DRUGS RELATED TO RESPIRATORY SYSTEM

BRONCHODILATORS

**Asthma**
Drugs may be administered by inhalation, oral or parental. Inhalation delivers drug directly to the airways resulting in a smaller dose and reduced side effects. Pressurised metered dose inhalers are effective and convenient. Spacer devices improve delivery in children. Breath actuated devices usually use powder. Inhalation is the safest route in pregnancy. Solutions for nebulisation are available for acute attacks – given over 5-10 minutes with oxygen as the carrier. Oral medication is given when inhalation is impossible. Systemic side effects are more common with this route. The intravenous route is used when nebulisation is inadequate or inappropriate.

Acute attack – must be treated promptly. Characterised by dyspnoea, exhaustion, tachycardia (>110) and very low peak expiratory flow. Treat with oxygen, salbutamol or terbutaline by nebuliser. Followed by steroids – prednisolone 30-60mg orally or hydrocortisone 200mg IV. Poor response – give ipratropium by nebuliser, aminophylline by slow IV injection. Treatment should never be delayed for investigations; patients should never be sedated and always be aware of the potential for pneumothorax. If condition still deteriorates consider ventilation.

Chronic obstructive pulmonary disease – may be helped by short-acting beta2 agonists or antimuscarinics/long acting beta2 agonists when more severe.

**Adrenoceptor Agonists (Sympathomimetics)**
Selective beta2 agonists such as salbutamol and terbutaline are the safest and most effective for mild to moderate symptoms of asthma. Recommended over the less selective beta agonists such as orciprenaline. Salmeterol is a longer acting beta2 agonist and is administered by inhalation. Should not be used for acute attack. Helpful in nocturnal asthma and can be added to existing steroid therapy, not replacing it. Regular treatment - short-acting agonists provides no clinical benefit, long-acting agonists is of benefit. Duration of action of inhaled doses of short acting is 3-5 hours, long acting 12 hours. Dose, frequency, maximum number of inhalations in 24 hours should be stated explicitly to the patient. The dose given by nebuliser is substantially higher. Salbutamol and terbutaline can be given IV in severe cases, SC and IM may also be used. Beta2 agonists should be used with caution in hyperthyroidism, CVS disease, arrhythmias, susceptibility to prolonged QT interval and hypertension. May cause ketoacidosis in diabetics, especially if given IV. Beware hypokalaemia. May cause fine tremor, nervous tension, headache, palpitations, peripheral dilatation, tachycardia, arrhythmias, sleep disturbance and muscle cramps. IM injection can be painful.

**Salbutamol** – dose orally 4mg (elderly 2mg) 3-4 times a day. Maxm single dose 8mg, but unlikely to be of extra benefit. SC / IM dose 500mcg every 4 hours. Slow IV 250mcg, repeat if necessary. IV infusion – 5mcg/min initially and adjust depending on heart rate (range 3-20mcg/min). Aerosol inhalation100-200mcg (1-2 puffs) 3-4 times a day for persistent symptoms. Prophylaxis for exercise induced bronchospasm 200mcg. Inhalation of powder 200-400mcg, 3-4 times a day for persistent symptoms. Bioavailability is lower with dry powder inhalers, hence higher dose. Counselling is essential in these patients regarding doses and frequency – no relief after three hours, contact doctor.

**Terbutaline** – orally 2.5mg TDS for 1-2 weeks, then 5mg TDS. SC / IM or slow IV 250-500mcg up to 4 times daily. Infusion solution 3-5mcg/ml – 1.5-5mcg/min for 8-10 hours.
Aerosol 250-500mcg 3-4 times a day for persistent symptoms. Powder 500mcg (one inhalation) four times a day. Nebulised 5-10mg 2-4 times daily. Counselling is essential in these patients regarding doses and frequency – no relief after three hours, contact doctor. **Salmeterol** – main use in patients who require long term regular bronchodilator treatment, not for immediate relief in acute attacks. Significant incidence of paradoxical bronchospasm. Dose by inhalation 50mcg (2 puffs) BD in severe airways obstruction. Same dose for COAD.

**KEY POINTS – BRONCHODILATORS**
1. Two main types – beta2 adrenoceptor stimulants and antimuscarinics (anticholinergics)
2. Some are given by inhalation – patients being given detailed instructions on devices
3. Bronchodilators with a long action are not suitable for treatment of acute attacks
4. Hypokalaemia is a potential risk with beta2 adrenoceptor stimulants
5. Hypokalaemia can be increased with combined therapies – monitor plasma potassium

**Anti-muscarinic**
Used by inhalation in patients already on high dose inhaled steroids. Can be nebulised in life threatening situations. More effective in relieving bronchoconstriction in COAD than in relieving asthma. Aerosol ipratropium has a maximum effect 30-60 mins after use with a duration of action 3-6 hours. Maintenance three times per day.

**Ipratropium** - caution in patients with glaucoma, prostatic hypertrophy. Be careful nebulised drug does not enter eye in glaucoma patients. Causes dry mouth, urinary retention and constipation. Aerosol 20-40mcg up to 80mcg, 3-4 times per day. Inhalation of powder 40mcg, 3-4 times per day, doubled in less responsive patients. Nebulised 100-500mcg up to 4 times per day. Because of paradoxical bronchospasm first dose under medical supervision.

**Theophyllines**
Used in reversible airways obstruction. Additive effect when given with beta2 agonist, including hypokalaemia. Theophylline is metabolised in the liver and considerable variation in half life occurs. Half life increases in heart failure, cirrhosis, viral infections, elderly and concurrent treatment with cimetidine, ciprofloxacin, erythromycin, fluvoxamine and oral contraceptives. Half life is decreased in smokers, chronic alcoholism and by drugs such as phenytoin, carbamazepine, rifampicin and barbiturates. This is important because of the narrow margin between therapeutic and toxic levels. A plasma theophylline level of between 10-20mg/litre is usually required for effective bronchodilatation. Frequency and severity of side effects increase with levels over 20mg/litre. Theophylline modified release preparations can produce adequate plasma levels for up to 12 hours. Given at night it can control nocturnal asthma and early morning wheezing. Theophylline is given by injection as aminophylline – a mixture of theophylline and ethylenediamine, which is 20 times more soluble than theophylline alone. Aminophylline must be given by very slow IV injection (at least 20 mins). It is too irritant for IM use. IV aminophylline is useful when nebulised beta2 agonists have failed to work. Essential to measure levels in patients taking oral theophylline before IV aminophylline – convulsions and arrhythmias can occur.

**Theophylline** – caution with heart disease, hyperthyroidism, peptic ulcer, hepatic impairment, epilepsy, elderly, fever. Avoid in porphyria. Beware hypokalaemia. Side effects include tachycardia, palpitations, nausea, headache, CNS stimulation, insomnia, arrhythmias and convulsions – especially if given by rapid IV injection. Doses of the five preparations vary and the patient must receive the one that they are already taking. Neulin 125mg 3-4 times a day after food; Neulin SA 175-350mg 12 hourly; Slo-Phyllin 250-500mg 12 hourly; Theo-Dur 300mg 12 hourly; Uniphyllin Continus 200mg 12 hourly increasing to 300mg after one week. Beware some cough and decongestants contain theophylline.
**Aminophylline** – allergy to ethylenediamine may cause urticaria, erythema and exfoliative dermatitis. Orally 100-300mg 3-4 times per day after food. Intravenously, if not already on theophylline, give 250-500mg (5mg/kg) by slow injection over 20 minutes. Infusion 500mcg/kg/hr, adjusting to plasma levels. If already on oral theophylline DO NOT give IV aminophylline unless plasma level available.

