%), transmitted by direct contact with nasal secretions from an infected individual or aerosol spread (less common)
   b. Other organisms include human parainfluenza virus (type 3 is second most common), influenza A, adenovirus, rhinovirus, picornavirus, occasionally *Mycoplasma pneumoniae*.

2. Risk factors include age <2 months of age; prematurity (<32/40); any chronic respiratory, congenital cardiac (particularly cardiac failure) or immunodeficiency disease; crowded living conditions, low socioeconomic status, passive smoke exposure, day care attendance or older siblings in day care.

3. Clinical features:
   a. 2-3 days of prodromal coryzal symptoms; followed by low-grade fever, cough, tachypnoea, hyperinflation, expiratory wheeze and inspiratory crackles. Severity as per above table.
      i. Infants often get worse in the first 72 hours of the illness, then start to improve.
      ii. Note that tachypnoea is defined as >60 breaths/min under 2 months; >50/min from 2 to 12 months; and >40/min over 12 months (c.f. adult rate of 15 breath/min).
   b. Admission criteria – all children with a history of apnoea, O₂ saturation <92% or clinical concern of hypoxia, dehydration or severe illness.
      i. Also consider underlying medical conditions, infants <2 months or born prematurely, severity of illness, inability to feed and duration of illness (i.e. first 72 hours).
      ii. There may also be social issues – e.g. no car/phone, parents can’t cope, crowded or difficult home environment.
   c. Diagnosis is clinical, and investigations are rarely required – nasopharyngeal aspiration and CXR may be used in those who don’t quite fit the clinical picture, or have underlying disease.

4. Management:
   a. Supportive – reassurance, fluids (po/ng/iv), nutrition, O₂, additional respiratory support.
   b. Poor evidence for antibiotics, β₂-agonists (can worsen V/Q mismatch → hypoxia), ipatropium, systemic steroids (NNT 700 for hospital stay decreased 0.43 days, symptoms reduced 1.6 days), nebulised adrenaline (only used in severe cases to avoid intubation).
   c. Prophylaxis:
      i. Palivumazab is a humanised monoclonal antibody given monthly (over 4-5 months); reduces hospital stay and symptoms by 50% and O₂ requirement by 33% (though doesn’t change incidence or days ventilated); recommended for premature infants and children <2 years with bronchopulmonary dysplasia; but too dang expensive.
      ii. Vaccination has been trialled; but most cases <6 months of age (passive maternal antibodies), there are 2 strains and many subtypes; prior safety issues; the useful epitopes are not immunogenic in infancy, and natural immunity is short-lived.

5. Prognosis:
   a. RSV-induced changes in bronchiolar epithelium may last months and symptoms may lag behind clinical signs of recovery. Bronchiolitis obliterans may occur with some aetiologies.
   b. 30-40% of infants develop subsequent wheezing until 7 years of age, particularly those with eosinophilia during RSV bronchiolitis.
   c. Risk factors for developing asthma include eczema, interval symptoms (wheeze without ‘colds’), family history of atopy (1st degree relatives) elevated IgE levels.

Pneumonia is an inflammation of lung tissue due to an infectious agent, stimulating a host response that results in tissue damage. It is more common and more severe in younger children, and is a leading cause of hospitalisation – in fact, admission rates in New Zealand are 3-10x higher than any other Pacific or Anglo-American nation. Rates are particularly high in Pacific Island (5.1x) and Maori (2.4x) children.

1. Aetiology – not identified in 40-80% of pneumonias in hospitalised children.
   a. <1 month – Group B *Streptococcus*, Gram negative organisms.
   b. 1-3 months – RSV, parainfluenza 1 and 2, *C. trachomatis*, *B. pertussis*, *S. pneumoniae*, *Haemophilus* species (less common in immunised infants).
   c. 3-24/12 – RSV and other respiratory viruses (parainfluenza, influenza, adenovirus, rhinovirus), mixed viral and bacterial infections; *S. pneumoniae*, *Haemophilus* species.
   d. >2 years – *S. pneumoniae*, *H. influenzae*, *Mycoplasma* species, respiratory viruses, *S. aureus*, others (*Klebsiella*, *Mycobacterium tuberculosis*, *Legionella*).

2. Risk factors include age <2 months, prematurity (<32/40), chronic respiratory or congenital cardiac diseases, poor growth, low socioeconomic status, passive smoke exposure and day care attendance.
Respiratory

3. Clinical features:
   a. There is often history of a preceding upper respiratory tract infection; followed by high fever, headache, malaise, lethargy, chills, productive cough, dyspnoea and reduced breath sounds
      i. Anorexia with dehydration is common, sometimes with nausea and vomiting, diarrhoea and abdominal pain
      ii. Note that wheeze may only occur in very young infants – in older children increased respiratory rate is the best indicator for severity
   b. Diagnosis is again largely clinical, but CXR may be useful to demonstrate lobar consolidation (S. pneumoniae, H. influenzae), patchy infiltrates (non-specific in infancy), hilar adenopathy (TB) or pneumatoceles (S. aureus, Gram-negative organisms)

4. Management:
   a. Treatment depends on organism, but pending culture/sensitivity results, first-line therapy is generally oral amoxicillin + clavulanic acid; second line is a macrolide e.g. erythromycin
      i. Under 5 – amoxicillin 40mg/kg/day tid for 7-10 days
      ii. Over 5 – erythromycin 40mg/kg/day qid for 7 days
   b. IV antibiotics may be used in very sick children; these include cefuroxime, cefotaxime, amoxicillin and erythromycin
   c. Prophylaxis mainly involves dealing with risk factors, notably low birth weight (RR for death 6.4 <1/12, 2.9 thereafter), malnutrition (RR 4.0) and no breast feeding (RR 2.0)

Red flags for underlying disease include failure to thrive, repeated vomiting, cardiac murmur, infections elsewhere (skin infections, gastroenteritis), possibility of foreign body, persistent asymmetric signs, no symptom-free period or unwell since birth, chest deformity or clubbing, poor treatment response or stridor.