**Corticosteroids**
Are effective in asthma by reducing airway inflammation and hence reducing oedema and secretion of mucus in the airways. Patients with COAD usually show no response to corticosteroids. Higher doses of inhaled corticosteroid may reduce symptoms and exacerbations slightly in patients with more severe COAD. Trial of corticosteroid can distinguish between COAD and asthma. Inhaled corticosteroids should be considered for prophylactic treatment of asthma when patients are using beta2 agonists more than once daily. Corticosteroid inhalers must be used regularly to obtain maximum benefit. Alleviation of symptoms occurs 3-7 days after initiation. Doses for CFC free corticosteroids may be different from those containing CFC’s. If inhaled corticosteroid causes coughing, a beta2 agonist beforehand may help. Transfer from oral corticosteroids to inhaled must be slow with a gradual reduction in oral dosage. High dose inhalers (500mcg BD) should only be used if there is clear benefit over the lower dose. Oral tablets may be needed during infection and exacerbations. Inhaled corticosteroids have considerably fewer systemic side effects than oral steroids. Prolonged high doses can cause bone demineralisation and osteoporosis. Spacer devices increase airway deposition and decrease oropharyngeal deposition which predisposes to candidiasis. Oral steroids for acute attacks over a short course – 30-60mg prednisolone daily for a few days. Dose reduced gradually after attack controlled. Long term steroids may be necessary in patients where response to other drugs is small. High dose inhalation is preferred to minimise oral intake of steroids. Oral should be given as single dose in the morning to reduce disturbance to circadian cortisol secretion. Titrated to lowest dose to control symptoms. Regular peak flow readings. Alternate day treatment is not very effective.

**Beclomethasone** – caution in active or quiescent tuberculosis, cover may be required during stress episodes (operation). Paradoxical bronchospasm can occur and may be prevented by inhalation of beta2 agonist. Can cause hoarseness, candidiasis (mouth and throat). Dose by aerosol 200mcg BD or 100mcg TDS/QDS. Powder 400mcg BD or 200mcg TDS/QDS. High dose inhalers 500mcg BD or 250mcg QDS, increasing to 500mcg if necessary. Powder 400mcg BD, increasing to 800mcg BD.

**Leukotriene receptor antagonists**
Block the effect of cysteinyl leukotrienes in the airways. Add on therapy for patients with mild to moderate asthma which is not controlled with inhaled corticosteroids and a short acting beta2 agonist. May be of benefit in exercise induced asthma. Should not be used to treat acute severe asthma. Churg-Strauss syndrome – history of asthma, rhinitis, sinusitis, systemic vasculitis, eosinophilia – can be associated with use of leukotriene receptor antagonists. Often triggered by reduction or withdrawal of oral corticosteroid therapy. The prescriber must make the patient aware of potential symptoms of eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications or peripheral neuropathy.

**Zafirlukast** – caution in the elderly, renal impairment, Churg-Strauss syndrome, hepatic impairment. Interacts with aspirin (increases levels zaf), erythromycin and theophylline (decreases levels of zaf), anticoagulant effect of warfarin increased. Can cause GIT
symptoms, headaches, arthralgia, myalgia, hepatitis, thrombocytopenia and respiratory infection in the elderly. Dose 20mg BD.

**Anti-histamines**
Treatment of nasal allergies and vasomotor rhinitis. Reduce rhinorrhea and sneezing, less effective in nasal congestion. Used to treat urticarial rashes, pruritus, insect bites, drug allergies. Injections of chlorphenamine or promethazine are used as an adjunct to adrenaline in the treatment of anaphylaxis. Also used in nausea and vomiting, insomnia. Duration of action and levels of drowsiness vary between drugs. Sedating antihistamines include trimeprazine and promethazine and non-sedating ones include acrivastine, loratadine and terfenadine. The non-sedating antihistamines cross the blood brain barrier to a lesser extent. Sedating antihistamines have a significant antimuscarinic effect and should not be used in prostatic hypertrophy, urinary retention, glaucoma. Caution in hepatic and renal impairment. Caution in epilepsy and the elderly. May cause palpitations and arrhythmias, extrapyramidal effects, blood disorders and liver dysfunction.

**Loratidine** – non-sedating. Used in treatment of hayfever and urticaria. Sedation and antimuscarinic effects low. Dose 10mg daily.

**Chlorpheniramine** – sedating. Used in treatment of hayfever, urticaria and anaphylactic reactions. Can cause exfoliative dermatitis, tinnitus, transient hypotension. Dose 4mg every 4-6 hours. SC / IM 10-20mg to a maximum of 40mg in 24 hours. IV 10-20mg over 1 minute.

**INFECTIONS**

**Anti-bacterial**
Two factors need to be considered – the patient and the likely causative organism. Factors related to the patient which must be considered include history of allergy, renal and hepatic function, resistance to infection (may be immunocompromised), ability to tolerate drugs orally, severity of illness, ethnic origin, age, and if female are they pregnant, breast feeding or on the contraceptive pill. A rational approach to antibacterial selection for urinary tract infection in a pregnant woman suffering from nausea – organism resistant to ampicillin but sensitive to nitrofurantoin (causes nausea), gentamicin (can only be given by injection and should be avoided in pregnancy), tetracycline (causes dental discoloration), co-trimoxazole (folate antagonist, theoretical teratogenic risk) and cefalexin. Safest antibiotics in pregnancy are the penicillins and cephalosporins, cefalexin would be safest in this patient. Selection of antibacterial must allow for a number of variables including changing hepatic and renal function, increasing bacterial resistance and side effects. Duration of therapy, dosage and route of administration depend on site, type and severity of infection and response.

Following precepts should be considered before starting therapy – viral infections should not be treated with antibacterials. Samples should be taken for culture and sensitivity testing (avoid blind prescribing). Knowledge of prevalent organisms and their sensitivity is of great help. Dose varies according to age, weight, renal function and severity of infection. A dose appropriate to the condition is essential. Avoiding toxic doses with narrow margin (toxic and therapeutic) drugs (aminoglycosides) by measuring plasma levels. Route of administration depends on severity of infection – IV for life threatening situations. Duration of therapy depends on the nature of the infection and the response to treatment. Unduly prolonged courses may develop resistance or side effects. A 5 day course is usually sufficient. TB and osteomyelitis require longer periods of treatment. Conversely a single dose of an antibacterial may cure uncomplicated UTI. Superinfection is likely to be associated with broad spectrum antibiotics such as cephalosporins leading to fungal infections and antibiotic associated colitis. If an organism is cultured a change to a more appropriate
antibiotic may occur. If no organism is cultured then clinical grounds are used for decision making.

**KEY POINTS – ANTIBIOTIC THERAPY**

1. Antibiotics are antibacterial, not antiviral agents
2. Nature of infective organism and sensitivity to antibiotics before treatment, if possible
3. Broad spectrum combinations not a good substitute for tailored treatment to organism
4. Know previous treatment and hypersensitivities, hepatic and renal function
5. Route of administration and duration depend on severity of infection
6. Topical use of antibiotics should be avoided

**Penicillins**

Are bactericidal and act by interfering with bacterial wall synthesis. Diffuse well into body tissues but penetration of CSF is poor (unless meninges inflamed). Excreted in urine in therapeutic concentrations. Most important side effect is hypersensitivity – rashes and anaphylaxis. If they have suffered anaphylaxis, urticaria or rash immediately after penicillin administration then they are at increased risk of immediate hypersensitivity to penicillin. They should not receive a beta-lactam antibiotic. A minor rash, or one which develops after 72 hours after penicillin is probably not allergic to penicillin and it should not be withheld in serious infections. A rare but serious toxic effect is encephalopathy due to cerebral irritation. May be due to excessively high doses in patients with renal failure. Should not be given intrathecally. There can be accumulation of electrolyte in renal failure patients. Diarrhoea is frequent. MRSA can be resistant to flucloxacillin as well, give vancomycin or teicoplanin instead.

**Benzylpenicillin** – is inactivated by bacterial beta-lactamases. Effective in streptococcal, pneumococcal, meningococcal and gonococcal infections. Also for anthrax, diphtheria, gas-gangrene, leptospirosis and Lyme disease. It is inactivated by gastric acid and absorption is low. Phenoxymethylpenicillin is gastric stable. Beware allergy and renal impairment. Side effects – hypersensitivity, neutropenia, thrombocytopenia, convulsions, diarrhoea and colitis. IM or slow IV injection 2.4-4.8g daily in four divided doses. Meningococcal disease 2.4g every four hours IV.

**Flucloxacillin** – effective against penicillinase producing staphylococci – sole indication for use. Can be given orally and by injection. Cholestatic jaundice has been seen several weeks after stopping flucloxacillin. Administration for longer than 2 weeks and age can increase the risk. Same side effects as benzylpenicillin. Dose 250-500mg QDS at least 30 minutes before food. Similar for IM. Slow IV of 250-2000mg every six hours.

**Amoxicillin** – active against Gram negative and positive organisms. Inactivated by penicillinase. Should not be used blind in hospital acquired infection without checking sensitivity. Well excreted in bile and urine. Given orally, absorption is better than ampicillin and is not decreased if there is food in the gut (ampicillin reduced absorption). Beware allergy and renal impairment. Causes rash, especially if glandular fever. Nausea, vomiting, diarrhoea, rash. 250mg orally TDS, doubled in severe infection. IM 500mg every 8 hours. IV same as IM but up to 1g every six hours.

**Co-amoxiclav** – amoxicillin plus beta-lactamase inhibitor clavulanic acid (no significant antibacterial activity). Should be reserved for infection caused by amoxicillin resistant organisms. Same side effects as amoxicillin as well as cholestatic jaundice, erythema multiforme, vasculitis, headache, convulsions. 250mg orally TDS, doubled in severe infection. IV injection over 3-4 minutes, 1g TDS.
Co-fluampicil – mixture of equal parts of flucloxacillin and ampicillin. Use in mixed infections involving beta-lactamase producing staphylococci. Oral dose 250/250mg every 6 hours, doubled in severe infection. Same for IM and slow IV.

Piperacillin – is a ureidopenicillin broad spectrum, more active than ticarcillin against pseudomonas. Should be used with an aminoglycoside in the treatment of pseudomonas septicaemia – synergistic effect. Should NOT be mixed in the same syringe or infusion. May lead to hypernatraemia. Same side effects as benzylpenicillin. Deep IM or slow IV over 3-5 minutes 100-150mg/kg daily up to 200-300mg/kg in divided doses.

Cephalosporins
Broad spectrum antibiotics used for septicaemia, pneumonia, meningitis, biliary tract infection, peritonitis and UTI. Similar pharmacology to penicillins, excretion being mainly renal. Penetrate CSF poorly (unless inflamed meninges). Cefotaxime suitable cephalosporin for infections of CNS. 10% of penicillin sensitive patients will be sensitive to cephalosporin. Interference with clotting.

Cefotaxime – greater activity against certain Gram negative bacteria. Less active than cefuroxime against Gram positive bacteria. Can get superinfection with resistant bacteria and fungi. Beware renal impairment, false positive glucose test and Coombs test. Contraindicated in cephalosporin sensitivity and porphyria. Diarrhoea, colitis, N&V, abdominal discomfort, hepatic disturbance, blood disorders. IM or IV injection 1g every 12 hours increasing in severe infections up to 8g daily.

Cefuroxime – less susceptible to beta-lactamase inactivation. Same side effects as cefotaxime. Orally 250mg BD, doubled for severe infection. UTI 125mg BD, pyelonephritis 250mg BD. IM/IV 750mg every 6-8 hours, 1.5g in severe infections. Surgical prophylaxis 1.5g IV at induction

Cephalexin – active orally. Useful for UTI. Same side effects as cefotaxime. Orally 250mg QDS or 500mg every 8-12 hours increasing to 1-1.5g every 6-8 hours.

Aztreonam – is a monocyclic beta-lactam antibiotic with an antibacterial spectrum limited to Gram negative aerobic bacteria, not active against Gram positive and should not be used blind. Less likely to cause hypersensitivity in penicillin sensitive patients. Reduce dose in renal impairment, beware hepatic impairment. N&V, diarrhoea, cramps, mouth ulcers, jaundice, blood disorders, urticaria and rashes. Deep IM or IV injection over 3-5 minutes 1g every 8 hours or 2g every 12 hours.

KEY POINTS – CEPHALOSPORINS
1. Bacteriocidal antibiotics with wide range of activity
2. Some are less susceptible to inactivation by beta-lactamases
3. Main side effect hypersensitivity and 10% penicillin sensitive patients are also sensitive
4. Exclude such sensitivity before cephalosporin therapy

Tetracyclines
Broad spectrum antibiotic which has developed resistance. Treatment of choice for chlamydia, rickettsia, brucella and spirochaete. Respiratory mycoplasmal infection and bronchitic exacerbations. Useful in acne. Tetracyclines are deposited in growing bone and teeth causing staining and dental hypoplasia – do not use in children under 12 years or pregnant women. With the exception of doxycycline, tetracyclines exacerbate renal failure.

Tetracycline – chronic bronchitis. Beware hepatic and renal impairment. Can cause N&V, diarrhoea, oesophageal irritation, exacerbation SLE and myasthenia gravis. 250mg QDS orally, doubling in severe infection.
**Doxycycline** – brucellosis, prostatitis. May be used in renal impairment. Avoid in porphyria and exposure to sunlight. Orally 200mg first day then 100mg daily.

### KEY POINTS – TETRACYCLINES
1. Broad spectrum antibiotics, limited by bacterial resistance
2. Use in infections caused by chlamydia, rickettsia and mycoplasma
3. Tetracyclines bind with calcium and deposited in teeth, avoid children <12 and pregnancy
4. Absorption decreased by milk, food and antacids (except doxycycline, minocycline)
5. Most tetracyclines may increase renal failure if present

**Aminoglycosides**
Bacteriocidal and active against some Gram positive organisms and many Gram negative. Gentamicin and tobramycin are active against Pseudomonas aeruginosa and streptomycin is active against mycobacterium tuberculosis. They are not absorb from the gut and are excreted via the kidneys. Side effects are dose related and include ototoxicity and nephrotoxicity – mainly elderly and those in renal failure. Restrict course to 7 days. If there is renal impairment increase time between doses, then consider reducing the dose. They impair neuromuscular transmission and should be avoided in myasthenia gravis. Should not be given with ototoxic diuretics such as frusemide, if unavoidable separate administration by as long a period as possible. Serum concentrations such be monitored. Normal patients first measurement after 3 or 4 doses, renal deficiency earlier. Take sample one hour after IM/IV (peak) and just before next dose (trough). It must be measured in all patients.

**Gentamicin** – used widely in the treatment of serious infections. Broad spectrum but inactive against anaerobes and haemolytic strep. If given as blind therapy use with metronidazole or penicillin or both. Dose 5mg/kg in divided doses every 8 hours (if renal function normal). Higher doses in serious infections and immunosuppressed patients. Beware elderly and renal impairment. Prolonged use muscle weakness and risk of ototoxicity. Can also cause colitis, N&V, hypomagnesaemia and rash. IM or slow IV over 3 minutes 3-5mg/kg daily TDS. Endocarditis 80mg BD. One hour peak level should be 6-10mg/L, pre-dose should be less than 2mg/L.

**Tobramycin** – More active against pseudomonas. Can be administered by nebuliser on a cyclical basis – 28 days followed by no drug for 28 days. Give other inhaled drugs first. Peak flow before and after nebulised tobramycin. Similar side effects to gentamicin plus cough and voice alteration. IM or slow IV 3mg/kg daily TDS, severe infections 5mg/kg. UTI single IM dose of 2-3mg/kg. One hour peak level should not exceed 10mg/L, pre-dose less than 2mg/L. Nebulised – 300mg every 12 hours for 28 days, repeat after a further 28 days.