Asthma is characterised by reversible airway obstruction, airway inflammation and airway hyper-responsiveness to a variety of stimuli. It is defined as episodic wheezing and/or cough in a clinical setting where asthma is likely, and other rarer conditions have been excluded. Other features that may aid diagnosis are the three 'R’s – recurrence, reactivity and response (to bronchodilators/antiinflammatories).

1. Epidemiology
   a. Wheezing is incredibly common in the industrialised world, with a cumulative prevalence of 30-60%. While 50% of children who wheeze in infancy stop by 6 years, about 40% continue
   b. The incidence of asthma varies according to definition, but is as high as 25-33% in New Zealand. Both genders are equally affected, and about 2/3 of cases are considered mild.
   c. Asthma typically begins in childhood, and about 50% develop persistent asthma – New Zealand has one of the highest rates for childhood asthma hospital admissions

2. Classification:
   a. Mild infrequent episodic asthma (75%; 270,000) – episodes at least 4-8 weeks apart
   b. Frequent episodic asthma (20%; 70,000) – episodes more often than 4-8 weeks apart
   c. Persistent asthma (5%; 20,000) – symptoms many or most days

3. Clinical features:
   a. Symptoms include wheeze, dry cough, breathlessness and chest tightness – frequency, timing (e.g. nocturnal, seasonal) and precipitating factors (e.g. exercise, allergens, irritants)
      i. Personal history of atopy (e.g. eczema or allergic rhinitis)
      ii. Family history of asthma, eczema or allergic rhinitis is helpful – 20% risk if one parent, 60% if both parents (baseline 6-7% risk); also history of atopy in siblings
   b. Examination is usually normal in the interval phase, though children may have indications of atopy (eczema, allergic shiners, allergic salute/crease) or chronicity (chest wall deformity)

4. Management:
   a. General principles:
      i. Goals are normal growth/development, participation in normal activities/exercise, no school absences, no asthma at night, normal lung function, minimal adverse effects
      ii. Management should be holistic including education, avoidance of triggers, physical fitness, drug therapy, early action in an acute attack and regular review
      iii. Promote self-reliance, recognition of early warning signs, recognition of own resources and strengths, and good use of medical management
      iv. All children should have an asthma plan that details what to do when they are well, when they have mild symptoms, when symptoms get worse, and in an emergency
   b. Acute asthma:
      i. At presentation assess wheeze (none=0, expiratory=1, expiratory and inspiratory=2, stethoscope=3) and accessory muscle use/indrawing (none=0, mild=1, moderate=2, severe=3) \( \rightarrow \) severity (1-2=mild, 3-5=moderate, 6=severe)
         1. Mild – salbutamol 100mcg x6 via spacer, consider prednisone on history

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Respiratory

2. Moderate – O₂ if SpO₂ <92%, salbutamol 100mcg x6 via spacer, prednisone or prednisolone (2mg/kg po od up to 60mg/day x3-5 days)
3. Severe – O₂, salbutamol 100mcg x6 via spacer or 5mg nebule, ipatropium 20mcg x4 via spacer or 0.25mg nebule; prednisone or prednisolone

ii. Reassess severity after 20 minutes:
1. Mild – salbutamol if indicated, prednisone/prednisolone if not already given
2. Moderate – O₂ if SpO₂ <92%, salbutamol every 20 minutes for up to 1 hour, consider prednisone or prednisolone if not already given
3. Severe – O₂, salbutamol every 20 minutes (continuously if not improving), ipatropium every 20 minutes up to 3 doses in the first hour only

iii. Reassess after 1 hour, if no improvement consider admission to hospital/ICU

C. Chronic asthma – remember to check compliance and technique; indications of poor control include days off school, night waking, poor exercise capacity and urgent visits to the doctor
i. Initially – short-acting β-agonist PRN
1. If >3 doses per week, add an inhaled corticosteroid (more effective in children than other drugs e.g. leukotriene modifiers, mast-cell stabilisers)
2. If poor control with >400mcg beclomethasone equivalent, add LABA
3. Increase inhaled corticosteroid further if required – note that the dose-response curve tends to plateau, so adding other drugs are better
4. Step-down treatment after 3-4 months stability

ii. Potential adverse effects of inhaled corticosteroids include:
1. Local – oral thrush, hoarseness, cough
2. Systemic – impaired growth (high doses not tailored to severity; asthma also suppresses growth), adrenal suppression, poor bone formation/resorption
3. Others – cataracts, bruising, dermal thinning, behavioural disturbance