### KEY POINTS – AMINOGLYCOSIDES
1. Wide range bacteriocidal antibiotics
2. Not absorbed orally
3. Side effects dose related, treatment should not exceed seven days
4. Excreted renally, decrease dose in renal impairment, increase dose interval
5. Otoxicity, nephrotoxicity – exacerbated by some potent diuretics
6. Plasma levels should be monitored

**Macrolides**
Similar spectrum to penicillin and is an alternative in allergic patients. Active against many penicillin resistant staph but resistance is building. Useful in respiratory infections, Legionnaires, chlamydia, mycoplasmas and campylobacter. Causes N&V, diarrhoea which can be avoided with lower doses.
**Erythromycin** – caution in hepatic and renal impairment, prolongation of QT interval, porphyria. Urticaria, rash, reversible hearing loss with large doses, cholestatic jaundice and cardiac effects. 250-500mg QDS up to 4g daily in severe infections. IV infusion 50mg/kg daily every 6 hours.

**KEY POINTS – MACROLIDES**
1. Penicillin like range of activity
2. Useful in penicillin sensitive patients
3. Useful against some penicillin resistant staphylococci

**Others**

**Chloramphenicol** – potent broad spectrum but can cause serious haematological side effects when given systemically. Reserve for life threatening conditions such as typhoid. Avoid repeat courses and prolonged treatment. Reduce dose in hepatic and renal impairment. Side effects – irreversible aplastic anaemia, peripheral neuritis, optic neuritis, erythema multiforme, N&V, diarrhoea, grey syndrome (abdominal distension, cyanosis and circulatory collapse). Orally or IV – 50mg/kg in 4 divided doses, can be doubled in severe infections. Pre-dose levels should not exceed 15mg/L.

**Clindamycin** – causes colitis, especially in middle aged to elderly women post-operative. If diarrhoea starts discontinue drug immediately. Active against Gram positive cocci. Well concentrated in bone and excreted in bile and urine. Recommended for staph joint and bone infection. Caution with hepatic or renal impairment. Diarrhoea, N&V, colitis, jaundice, blood disorders. Orally 150-300mg every 6 hours, up to 450mg every 6 hours in severe infections. Deep IM or IV infusion – 0.6-2.7g daily in 2-4 divided doses. Single dose IV should not exceed 1.2g.

**Fucidin** – narrow spectrum antibiotic. Used in treatment of penicillin resistant staph infections, especially osteomyelitis. Use with another antibiotic to prevent resistance developing. Beware hepatic impairment. Can cause N&V, reversible jaundice (after high dose or rapid injection), rash, acute renal failure and blood disorders. Orally 500mg TDS, doubled for severe infection. IV 500mg TDS, less than 50kg give 6-7mg/kg TDS daily.

**Vancomycin** – bacteriocidal against aerobic and anaerobic Gram positive bacteria. Used IV against multi-resistant staph. Long duration of action, 12 hourly. Plasma levels after 3-4 doses, renal impairment sooner. Ototoxic and nephrotoxic. Not effective by mouth in serious infection – not significantly absorbed. Can be used to treat antibiotic associated colitis – orally 125mg QDS 7-10 days. When given IV avoid rapid infusion. Caution in renal impairment, elderly, history of deafness – blood counts, urinalysis, renal function tests in all patients. Blood disorders – neutropenia – after one week or cumulative dose of 25g. IV infusion 500mg over 60 minutes QDS or 1g over 200 mins every 12 hours.

**Teicoplanin** - bacteriocidal against aerobic and anaerobic Gram positive bacteria. Similar to vancomycin, but significantly longer duration of action, hence daily doses. Can be given IM or IV. Monitor auditory and renal function. N&V, diarrhoea, rash, pruritis, bronchospasm, blood disorders, abn. liver function tests, tinnitus and renal failure. IV/IM 400mg every 12hrs for three doses, then 200mg daily. Higher dose in patients over 85kg.

**Colistin** – polymixin antibiotic active against Gram negative organisms. Not absorb orally and is toxic IV. Mainly used for bowel sterilisation, but not for bowel infections. Can be nebulised. Caution in renal impairment and porphyria. Contraindicated in myasthenia gravis. Can cause perioral and peripheral paraesthesia, vertigo, muscle weakness, nephrotoxicity, bronchospasm. Orally 1.5 to 3 million units TDS. IM/IV 2 million units TDS. Inhalation 1 million units every 12 hours.
**Co-trimoxazole** – sulphamethoxazole + trimethoprim synergistic. Can cause Stevens Johnson syndrome and blood dyscrasias. Caution in renal and hepatic impairment, avoid in blood disorders (monitor blood count), discontinue if rash or blood disorder. Contraindicated in porphyria. N&V, rash, SLE, anorexia, arthralgia, liver damage, pancreatitis, renal problems. 960mg orally every 12 hours, same IV. Increase to 1.44g in severe infection.

**Trimethoprim** – for urinary and respiratory infections. Side effects less severe when used alone (without sulphamethoxazole). Orally 200mg every 12 hours, slow IV 200mg every 12 hours.

**KEY POINTS – SULPHONAMIDES**
1. High fluid intake necessary to avoid crystalluria
2. Best avoided in the elderly and patients with folate deficiency
3. Trimethoprim preferred for most infections

**Metronidazole** – high activity against anaerobic bacteria and protozoa. Used in treatment of antibiotic associated colitis (400mg orally TDS). Disulfarim-like reaction with alcohol. Beware hepatic impairment, monitor if treatment exceeds 10 days. N&V, unpleasant taste, headache, urticaria, abnormal LFT’s, aplastic anaemia. Anaerobic infection 800mg orally then 400-500mg TDS. IV 500mg every 8 hours. PR 1g every 8 hours.

**Quinolones**
Active against Gram negative and positive bacteria. Respiratory and UTI. Should be used with caution in patients with a history of epilepsy and myasthenia gravis. Avoid exposure to excessive sunlight. Taking NSAID’s at same time might predispose to convulsions. Can cause arthropathy in adolescents.

**Ciprofloxacin** – N&V, dyspepsia, convulsions, arthralgia, tendonitis, renal failure and hepatic dysfunction. Orally 250-750mg BD for respiratory, 250-500mg UTI for three days. IV 400mg over 60 minutes, 200-400mg BD

**KEY POINTS – QUINOLONES**
1. Ciprofloxacin has widest range of activity, effective against Gram +ve and –ve pathogens
2. Use with caution in epileptics – may cause convulsions
3. Action may increase if NSAID’s are also taken
4. Withdraw treatment if neurological or other disturbances occur after first dose

**Anti-malarial**
Chloroquine is used for the prophylaxis of malaria in areas of the world where the risk of chloroquine-resistant falciparum malaria is still low. It is no longer recommended as treatment because of widespread resistance.

**Chloroquine** – caution in renal impairment and pregnancy. May exacerbate psoriasis and neurological disorders. Side effects include GIT disturbance, headache, convulsions, marrow suppression, urticaria. Dose 300mg weekly.

**Anti-fungal**
Aspergillosis usually respiratory tract and treated by IV amphotericin. Candidiasis can be treated topically but deep seated infection needs IV amphotericin or fluconazole. Cryptococcus in immunocompromised patients needs IV amphotericin or fluconazole. Histoplasmosis – fulminating give amphotericin IV.

**Amphotericin** – used in systemic fungal infections. Active against most fungi and yeasts. Highly protein bound and penetrates tissues poorly. Given IV side effects common. Monitor
hepatic and renal function, blood count and electrolytes. Arrhythmias if infused rapidly. Anorexia, N&V, anaphylaxis (test dose first), low potassium and magnesium, blood disorders, neurological disorders. Orally 100-200mg QDS. IV 1mg over 15 minutes then 5mg/kg daily for at least 14 days.