Asthma delivery devices:
1. Metered dose inhalers are commonly used in adults, but are not suitable for use in many children due to difficulties coordinating inhalation. Particles in the aerosol cloud generated range from <1-100μm; whereas the maximum particle size for inhalation is 5μm (majority is swallowed/absorbed)
   a. Autohalers are modified MDIs that have a breath-activated flap that prevents drug delivery until a certain inspiratory pressure is reached; however this may be uncomfortable for some
2. Spacers give better delivery to the lungs and minimise systemic adverse effects – larger particles cling to the walls of the spacer and smaller particles are more available for inspiration. Notes:
   a. One actuation at a time is best – the MDI doesn’t deliver as well on subsequent puffs, and the second puff leads to turbulence within the spacer (causing particles to coalesce/deposit)
   b. Static charge on new spacers also causes deposition – to make a ‘used’ spacer; put 10 puffs of the MDI into the spacer, or wash in detergent and drip-dry (lasts 1-2 weeks if unused)
   c. Optimal technique – shake MDI, insert into ‘used’ spacer, seal around mask or mouthpiece (latter prevents nasal filtration), activate one puff, take 5 tidal breaths, remove spacer
3. Inhaled powder devices include turbuhalers and accuhalers (replaced diskhalers). While more portable than a spacer, they need a high inspiratory flow rate so can’t be used by preschoolers.
4. Nebulisers are still in use, but a number of studies have shown that spacers are just as effective (if not more effective) if used properly. Nebulisers also take more time to deliver and cost much more.

• Conditions without Cough or Wheeze

Pharyngitis is an inflammatory illness of the mucous membrane and underlying structures of the throat, invariably associated with the symptom of sore throat. Pharyngitis with nasal symptoms is usually viral, while pharyngitis without nasal symptoms can be caused by a range of agents (including S. pyogenes)
1. Aetiology – S. pyogenes, EBV, rhinovirus, echovirus, Coxsackievirus, herpes simplex, adenovirus, influenza virus, parainfluenza virus
2. Clinical features – sudden onset fever and sore throat with anorexia; there may be headache, nausea, vomiting, lassitude and sometimes abdominal pain
3. Complications – usually lasts 4-10 days, but in 0.3-3% of untreated S. pyogenes throat infections rheumatic fever occurs; others include retro- or parapharyngeal abscess, septicaemia or toxic shock
4. Management – must swab (Group A Streptococcus) and penicillin if positive (10 days, child is infectious for 24 hours after antibiotics started); symptomatic relief with warm fluids or paracetamol

Otitis media is subdivided into acute otitis media, otitis media with effusion (secretory otitis media) and chronic supplicative otitis media including perforation.
1. Acute otitis media presents with earache, irritability, pulling at ears, fever, malaise, hearing loss
   a. Aetiology – Pneumococcus, other Strep., H. influenzae, M. catarrhalis, S. aureus
   b. Signs – bulging red tympanic membrane → may rupture and discharge

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c. Complications – incomplete resolution (Æ OME), recurrent (Æ tympanosclerosis, permanent perforation), acute mastoiditis (red swelling, systemic disturbance)
d. Treatment – analgesics ± oral antibiotics, assess resolution; recurrent Æ grommets, treat nasopharyngeal sepsis (adenoidectomy), low-dose prophylactic antibiotics

2. Otitis media with effusion is relatively silent – there may be conductive hearing loss, behavioural change, poor school performance, balance disturbance. Often picked up during screening
a. Aetiology – multifactorial including poor Eustachian tube function, URTI, recent AOM, palatal abnormality (e.g. cleft), nasopharyngeal abnormality (adenoids, malignancy)
b. Signs – dull, hypervascular, immobile drums ± retraction
c. Complications – language/educational delay, middle ear changes (atelectasis, adhesive otitis media, cholesteatoma)
d. Treatment – most resolve spontaneously, may try antibiotics after 4/52 (e.g. 4/52 o cotrimoxazole), treat any nasal pathology, consider grommets if continues 3/12

3. Chronic suppurative otitis media
   a. Mucosal CSOM (‘tubo-tympanic’ disease) – repeated infection Æ chronic tympanic perforation Æ hearing loss, otorrhoea, middle ear fibrosis, tympanosclerosis, ossicle defects
      i. Signs – central perforation Æ purulent discharge, white plaques of tympanosclerosis on the tympanic membrane, conductive hearing loss
      ii. Generally benign, but occasionally leads to intracranial complications
      iii. Treatment – swab and culture, local ear toilet, topical antibiotics/steroid drops ± oral antibiotics, repair membrane/ossicle (myringoplasty, ossiculoplasty)
   b. Cholesteatoma (‘attico-antral’ disease) – chronic, offensive-smelling discharge, hearing loss
      i. Combination of chronic negative middle ear pressure and chronic inflammation Æ expanding cyst-like lesion in the middle ear, attic or mastoid
      ii. Signs – attic or postero-superior marginal perforations
      iii. Treatment – local treatment as per mucosal CSOM, surgery to remove the disease and restore hearing where possible (mastoidectomy, tympanoplasty)

Sinusitis is a bacterial infection of the paranasal sinuses, sometimes complicating the common cold. Note that strictly speaking sinusitis and post-nasal drip do not cause cough; whereas nasal obstruction causes loss of filtration, warmth and humidification which can potentially cause cough.