**Fluconazole** – well absorb orally and good penetration into CSF. Beware renal and hepatic impairment. Nausea, diarrhoea, headache, rash, abnormal LFT’s, alopecia, pruritis. Oral 150mg single dose in thrush. Mucosal candidiasis 50mg daily for 7-14 days. IV 400mg initially then 200mg daily.

**Nystatin** – mainly for candida infections. N&V, diarrhoea, rash, oral irritation. Orally 500,000 units QDS, doubled in severe infection.

**Miconazole** – for oral infections and intestinal. Oral gel can result in systemic absorption. Beware hepatic impairment. N&V, diarrhoea and hepatitis. 5-10mls in the mouth after food every six hours.

### KEY POINTS – ANTIFUNGAL AGENTS
1. When used for oral fungal infections, remove dentures
2. Dermatophyte infection of hair, remove as much infected hair as possible
3. Combined use of azole antifungal agents and astemizole, ccisapride and terbinafine may result in cardiac arrhythmias
4. Should not be used for superficial fungal infections

**Anti-viral**
Majority of viral infections resolve spontaneously in immunocompetent subjects.

**Aciclovir** – active against herpes virus. Does not eradicate virus. Systemic treatment of chickenpox and shingles, topical treatment of herpes simplex infections (inc eye). Maintain adequate hydration, beware renal impairment. N&V, diarrhoea, fatigue, rash, urticaria, hepatitis, neurological symptoms, renal failure. 200mg five times daily orally for treatment of herpes simplex – 5 days. Herpes zoster – 800mg five times daily for 7 days. IV infusion 5mg/kg TDS for 5 days.

**Famciclovir** – pro-drug of penciclovir. Used in herpes zoster and genital herpes. Used as cream. N&V, headache, confusion, rash. 250mg TDS for 7 days in herpes zoster. Genital herpes same but 5 day course.

**Valganciclovir** – induction and maintenance treatment of CMV in AID’s patients. Pro-drug of ganciclovir. Monitor blood count. Side effects N&V, diarrhoea, leucopaenia, anaemia, GIT bleed. 900mg twice daily for 21 days; if retinitis worsens repeat 21 day course. Maintenance 900mg daily.

### KEY POINTS – ANTIVIRAL AGENTS
1. Mainly virustatic, not virucidal in action
2. Early treatment necessary
3. Some are inactivated by gastric acid and should be taken fasting or between meals
4. Some given by injection are skin irritants – avoid direct skin contact

### HIV INFECTION
The most frequently used treatment regimens include a protease inhibitor combined with two nucleoside analogue reverse transcriptase inhibitors (e.g saquinavir with zidovudine and zalcitabine). Such combinations are referred to as highly active antiretroviral therapy (HAART) and involve complex regimens that require compliance by the patient and careful assessment of the progress of viral suppression. Combination drug therapy should be started before substantial immunodeficiency is present. The goal is to suppress the virus before
resistant mutants emerge or irreversible immune damage occurs. When resistance occurs, changes in drug therapy should involve the addition or change of at least two drugs. Optimal treatment should reduce the viral load to below detectable limits. This may take six months of adequate therapy to achieve. Failure to achieve full suppression of viral load should prompt a change in therapy if compliance is believed to be good. Poor compliance is likely to encourage the development of drug resistance. Prophylaxis after accidental exposure to the virus is now recommended. The regimen depends on the level of risk: two drugs are often used for moderate risk or three drugs if the risk is high.

**TUBERCULOSIS**

TB is treated in two phases – initial phase using at least three drugs and a continuation phase using two drugs in fully sensitive cases. Initial phase reduces the bacterial population as rapidly as possible and prevents the emergence of drug-resistant bacteria. Daily use of isoniazid, rifampicin, pyrazinamide and ethambutol is the treatment of choice, preferably as a single tablet. Ethambutol can be omitted if risk of resistance to isoniazid is low. Beware immunosuppressed patients, those previously treated for TB and those who have had contact with drug resistant TB. Streptomycin can be used in resistant cases. Initial phase drugs should be continued for 2 months and then until susceptibility results are known. Continuation phase – for a further 4 months with isoniazid and rifampicin, preferably as combination drug. Rifater is a combination drug – rifampicin, isoniazid and pyrazinamide. Rifinah is rifampicin and isoniazid. Supervised treatment is isoniazid, rifampicin, pyrazinamide and ethambutol 3 times a week for 2 months followed by isoniazid and rifampicin 3 times a week for four months. Care with immunocompromised patients – resistance is common. Monitor hepatic function in all patients and check renal function before dose calculation. Isoniazid is a cheap and highly effective drug. Can cause peripheral neuropathy – if it develops gives pyridoxine 10mg daily. Rifampicin can cause disruption to LFT’s, usually transient. Six syndromes with intermittent treatment (20-30% cases) – flu like, abdominal and respiratory symptoms, shock, renal failure and thrombocytopaenic purpura. It induces liver enzymes. Pyrazinamide is bactericidal and is only useful in the first couple of months. Ethambutol if isoniazid resistance. Visual disturbance, colour blindness, decreased acuity, restriction of fields. Eyesight usually recovers on stopping the drug.

**Isoniazid** – beware renal and hepatic impairment. Slow acetylators are at risk from toxicity. Alcoholics, malnourished, HIV and diabetics a risk from neuropathy. Side effects – N&V, dry mouth, neuropathy, convulsions, psychosis, SLE like syndrome. Dose 300mg daily.


**Pyrazinamide** – beware hepatic impairment, gout and diabetes. Side effects – hepatotoxicity with fever, anorexia, hepato-spleno-megaly, jaundice, N&V and arthralgia. Dose 1.5 to 2grams daily.

**Ethambutol** – beware renal function, visual acuity. Side effects – optic neuritis, visual disturbance. Dose 15mg/kg daily.

Rifater - isoniazid, rifampicin and pyrazinamide. Under 40kgs (3 tabs daily), 40-49kgs (4 tabs daily), 50-64kgs (5 tabs daily) and over 65kgs (6 tabs daily).

Rifinah – isoniazid and rifampicin. Under 50kgs (3x150mg tabs daily), over 50kgs (2x300mg tabs daily).
IMMUNOSUPPRESSANTS
Used to suppress rejection in organ transplant recipients and to treat a variety of chronic inflammatory and autoimmune diseases. Use of these drugs may result in rapid spread of infection. Steroids may suppress the clinical signs of infection. Azathioprine is used when steroid therapy alone is providing inadequate control. It is metabolised to mercaptopurine (reduce dose if on allopurinol). Can develop myelosuppression and hepatic toxicity. If low thiopurine methyltransferase (TPMT) enzyme activity, higher risk of myelosuppression. Mycophenolate mofetil is metabolised to mycophenolic acid and is more selective than azathioprine. Prophylaxis of acute rejection in organ transplant when used with ciclosporin and corticosteroid. Risk of infection and leucopaenia are higher. Ciclosporin is a calcineurin inhibitor and is virtually free of myelotoxicity. It is nephrotoxic. Tacrolimus is also a calcineurin inhibitor but the neurotoxicity and nephrotoxicity is greater than ciclosporin. Cardiomyopathy has also been reported.

Azathioprine – monitor FBC weekly. Side effects – hypersensitivity including malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia. Dose related marrow suppression, liver impairment, cholestatic jaundice, hair loss, infections. Dose – oral, IV over one minute or IV infusion. 1-3mg/kg daily adjusted to response. For organ rejection suppression up to 5mg/kg daily then 1-4mg/kg daily according to response.

Mycophenolate mofetil – monitor FBC weekly. Beware active GIT disease. Side effects – diarrhoea, vomiting, constipation, nausea, dyspepsia, pancreatitis, abdominal pain, infection (viral, fungal), anaemia, renal damage. Dose – oral 1g twice daily within 72hrs of renal transplant or IV infusion 1g twice daily starting within 24hrs to a maximum of 14 days. Cardiac transplant – 1.5g twice daily orally within 5 days of transplant. Liver transplant – IV infusion 1g twice daily within 24hrs for 4 days (up to maxm 14 days) then by mouth 1.5g twice daily.

Ciclosporin – organ rejection suppression as well as dermatitis and psoriasis. Monitor renal function and LFT’s. Side effects – dose dependent increase in serum creatinine and urea, hair loss, headache, hypertension, GIT disturbance, rash, raised uric acid, weight gain. Dose for organ transplants 10-15mg/kg daily orally 4-12 hours prior to surgery followed by the same dose for 1-2 weeks reducing to 2-6mg/kg daily for maintenance. Adjust dose to blood ciclosporin level and renal function. Lower dose if given with steroids. One third of dose can be given by IV infusion over 2-6hrs. For bone marrow transplant – 3-5mg/kg daily by IV infusion over 2-6hrs from day before transplant to 2wks post-op or 12.5mg/kg daily orally for 3-6 months.


RHEUMATOLOGY
Certain drugs such as gold, penicillamine, hydroxychloroquine, chloroquine, drugs affecting the immune response and sulfasalazine may suppress the disease process in rheumatoid arthritis. They are sometimes known as disease-modifying antirheumatic drugs (DMARDs). They do not produce an immediate therapeutic effect but require 4 to 6 months of treatment for a full response. If no objective benefit within 6 months it should be discontinued and another drug tried. These drugs may not only improve the symptoms and signs of
inflammatory joint disease but also the extra-articular manifestations such as vasculitis. They reduce ESR, C-reactive protein and sometimes the titre of rheumatoid factor.

**Gold** – may be given IM or orally. Deep IM injection, 10mg test dose followed by 50mg weekly until evidence of remission. Benefit not expected until 300-500mg have been given. Discontinue after 1g if no remission. Once remission – injections every 4 weeks up to five years. If relapse back to weekly injection. Oral gold (auranofin) is less effective. Gold should be discontinued if blood disorder or proteinuria. Other side effects – pruritis, rash, diarrhoea, abdominal pain, nausea.

**Penicillamine** – similar action to gold. Discontinue if no improvement within a year. Takes 6-12 weeks before improvement. After 6 months remission reduce dosage to every 12 weeks. Regular blood counts, check urine for proteinuria. Nausea can be reduced by taking it with food, loss of taste can occur. Hypersensitivity to penicillin can rarely lead to problems. Dose 125-250mg daily before food for 1 month, increased by similar amounts at intervals of not less than 4 weeks to usual maintenance of 500-750mg daily in divided doses.

**Methotrexate** – initial dose of 7.5mg by mouth once a week, adjusted according to response to a maximum of 15mg once a week. Regular FBC, renal function and LFT’s. Beware pulmonary toxicity in rheumatoid patients – cough, dyspnoea, fever.

**Allopurinol** – long term control of gout. Well tolerated and useful in patients with renal impairment. Once daily, but when dose over 300mg give as divided dose. Ensure adequate fluid intake. Side effects – rash (withdraw treatment), exfoliation, fever, lymphadenopathy, GIT disorder, headache, visual and taste disturbance, neuropathy. Dose 100mg daily after food then adjust to uric acid concentration in blood, up to a maximum of 700-900mg daily.

**Probenecid** – used to prevent nephrotoxicity with cidofovir. Increases excretion of uric acid. Similar side effects. Dose 500mg daily.

**THYROID DISEASE**

**Hypothyroid**
Levothyroxine sodium is treatment of choice for maintenance therapy. The initial dose should not exceed 100mcg daily, preferably before breakfast or 25-50mcg in the elderly or those with cardiac disease. Maintenance is achieved by increasing the dose 25-50mcg every four weeks – usual range 100-200mcg daily. Liothyronine sodium similar action but metabolised rapidly and has more rapid effect. 20mcg equivalent to 100mcg levothyroxine. Effects develop in a few hours and disappear within 24-48hrs of stopping treatment. May be used in severe hypothyroid states. IV liothyronine is the treatment of choice in hypothyroid coma.

**Thyrooxine** – beware panhypopituitarism or adrenal insufficiency. Caution in elderly, cardiac disease, diabetes mellitus. Pre-therapy ECG essential. If increase in metabolism is too rapid may precipitate cardiac problems – signs diarrhoea, nervousness, tachycardia, insomnia, tremor, anginal pain, loss of weight and muscle weakness. 50-100mcg initially, 50mcg if over 50yrs, before breakfast. Increase by 50mcg every 4 weeks until maintenance. If existing cardiac disease give 25mcg daily or 50mcg alternate days.

**Liothyronine** – same cautions. Oral dose 10-20mcg daily increasing gradually to 60mcg daily in 2-3 divided doses. Elderly smaller initial dose. IV 5-20mcg every 12 hours or every 4 hours if necessary or 50mcg then 25mcg every 8 hours reducing to 25mcg BD

**KEY POINTS – THYROID DRUGS**
1. Early diagnosis and treatment are essential in cretinism
2. In hypothyroidism, maintenance doses should be taken before breakfast
3. Liothyronine is used when a rapid onset is required – IV in hypothyroid coma
Hyperthyroid
Antithyroid drugs are used to control hyperthyroidism for long term management or prepare patients for thyroidectomy. Carbimazole is commonest used drug. Bone marrow suppression may present with sore throat before decrease in white cell count – carbimazole should be stopped immediately.

Carbimazole – caution in hepatic disease. Can cause nausea, GIT disturbance, headache, arthralgia, alopecia, bone marrow suppression. Rashes and pruritis are common. Daily dose of 15-40mg until euthyroid, usually 4-8 weeks, then reduce to maintenance of 5-15mg daily (therapy for 12-18 months).

Propylthiouracil – similar cautions to carbimazole. Used if sensitivity to carbimazole. Can cause leucopaenia, cutaneous vasculitis, thrombocytopenia, aplastic anaemia. Dose 200-400mg daily.

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<thead>
<tr>
<th>KEY POINTS – THYROID INHIBITORS</th>
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<td>1. Bone marrow suppression may occur</td>
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<td>2. Withdraw treatment if any evidence of neutropenia</td>
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<tr>
<td>3. Advise patients to report sore throats or other indications of infection</td>
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<tr>
<td>4. White cell count if any evidence of infection</td>
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POSTERIOR PITUITARY HORMONES
Diabetes insipidus can be treated with desmopressin. Dosage is tailored to produce a diuresis every 24hrs to prevent water intoxication. If post-surgery diabetes insipidus – treat for limited period. It has no vasoconstrictor effect and can be given orally or intranasal. It can also be used to boost the levels of factor VIII.

Desmopressin (DVAVP) – caution in renal impairment, CVS disease and hypertension. Side effects – fluid retention, hyponatraemia, stomach ache, headache, N&V. Dose for diabetes insipidus – orally 300micrograms in 3 divided doses, maintenance 300-600micrograms in 3 divided doses daily (range 200mg to 1.2grams). Primary nocturnal enuresis – 200mcg bedtime to maxm 400mcg. Intranasal 10-40mcg daily in 2 divided doses. Primary nocturnal enuresis – 20mcg bedtime to maxm 40mcg. Injection 1-4mcgs daily

STEROID THERAPY
In comparing the relative potencies of the corticosteroids in terms of the anti-inflammatory effect (glucocorticoid effect) it should be borne in mind that high glucocorticoid effect is of no advantage unless it occurs in conjunction with relatively low mineralocorticoid activity. Equivalent glucocorticoid effects are

- Prednisolone 5mg = Betamethasone 750mcg
- Cortisone acetate 25mg = Dexamethasone 750mcg = Hydrocortisone 20mg = Methylprednisolone 4mg = Triamcinolone 4mg.