2. Clinical features – rhinorrhoea (frequently purulent), occasionally with fever, cough, pain and headache, sore throat, periobital swelling, vomiting and sometimes malodorous breath
3. Complications – orbital infection, meningitis, osteomyelitis, cavernous sinus thrombosis, abscesses of the epidura, subdura or brain. Relationship to lower respiratory tract diseases unclear.
4. Management – analgesics for symptoms, empiric antibiotics (e.g. amoxicillin) pending culture results; parenteral antibiotics may be necessary for complications; surgical drainage rarely necessary

Epiglottitis is a serious infection of the epiglottis and supraglottic structures resulting in acute airway obstruction and high risk of mortality. It is rare, but should be considered in children presenting with dyspnoea with stridor.

1. Aetiology – almost always H. influenza type B, very rarely other bacteria, viruses or Candida
2. Clinical features – may have prodromal upper respiratory symptoms then acute onset of sore throat, dysphagia, respiratory distress, drooling, irritability, restlessness, anxiety and high fever
3. Complications – total airways obstruction, pneumonia, atelectasis, exudative tonsillitis, cervical lymphadenitis and otitis media; other rare (meningitis, septic arthritis, pericarditis)
4. Management – secure the airway ASAP (nasotracheal intubation ± CPAP to reduce idiopathic pulmonary oedema); 2nd or 3rd generation cephalosporin pending sensitivities; treat contacts

MISCELLANEOUS ADULT LUNG DISEASES

- Interstitial Lung Disease

Interstitial lung diseases are a heterogenous collection of diseases characterised by cough, dyspnoea, clubbing, fine basal crackles and interstitial changes on CXR (nodules, reticular thickening), with restricted lung function (reduced lung volume and diffusion, and desaturation on exercise). Diagnosis is usually on the basis of high-res CT findings or open lung biopsy.

Cryptogenic fibrosing alveolitis is a slowly progressive disorder most commonly seen in older patients.

1. Most likely the result of abnormal healing response to injury by alveolar epithelial cells (fibroblasts prevent re-epithelialisation); associated with connective tissue disorders (scleroderma and RA)
2. Patients present with insidious onset cough and dyspnoea, may have clubbing but almost always have fine basal crackles (‘velcro’) on auscultation
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3. CXR shows peripheral basal interstitial shadowing, which is well demonstrated on high-res CT which is diagnostic for most patients. Lung functions show classical changes of interstitial lung disease.
4. Management involves oxygen, glucocorticoids, cyclophosphamide, interferon-γ; however transplant may be required (often heart/lung due to cor pulmonale).
5. Median survival is 5 years; in a rapidly progressive form (Hamman-Rich syndrome) survival is generally less than 6 months.

Extrinsic allergic alveolitis is a diffuse inflammatory disease caused by repeated inhalation of dust made up of animal proteins, plant proteins or reactive inorganic compounds.
1. Aetiology – thermophilic actinomyocyte (farmer’s lung, air conditioner lung, bagassosis), avian protein and blood (bird breeder’s lung), rat urine and protein (rat handler’s lung), toluene/methylene diisocyanate (isocyanate lung), Bacillus subtilis enzymes (washing powder lung)
2. Clinical features – may present with acute or chronic hypersensitivity pneumonitis:
   a. Acute – fever up to 40°C, cough, dyspnoea, malaise, body aches, rarely haemoptysis or sputum production, hypoxia, fine mid- to end-inspiratory crackles
      i. CXR shows diffuse interstitial infiltrate with hazy background, fine nodular shadows, linear striated shadows and occasional lower lobe consolidation
   b. Chronic – chronic cough, dyspnoea and exercise intolerance, anorexia and weight loss, fatigue, progressive hypoxia/cyanosis, clubbing, find mid- to end-inspiratory crackles
      i. CXR shows reticulonodular pattern with coarse linear shadows and nodules; no hilar adenopathy, effusion or pneumothorax; upper lobe ring shadows and bronchiectasis
3. Management – avoidance is primary therapy; corticosteroids for 1-2 weeks may resolve symptoms though alternate day therapy may be needed if exposure cannot be discontinued

Sarcoidosis is a multisystem disorder characterised by formation of granulomas at the site of disease activity, probably due to cytokine dysregulation (IL-12).
1. Patients most commonly present with bilateral hilar adenopathy, pulmonary infiltrates and ocular or skin lesions, but many other organs may be involved (e.g. liver, spleen, lymph nodes, heart, CNS)
2. Investigations – serum angiotensin converting enzyme elevated (>60%); lymphopaenia, anaemia or leukopaenia (>50%), abnormal LFTS (high ALP), hypercalciuria (10%), Kveim-Siltzbach skin test
3. CXR allows staging using Scadding’s classification:
   a. Stage 0 – normal
   b. Stage 1 – hilar adenopathy alone
   c. Stage 2 – hilar adenopathy with parenchymal infiltrates
   d. Stage 3 – parenchymal infiltrates alone
   e. Stage 4 – pulmonary fibrosis
4. Management – may require no specific therapy if asymptomatic; systemic corticosteroids may be useful for symptomatic patients (high-dose prednisone tapering over a year) though many relapse
5. Prognosis – 80% have spontaneous resolution within two years; 10% have significant fibrosis but no further worsening of disease; 10% will have chronic disease and a few will visit the grim reaper.

Other important interstitial lung diseases include adult respiratory distress syndrome, those associated with connective tissue disorders and drug-induced interstitial lung disease (e.g. amiodarone, nitrofurantoin). Note that some conditions may mimic ILD, namely miliary TB and pulmonary oedema.

Pleural Disease

Pleural physiology:
1. The pleura (visceral and parietal with a space containing about 10mL of fluid) allow movement of the lungs relative to the chest wall; note giraffes have no pleural cavity and dogs only have one pleura.
2. Visceral pleura is thick (60μm) and mechanically supports the lung (‘interdependence’); the parietal pleura (30μm) is thin and is the major site of fluid production; and stomas are even thinner (2-10μm)
3. There is huge reserve for resorption (20-30 times normal capacity) via lymphatics (bulk flow, no active transport). Everything seems to work according to Starling’s law of filtration, which I’ve forgot.

Pleural effusion:
1. Classification (Light’s criteria is 98% sensitive, 83% specific)
   a. Transudate – protein <50% serum, LDH <60% serum; (cells usually <1000/μL)
      i. Increased hydrostatic pressure e.g. CHF
   b. Exudate – protein >50% serum, LDH >60% serum or >67% upper limit of normal; (pH <7.4)
      i. Increased permeability of pleural membrane due to infection, malignancy, inflammation, vascular disorders, GI conditions (e.g. pancreatitis)
2. Clinical features:
Respiratory

a. History of respiratory infections, dyspnoea, cough (lung distortion), pleuritic pain (parietal pleural inflammation); gas exchange normal (decrease in volume only ~1/3 that of effusion)
b. CXR (bilateral decubitus) – determine quantity/loculation, localise masses (silhouette sign – heart border lost with anterior fluid; diaphragm border lost with posterior fluid)
c. Pleural fluid for appearance, pH, LDH, glucose, protein, amylase (USA), cell counts and differential, others e.g. ANA, RF and complement if collagen vascular disease suspected
   i. Bloody – Hct <1% insignificant, 1-20% cancer, PE or trauma, >50% haemothorax
   ii. Cloudy or turbid – cells (empyema), high lipids → ↑TGs on centrifuge (chylothorax)
   iii. Putrid odour – empyema (anaerobic)
d. Others – pleural biopsy if pleural fluid not diagnostic (picks up malignancy, TB – few organisms in fluid), USS, CT, bronchoscopy (low yield), thoracoscopy and open biopsy

3. Management:
   a. Treat the underlying cause e.g. CHF patients should get diuresis and observation for 24-48 hours; note that management difficulties usually arise in patients with malignant effusion
   b. Indications for referral – massive unilateral effusion, suspected tuberculosis aetiology, complicated parapneumonic effusion/empyema, chylothorax, no diagnosis after biopsy
   c. Criteria for complicated parapneumonic effusion/empyema needing immediate ICT drainage
      i. pH <7.2
      ii. Glucose <2.5mmol/L
      iii. LDH >1000
      iv. Also turbid fluid with high WCC, organisms seen on Gram stain or culture, frank pus and/or loculation demonstrated on USS or CT

Pneumothorax is air in the pleural space. It may be secondary to underlying lung disease (obstructive, restrictive, cavitatory and trauma, possibly asthma) or primary (spontaneous, possibly with predisposing subpleural blebs seen in 75% of cases). The patients in this latter group tend to be young men aged 25-35 years with tall and thin body habitus; >90% are smokers and there is a slight familial tendency.

1. Pathophysiology:
   a. Small pneumothorax – usually asymptomatic or present with mild dyspnoea on exertion
   b. Larger pneumothorax leads to reduced vital capacity, increased A-a gradient, reduced V/Q ratio and shunting (presenting with hypoxia); note hypercapnia doesn’t occur in 1° disease

2. Clinical features –
   a. History of chest pain, shortness of breath, mediastinal or subcutaneous emphysema, ‘sloshing’ sensation in chest; symptoms occur at rest and may be subtle in 2° disease
   b. Examination findings include decreased chest expansion, hyper-resonance and decreased breath sounds; tension pneumothorax may present with respiratory distress, cardiovascular collapse (cyanosis, peripheral shut down, hypotension, tachycardia), mediastinal shift
   c. CXR shows a thin, visceral pleural line (<1mm width) displaced from the chest wall; small apical pneumothorax on expiration (not recommended); differentiate bulla (has meniscus)
      i. Size in % = 100 x (1-lung3 / hemithorax3) – or just draw the dammed thing
         1. Small – shallow rim of air around lung
         2. Moderate – lung collapsed halfway towards heart border
         3. Large – airless lung separated from diaphragm
      ii. Note adhesions and pleural fluid – these can tear/bleed if ICT is placed nearby

3. Management:
   a. Observation ± supplemental O2 – consider if no underlying disease, small pneumothorax or not short of breath, social circumstances; resolves 1.25% per day; >3L aspirate → failure
   b. Aspiration – more rapid resolution, but not without complications; note that size is not a complication. If fails to resolve, increasing pneumothorax or respiratory distress → ICT
   c. ICT – if there is underlying lung disease; attach to UWSD and suction after 24 hours; may use Heimlich valve. Allows rapid re-expansion, but don’t clamp the tube during transport!
      i. Refer if pneumothorax doesn’t improve on post-ICT CXR, or there is an ongoing air leak (>2/7), worsening subcutaneous emphysema, re-expansion pulmonary oedema, pleural effusion (blood or infective) or recurrent/bilateral pneumothorax
   d. Surgical pleurodesis via thoracoscopy