Cortisone and hydrocortisone have a higher mineralocorticoid effect resulting in more fluid retention, therefore unsuitable for long term treatment. Used for adrenal replacement therapy. Cortisone requires conversion in the liver to hydrocortisone. Hydrocortisone useful in short term emergencies and as topical cream for skin conditions – side effects less marked. Prednisolone is predominantly glucocorticoid and is the most commonly used orally. Dexamethasone has high glucocorticoid activity with insignificant mineralocorticoid activity. Suitable for high dose therapy where fluid retention would be unadvisable – cerebral oedema. Long duration of action, useful for suppression of corticotrophin secretion.

Disadvantages of corticosteroids – mineralocorticoid side effects include hypertension, sodium and water retention, potassium loss. Most marked with fludrocortisone, but significant with hydrocortisone. Glucocorticoid side effects include diabetes, osteoporosis,
vascular necrosis of the femoral head, mental disturbance (paranoia, depression), muscle wasting, peptic ulceration. High doses can cause Cushing's Syndrome – moon face, striae, acne – usually reversible on withdrawal of treatment, which must be gradual to prevent symptoms of acute adrenal insufficiency.

During prolonged treatment with corticosteroids, adrenal atrophy may develop and may persist for years after stopping. Abrupt withdrawal can lead to insufficiency presenting as hypotension or even death. Can also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss. Intercurrent infection or trauma (including surgery) may require a temporary increase in corticosteroid dose. If a patient is taking more than 10mg prednisolone daily within three months of surgery then 25-50mg hydrocortisone at induction for minor surgery; 25-50mg at induction followed by 25-50mg TDS for 24hrs in moderate and 72hrs in major surgery. There is an increased susceptibility to infection which may be severe. Septicaemia, TB, viral ocular infection, severe forms of chickenpox, measles.

Corticosteroids can be life saving in conditions such as exfoliative dermatitis, pemphigus, acute leukaemia and acute transplant rejection. Can be used in acute hypersensitivity reactions, by inhalation in asthmatics, topically for skin and ulcerative colitis (PR) and systemic connective tissue diseases. High dose (40-60mg) to start and reduce to lowest possible maintenance dose. Withdrawal should be gradual – rapidly to physiological equivalents (prednisolone 7.5mg daily) and then slowly.

**KEY POINTS – CORTICOSTEROID THERAPY**
1. Potent drugs, use lowest effective dose
2. In long term treatment, side effects may be worse than the original illness
3. In chronic conditions, withdraw treatment very slowly allowing return to normal function
4. Corticosteroids taken in the morning, reduces suppression of pituitary-adrenal function
5. All patients should carry a steroid warning card
6. Careful during surgery when measures need to be taken to prevent hypotension

**Prednisolone** – suppression of inflammatory and allergic disorders, bowel disease, asthma, rheumatic disease and immunosuppression. Caution with infection, elderly, recent MI, CCF, hepatic and renal impairment, diabetes mellitus, osteoporosis, glaucoma. Contraindicated in systemic infection. Side effects as described + cataracts, skin thinning, poor healing, thromboembolism. Initially 10-20mg daily (up to 60mg) orally in morning after breakfast. Maintenance 2.5-15mg daily, Cushingoid side effects with doses over 7.5mg.

**Dexamethasone** – used in cerebral oedema, congenital adrenal hyperplasia, N&V with chemotherapy, rheumatic disease. Orally 0.5-10mg daily, IM or slow IV 0.5-20mg. Cerebral oedema 10mg initially then 4mg IM QDS for 2-10 days. Shock IV 2-6mg/kg repeated after 2-6 hours.

**Hydrocortisone** – orally replacement therapy 20-30mg daily in divided doses. IM or slow IV 100-500mg three to four times a day.

**DIABETES MELLITUS**
Diabetes mellitus occurs because of lack of insulin or resistance to its action. Type 1 diabetes is also referred to as insulin dependent diabetes mellitus (IDDM). Usually follows autoimmune destruction of the pancreatic beta cells. Requires administration of insulin. Type 2 diabetes is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Usually treated with diet +/- oral hypoglycaemics. Treatment aimed at alleviating symptoms and minimising the risk of long term complications. It is a strong risk factor for CVS disease and use of an ACE inhibitor may be beneficial. Optimal glycaemic control
reduces long term risks of microvascular complications. A measure of total glycated (or glycosylated) haemoglobin (HbA\textsubscript{1c}) or a specific fraction (HbA\textsubscript{1c}) provides a good indication of long term control. The ideal (HbA\textsubscript{1c}) level is 7%. Control of any hypertension is important.

**Insulins**

Plays a key role in the regulation of carbohydrate, fat and protein metabolism. Insulin is inactivated by GIT enzymes and must be given by SC injection. If it is injected into a limb site and is followed by exercise of that limb, absorption will be enhanced. Insulin is needed in all patients presenting with ketoacidosis. Acute onset diabetes - start with soluble insulin TDS with a medium acting insulin at bedtime. Otherwise start with a mixture of short and medium acting insulins (30% soluble, 70% isophane) given twice daily. Increase doses carefully to avoid hypoglycaemia. Insulin requirements may be increased by infection, stress, surgery, puberty and pregnancy. Decreased requirements in renal and hepatic impairment and Addison’s disease. When prescribing the word unit should not be abbreviated. Patients are advised to maintain a blood glucose between 4 and 10mmol/L. An HbA\textsubscript{1c} concentration of less than 7% (range 4-6%) or an HbA\textsubscript{1c} of less than 8.8% (range 5-7.5%). Hypoglycaemia which becomes more frequent masks the signs of impending hypoglycaemia. Beta blockers also blunt the awareness. If converting from beef insulin to human the total dose should be reduced by 10%. Pork to human does not usually require a change. Insulin regime for patients undergoing surgery:-

- Usual insulin the night before
- 5% glucose + KCl (10mmol/L) 125ml/hr
- Soluble insulin 1 unit/ml in 0.9% Normal Saline (60 units in 60ml) and infuse separately
- Blood glucose < 4mmol/L = 0.5 units/hr; 4-15mmol/L = 2 units/hr; 15-20mmol/L = 4 units/hr
- Blood glucose > 20mmol/L = review

Shocked or severely ill patients will require 2-4 times these rates. Blood glucose should be measured hourly until stable then 2hrly. The duration of action of IV insulin is only a few minutes and the infusion must not be stopped unless the patient is hypoglycaemic (<3mmol/L).

**Short-acting**

Short duration with rapid onset of action. Soluble is given 15-30 minutes before meals. When given SC rapid onset of action (30-60mins) with a peak at between 2-4 hours and a duration of 8hrs. Human more rapid onset, but shorter duration. Given IV half-life about 5mins.

*Soluble insulin* – reduce dose in renal impairment. May get fat hypertrophy at injection site.

*Insulin Aspart, Glulisine* – recombinant human insulin analogue. Fast onset, short duration

*Insulin lispro* – faster onset and shorter duration than soluble insulin. Fasting and pre-meal glucose higher, post-meal glucose lower. Hypoglycaemia slightly less frequent.

**Intermediate and long-acting**

Onset of action at 1-2 hours, maximal effect at 4-12 hours, duration of 16-35 hours. Some are once daily and others twice daily.

*Insulin Glargine, Detemir* – human insulin analogues. Glargine daily, Detemir daily or BD

*Insulin zinc* – prolonged duration of action.

*Isophane* – suspension of insulin with protamine. Protamine can cause allergic reactions.

*Protamine zinc* – once daily. Binds with soluble if in same syringe.
**Biphasic**
Biphasic isophane – mixture of 25% lispro and 75% insulin lispro protamine. Also 50%-50% mixture available. Mixtures of soluble and isophane – 10% soluble:90% isophane; 20:80; 30:70 (Mixtard); 40:60; 50:50

**NICE Guidelines Glargine**
Option for type one diabetes. Good control (HbA1c 6.5-7.5%) reduces complications. Insulin glargine is a long acting human insulin analogue and allows a more consistent release during the day, mimicking natural basal insulin release. SC injection giving no peaks during 24 hours. Meal times would coincide with injection of another form of insulin.