4. Prognosis:
   a. Recurrence (same side) 20% after 1 episode, 40% after 2, 80% after 3; 40% at 4 years
   b. Recurrence (opposite side) 10-20%
   c. Risk greatest in the first few months, more likely if subpleural blebs present, smoker

**Tuberculosis**

Tuberculosis is the most common cause of death by an infectious agent. Incidence varies in different countries and different ethnic groups – in New Zealand, notification rates were 2.7 per 100,000 for
Europeans, 18.9 per 100,000 for Maori, 43.9 per 100,000 for Pacific Islanders and 101 per 100,000 for other ethnicities. Incidence has been increasing since the 1990s due to poverty (crowded housing, poor nutrition, inadequate medical care), HIV and immigration. About 10% are reactivations, while about 3% die.

Pathogenesis:
1. M. tuberculosis complex includes six organisms, though only M. tuberculosis, M. bovis and M. bovis Bacille Calmette Guerin are clinically important.
   a. These organisms are strictly aerobic and have a thick lipid-containing cell wall (source of virulence and persistence) allowing them to survive and multiply (slowly) intracellularly
   b. They can lie dormant for long periods, and are resistant to conventional antibiotics as well as a low level of natural resistance against TB antibiotics
2. M. tuberculosis enters the body via respiratory droplets, settling in the lungs. Alveolar macrophages ingest the mycobacteria, where the non-specific immune response is insufficient and they multiply
   a. After 2-12 weeks (10^2 or 10^3 mycobacteria) a specific immune response occurs – either pure TH1 (cell mediated \(\rightarrow\) INF-\(\gamma\), IL-2) or mixed TH1 and TH2 (humoral \(\rightarrow\) IL-4, IL-5) which is bad
   b. In the minority of cases (<10%) the response is inadequate and primary progression occurs – with either huge cavitation (mixed TH2 response), miliary TB or nasty bronchopneumonia
   c. Otherwise the TH1 response is sufficient to contain the TB – granuloma formation occurs (Ghon focus), and these undergo central liquefaction (caseation)
      i. This leaves a fibrotic calcified scar lesion with some viable organisms (usually in the apex – high O2 tension) associated with a scarred hilar lymph node (Ghon complex)
      ii. Symptoms are uncommon and minimal – mostly relating to hilar lymphadenopathy with collapse (Brock’s syndrome – collapse \(\rightarrow\) bronchiectasis) or pleural effusion
3. Secondary TB is either due to reactivation of scars or reinfection. Risk factors include malignancy, alcoholism, diabetes, chronic dialysis, partial gastrectomy/malnutrition, immunosuppression, lymphoma and the frail elderly; with the highest risk in the first 2 years (50% of reactivation TB)
   a. May be restricted to the lungs or extrapulmonary (secondary systemic TB) which presents non-specifically or as chronic infection of the target organ
   b. Damage relates to a type 4 (cell-mediated) hypersensitivity response from an already sensitised immune response – the higher the TH2, the worse the damage as more mediators are released but the mycobacteria are less well contained \(\rightarrow\) widespread caseation
4. Miliary TB is the result of acute diffuse dissemination of TB bacilli, seeding sites that include lungs, meninges, bones, joints, lymph nodes, kidneys, adrenals, liver and spleen (may occur at any stage)

Clinical features:
1. Presentation:
   a. Primary infection – usually silent; may present with cough and fixed wheeze (atelectasis 2\(^\circ\) to hilar lymphadenopathy), pleural effusion, rash (erythema nodosum – allergic response)
   b. Progression, reactivation or miliary TB – symptoms of target organ damage; non-specific symptoms of fatigue, malaise, anorexia, weight loss, fever and cough
   c. Complications:
      i. Short-term – pleural effusion, empyema, bronchopneumonia, sinus tract formation, lymph node rupture
      ii. Long-term – bronchiectasis, cor pulmonale, mycetoma, adrenal insufficiency, sterility, bronchostenosis
2. Investigations:
   a. Mantoux testing (result is diameter of area of induration) – positive response means that a patient has been exposed to complex or non-TB mycobacterium; clinical context is important
      i. Criteria is >5mm for HIV patients, children/adolescents with recent TB contact, fibrotic CXR, major immunosuppression (transplant, steroids)
      ii. Criteria is >10mm for previous residence in a high-incidence country, IV drug users, TB lab personnel, adult contacts of a TB case, conditions with increased risk of infections or children exposed to adults with high risk
      iii. Criteria is >15mm for people with no risk factors and past BCG vaccination
   b. Microbiology:
      i. Sputum smear test and staining with fluorochrome (greater sensitivity) and ZN stain
      ii. Culture in liquid media gives ID in 7-10 days, sensitivity in 12-15 days (c.f. 6 weeks)
      iii. DNA probes give rapid identification; PCR useful but doesn’t differentiate dead/live
      iv. Others – MSU (sterile pyuria), FNA of enlarged lymph nodes (AFB and cytology)
   c. Imaging:
      i. CXR – apical shadowing, cavitation, miliary shadowing (1-2mm nodules bilaterally)
      ii. Bronchoscopy with bronchial washings
Respiratory

Management:

1. **General principles**
   a. Screening contacts and migrants from high-incidence countries
   b. Vaccination (BCG) in neonates – reduces risk by about 50%
   c. Chemoprophylaxis – limited treatment to eradicate latent TB infection (6-12/12 isoniazid)
   d. Control in hospital – isolate infectious cases in ventilated, negative pressure rooms; face masks for patient and/or medical staff; pre-employment screening (2-step Mantoux + CXR)

2. **Medications:**
   a. First line – rifampicin (R), isoniazid (H), pyrazinamide (Z), ethambutol (E) e.g. 2RHZ + 4RH
   b. Second line – aminoglycosides, ethionamide, capreomycin, para-amino-salicylic acid
   c. Always use at least 2 medications due to natural resistance (10%); never add a single drug to a failing regimen (usually requires a longer course as well)
   d. May be self-administered or given by a health professional (directly observed therapy) once daily, twice weekly or thrice weekly (final two weeks daily)

3. **Resistance:**
   a. Resistance may be primary (original organism transmitted from a known resistant index case) or secondary (results from inadequate treatment)
   b. In NZ, 10% of isolates have some resistance (usually isoniazid and streptomycin); while 1% are multi-drug resistant (isoniazid and rifampicin, or more than one drug)
   c. Resection of localised severe disease is sometimes necessary

<table>
<thead>
<tr>
<th>CXR</th>
<th># of MTB</th>
<th>Drugs</th>
<th>Duration</th>
<th>???</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTBI</td>
<td>Normal (or almost)</td>
<td>Few</td>
<td>1-2</td>
<td>6-9H or 2RI</td>
</tr>
<tr>
<td>Prevention??</td>
<td>Scarring, volume loss</td>
<td>Many</td>
<td>2-4</td>
<td>4-6/12</td>
</tr>
<tr>
<td>Active</td>
<td>Old consolidation, cavitation, miliary</td>
<td>Most</td>
<td>3-4</td>
<td>6/12 minimum</td>
</tr>
</tbody>
</table>

**Sleep**

- **Sleep Overview**

Sleep can be defined as a state of sustained quiescence in a species-specific posture accompanied by reduced responsiveness to external stimuli, plus in mammals: quick reversibility, characteristic EEG changes and spontaneous occurrence with endogenous periodicity. (Screw this, I'm going to bed)

1. **Stage 1** (2.5%)
   a. Light sleep in the first few minutes of sleep
   b. Difficult to distinguish from wakefulness

2. **Stage 2** (25-30%)
   a. Clear-cut sleep, sleep spindles and K-complexes on the EEG
   b. Increases in duration with each successive cycle through the night

3. **Stage 3**
   a. Slow waves with large amplitude – first stage of slow wave sleep
   b. Usually a precursor of stage 4 sleep, though in older patients only stage 3 may be seen

4. **Stage 4** (30%)
   a. Well-established slow-wave sleep with low arousal thresholds
   b. Huge levels in children, falling to 30% in young adults and fading with age (absent in elderly)

5. **Stage 5** (15-25% in 4-6 episodes)
   a. REM sleep – very fast EEG frequencies with profound loss of muscle tone, phases of eye movements; often autonomic instability with wild swings in HR, BP, RR and frequency
   b. Brain is metabolically active with high $O_2$ consumption – most if not all dreaming occurs here

Up to 30% will report difficulty sleeping in the preceding year, and 12-15% report feeling unrefreshed and/or excessively sleepy (a subjective sensation of the need to fall asleep) during the day.

1. Excessive daytime sleepiness (inappropriate sleepiness without clear cause) is most apparent when the individual is unstimulated (e.g. studying for exams), and is clearly different from fatigue
2. Assessing daytime sleepiness can be done via questionnaires, the Epworth sleepiness score, or objective tests (EEG monitoring, multiple sleep latency test, maintenance of wakefulness test)
3. Sleep hygiene is crucial – this includes sleeping at regular hours, a comfortable sleeping environment, and a clear influence of habits surrounding going to bed

**Disorders of sleep initiation and maintenance:**

1. **Insomnia** is a subjective impression that sleep is inadequate (usually quantity, often quality) due to problems with initiating sleep, repeated awakenings and/or getting back to sleep
   a. Acute insomnia (<3 weeks) is a almost universal experience, often occurring with acute life crises. It is usually self-limiting but can progress to chronic insomnia
Respiratory

b. Chronic insomnia (>3 months) may be present for months before the patient complains
   i. Primary – type A personalities; may have a history of mental illness; treatment is to help them cope and defuse anxieties (e.g. misinterpretation → actually sleeps well)
   ii. Secondary – to physical illness (e.g. pain, nocturia, hepatic failure – sleep inversion due to altered hormone clearance) or mental illness (e.g. depression, mania)

2. Narcolepsy is a rare genetic condition (0.1-0.25% of the Caucasian population) leading to a deficiency of hypocretin-secreting cells in the brainstem
   a. Characterised by hypersomnolence with attacks of overwhelming need to sleep
      i. May have hallucinations – hypnagogic (sleep onset), hypnopompic (on waking), often associated with paralysis on waking due to hypotonia of REM
      ii. 70% also have cataplexy where emotional stimulus → REM hypotonia while awake
   b. Diagnosis is by a multiple sleep latency test to demonstrate excessive sleepiness and sleep-onset REM (may be seen in normal patients, but more so in narcoleptics)
   c. Treatment is difficult but includes regular daytime naps, stimulants (amphetamines) and tricyclic antidepressants (suppress REM sleep)

3. Periodic limb movement disorder is characterised by stereotyped rhythmic twitches of the limbs (usually the legs) during sleep occurring every 10-15 seconds.
   a. Often an incidental finding in sleep studies; the minority may present with insomnia due to twitches or excessive sleepiness due to sleep fragmentation
   b. Diagnosis is by a combination of the sleep study findings (frequency and impact of the jerks on sleep), the clinical picture and the patient’s symptoms
   c. Treatment is very difficult but includes sedatives (e.g. clonazepam – may aggravate sleep disordered breathing) and drugs used in movement disorders (e.g. carbidopa, bromocriptine)

4. Disorders of circadian rhythm are extremely common, occurring when the body’s internal clock becomes out of phase with the day/night cycle. This may be caused by irregular lifestyle (i.e. daylight exposure), especially if meals and sleep times are disjointed and fragmented
   a. Most people are able to retrain their internal clocks fairly easily, while others have difficulties leading to night owls who become chronically sleep deprived (shift workers similar problems)
   b. Diagnosis is by history and recording a sleep diary to determine the patient’s sleep, exercise and eating patterns – sleep studies are of limited value
   c. Treatment is difficult – increasing the stimuli to normal sleep may be sufficient, otherwise bright light therapy can be used to gradually retrain the sleep/wake cycle

• Sleep Disordered Breathing

Physiological changes in sleep:
1. We reset our chemoreceptors, minute ventilation and O₂ consumption drops, and posture changes altering functional residual capacity and the mechanics of breathing
2. Additionally the progressive hypotonia of deepening sleep affects accessory muscles, intercostals and muscles of the upper airway causing a variable degree of airway narrowing and resistance
3. This increases load on the diaphragm, which can be intolerable if there is severe upper airway narrowing and/or obesity leading to respiratory failure. Alternatively the upper airway may be sucked shut, leading to asphyxia and apnoea, triggering arousal from sleep

Terminology
1. Apnoea – pause in breathing, usually brief; if prolonged (>10s) can be potentially pathological
2. Hypopnoea – shallow breathing
3. Respiratory related arousal – minor variations in breathing pattern causing sleep fragmentation
4. Respiratory disturbance index - # of apnoeas + # hypopnoeas + # RERA per hour

Snoring is common and is an indication of upper airway narrowing resulting in turbulence, with resulting vibration of the walls of the upper airway and soft palate. Up to 40% of middle-aged men and 20% of middle-aged women snore regularly. It may be affected by obesity, possibly by narrowing/altering the upper airway.
1. Simple snoring – lung, regular, all positions; no sleep disruption or sleepiness
2. Upper airways resistance syndrome – loud snorers who are sleepy but have no apnoeas or hypopnoeas. Progressive respiratory effort but normal flow, so possibly due to increased resistance
3. Obstructive sleep apnoea – apnoeas or hypopnoeas due to upper airway narrowing or full-blown obstruction leading to clinical symptoms (sleepiness, poor concentration, memory problems)
   a. Episodes disrupt sleep, though micro-arousals are hard to detect on EEG – note that the extent of daytime sleepiness does not correlate well with severity
   b. Affects 2-4% of middle-aged men, 1-2% of middle-aged women, with possibly increased incidence in Maori and Pacific Islanders due to facial shape
   c. Risk factors – throat shape (retrognathia), BMI (fat around throat), age (airway collapse), male gender, medical conditions (e.g. myxoedema, acromegaly)
Respiratory

d. Treatment:
   i. Conservative – weight loss (variable results), sleep position (not on back)
   ii. Mandible advancement devices to hold the tongue forward or pull the jaw forward; occasionally successful but more useful for simple snoring or mild OSA
   iii. Nasal CPAP – increases quality of life, decreases sleepiness and improves psychometric function, but approximately 10-15% cannot use this therapy
   iv. Surgery is largely used for ‘simple snoring’ but has limited success rate, though jaw reconstruction for small or retrognathic jaws may have some application

Central apnoea and hypoventilation

1. Trigger failure
   a. Normal – associated with movement or transition though sleep stages
   b. Ondine’s curse – congenital failure of automatic control of breathing; named after the suitor of Neptune’s daughter who was cursed to lose automatic control over all bodily functions.
   c. Cheyne-Stokes respiration (2° to heart failure or drugs) – most common cause of central apnoea in adults, characterised by waxing/waning respiration with apnoea, hyperventilation

2. Nocturnal hypoventilation – many reasons including brain damage and morbid obesity
   a. Normal to hypoventilate in sleep with reduced respiratory drive, but because of the shape of the O₂ dissociation curve we are protected from desaturation during this fall
   b. If there is severe respiratory disease, respiratory muscles that are only just coping during the day get less stimulus and ventilation may be inadequate at night → hypoxia, hypercapnia
   c. Non-invasive ventilation via self-sealing nose mask every night may be used and may reverse respiratory failure, but is fairly demanding treatment

3. Disorders of alertness and sleep promotion – rarely patients present with daytime somnolence but sleep normally and have no sleep disruption or sleep-disordered breathing (‘idiopathic hypersomnolence’). Some have poor sleep quality and may have history of drug/alcohol abuse, toxin exposure or major brain injury. Others have non-restorative sleep despite normal architecture.