**KEY POINTS – INSULINS**
1. Usually injected subcutaneously
2. Soluble insulin as a rapid action and is given 15-30 minutes before food
3. Vials of insulin suspension should be rotated and inverted, not shaken
4. Rotate injection sites

**Oral hypoglycaemics**
Only prescribe after 3 months restriction of carbohydrate diet and exercise.

**Sulphonylureas**
Augment insulin secretion in remaining pancreatic beta cells. May cause hypoglycaemia with excessive dose. Can encourage weight gain. Chose smallest dose to achieve adequate control of blood glucose. Avoid in hepatic dysfunction, renal impairment and porphyria. Omit before surgery, insulin may be required to cover the peri-operative period. Can cause GIT disturbance, jaundice, hypersensitivity.

**Glibenclamide** – associated with a greater risk of hypoglycaemia. Avoid in the elderly. 5mg daily with or immediately after breakfast.

**Gliclazide** – shorter acting and better tolerated by the elderly. 40-80mg daily up to 160mg as a single dose with breakfast.

**Tolbutamide** – shorter acting and better tolerated by the elderly and those with renal impairment. 500-1500mg daily in divided doses.

**Biguanides**
Decrease gluconeogenesis and increase peripheral utilisation of glucose. Needs to be some residual function in the pancreatic beta cells.

**Metformin** – drug of choice in obese patients. Hypoglycaemia is not a problem. GIT side effects are common. It can provoke lactic acidosis especially in renal impairment. 500mg with breakfast and evening meal for 7 days, then 500mg with breakfast, lunch and evening meal.

**Treatment hypoglycaemia**
Initially 10-20g of glucose orally. If unconscious, give glucagon if insulin induced. It mobilises glycogen from the liver. It can be given IM, IV or SC in a dose of 1mg. Alternatively 50ml of 20% glucose IV solution into a large vein.

**Glucagon** – can cause N&V, diarrhoea and lowering of potassium. 1mg IV,IM or SC.

**KEY POINTS – ORAL HYPOGLYCAEMICS**
1. Effective only when some residual beta-cell activity is present
2. Insulin therapy may be required during illness, surgery and pregnancy
3. Elderly more at risk of hypoglycaemia, particularly with long-acting sulphonylureas
Suggested treatments are shown in the boxes below – when the pathogen has been isolated treatment may be changed to a more appropriate antibacterial agent. If no bacterium is cultured, continue or stop on clinical grounds.

### GASTRO-INTESTINAL SYSTEM
Gastro-enteritis – antibacterial not usually indicated
Campylobacter enteritis – ciprofloxacin or erythromycin
Invasive salmonellosis - ciprofloxacin or trimethoprim
Shigellosis - ciprofloxacin or trimethoprim
Typhoid fever - ciprofloxacin or cefotaxime or chloramphenicol
Antibiotic associated colitis – oral metronidazole or oral vancomycin
Biliary tract infection - a cephalosporin or gentamicin
Peritonitis – a cephalosporin (or gentamicin) + metronidazole (or clindamycin)
Peritoneal dialysis assoc peritonitis – vancomycin + gentamicin in dialysis fluid
Or vancomycin in dialysis fluid + oral ciprofloxacin

### CARDIOVASCULAR SYSTEM
Endocarditis caused by streptococci – benzylpenicillin (vancomycin if allergic) + low dose gentamicin (80mg BD). Treat for 4 weeks, stop after 2 weeks if penicillin sensitive.
Endocarditis caused by enterococci – amoxicillin (vancomycin if allergic) + low dose gentamicin (80mg BD). Treat for 4 wks, if gentamicin resistant, change to streptomycin 6wks
Endocarditis caused by staphylococci – flucloxacillin (benzylpenicillin if sensitive, vancomycin if allergic) + gentamicin (or fusidic acid). Treat for 4wks, stop gent after 1wk

### RESPIRATORY SYSTEM
Epiglottitis caused by haemophilus influenzae – cefotaxime or chloramphenicol (IV)
Chronic bronchitis exacerbations – amoxicillin or tetracycline (or erythromycin)
Uncomplicated community acquired pneumonia – amoxicillin or benzylpenicillin (erythromycin if allergic). Add flucloxacillin if staph suspected
Severe community acquired pneumonia of unknown aetiology – erythromycin + cefuroxime or cefotaxime. Add flucloxacillin if staph suspected
Suspected atypical pneumonia – erythromycin (severe Legionella + rifampicin
Hospital acquired pneumonia -  broad spectrum cephalosporin or antipseudomonal penicillin

### CENTRAL NERVOUS SYSTEM
Meningitis – initial blind therapy – benzylpenicillin (cefotaxime if allergic) or chloramphenicol if cephalosporin allergy
Meningitis (meningococci) – benzylpenicillin or cefotaxime 5 days, rifampicin 2 days
Meningitis (pneumococci) – cefotaxime 10-14 days, benzylpenicillin if sensitive, if highly resistant add vancomycin or rifampicin
<table>
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<tr>
<th>Meningitis (haemophilus infl) – cefotaxime 10 days chloramphenicol if allergy or resistance. If haemophilus type b give rifampicin 4 days pre-discharge</th>
<th>Meningitis (listeria) – amoxicillin + gentamicin 10-14 days</th>
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<td><strong>URINARY TRACT</strong></td>
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<td>Acute pyelonephritis – broad spectrum cephalosporin or quinolone 14 days</td>
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<tr>
<td>Acute prostatitis – quinolone or trimethoprim 28 days. Severe inf cefuroxime+gentamicin</td>
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<tr>
<td>Lower urinary tract infection – trimethoprim or amoxicillin or nitrofurantoin or oral cephalosporin 3 days</td>
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<td><strong>BLOOD</strong></td>
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<tr>
<td>Septicaemia – initial blind therapy – community acquired – aminoglycoside + broad spectrum penicillin or broad spectrum cephalosporin alone</td>
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<tr>
<td>Hospital acquired – aminoglycoside + broad spectrum antipseudomonal penicillin or ceftazidime or meropenem alone or imipenem alone</td>
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<tr>
<td>Meningococcal septicaemia – benzylpenicillin or cefotaxime, rifampicin 2 days pre-discharge</td>
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<td><strong>OTHERS</strong></td>
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<td>Purulent conjunctivitis – chloramphenicol or gentamicin eye drops</td>
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<td>Dental infection – phenoxyethylpenicillin or amoxicillin, or erythromycin or metronidazole</td>
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<tr>
<td>Sinusitis – amoxicillin or doxycycline or erythromycin 3-10 days</td>
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<tr>
<td>Otits media – amoxicillin (erythromycin if allergic)</td>
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<tr>
<td>Otitis externa – flucloxacillin</td>
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<td>Throat infection – phenoxyethylpenicillin (erythromycin if allergic) or oral cephalosporin</td>
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<td>Cellulitis – phenoxyethylpenicillin+flucloxacillin (erythromycin if allergic) or co-amoxiclav</td>
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<td>Animal bites – co-amoxiclav</td>
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<tr>
<td><strong>ANTI-BACTERIAL PROPHYLAXIS</strong></td>
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<tr>
<td>Prevention of endocarditis in patients with heart valve lesions, septal defect, patent ductus or prosthetic valve.</td>
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<tr>
<td>Dental (no GA) – oral amoxicillin 3g one hour before procedure. If penicillin allergic or penicillin in last month give clindamycin 600mg one hour before procedure</td>
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<tr>
<td>Dental (under GA) – amoxicillin 1g at induction then 500mg six hours later; if prosthetic valve add gentamicin 120mg at induction. If allergic or penicillin in last month IV vancomycin 1g over 100 minutes then gentamicin 120mg at induction or teicoplanin 400mg IV + gentamicin 120mg at induction or IV clindamycin 300mg over 10 minutes then oral clindamycin 150mg six hours later</td>
<td></td>
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</tbody>
</table>