CHEMOTHERAPEUTIC DRUGS

(a) ***To outline the pharmacology of antimicrobial drugs.***

(b) ***To outline the interactions between antimicrobial and drugs used peri-operatively.***

> "Anti-microbial agents" → drug that kills or suppresses growth of a microorganism
>
> "Antibiotic" → chemical substance produced by microorganism that can kill or inhibit growth of another microorganism

(I) β-Lactam Agents:

- (1) Penicillins:
  - *Overview* – Contain "6-aminopenicillanic acid" nucleus → consists of (i) β-lactam ring and (ii) Triazolidine ring
  - *Types:*
    - (i) Narrow-spectrum (Eg. benzylpenicillin)
    - (ii) Narrow-spectrum resistant to staphylococcal β-lactamase (Eg. flucloxacillin)
    - (iii) Extended-spectrum (Eg. ampicillin, amoxycillin)
    - (iv) Anti-pseudomonal (Eg. piperacillin, ticarcillin + clavulinic acid)
  - *Mechanism* – Bactericidal → β-lactam ring inhibits bacterial cell wall synthesis (↓ peptidoglycan cross-linkage 2° to inhibition of transpeptidases/carboxypeptidases) → cell lysis due to weakened cell wall

    > Important to note – β-lactamase (encoded by bacterial chromosomes/plasmids) hydrolyse β-lactam ring and foster "resistance" → this can be minimised by combining penicillin with "Clavulinic acid" (irreversibly inhibits β-lactamase)

  - *Pharmacokinetics* – Absorbed via various routes (PO, IM, IV); good tissue penetration (incl BBB and bone); excreted renally by tubular secretion (Nb. Probenecid inhibits renal tubular secretion and ↑ plasma levels → but also inhibits CSF excretion and causes CNS toxicity!)
  - *Side-effects/Issues* – (i) Hypersensitivity reactions (10% of pop'n → 0.01% anaphylaxis) → cross-sensitivity exists b/t β-lactam agents in 10% of allergic pts, (ii) CNS toxicity (encephalopathy and convulsions) → esp with benzylpenicillin, (iii) GI effects(diarrhoea, N/V, pseudomembranous colitis), (iv) Cholestatic jaundice → esp flucloxacillin, (v) Skin rash (esp with concurrent infectious mononucleosis), (vi) BM suppression
- (2) Cephalosporins:
  - *Overview* – Similar penicillin nucleus → except thiazolidine ring replaced by 6-membered hydrothiazine ring
  - *Types* – 3 generations exist → each has Gram +ve cover, but ↑ Gram –ve cover with each generation:
    - (i) 1st generation (Eg. cephazolin)
    - (ii) 2nd generation (Eg. cefuroxime)
    - (iii) 3rd generation (Eg. ceftriaxone))
  - *Mechanism* – Similar to penicillin BUT β-lactam ring more resistant to β-lactamase
  - *Pharmacokinetics* – Given PO or IV; widely distributed (incl CSF, placenta, inflamed tissues); some are metabolised while others are excreted renally
  - *Side-effects/Issues* – (i) Hypersensitivity reactions (similar to penicillins), (ii) liver dysfunction
- (3) Carbapenams:
  - *Types* – Imipenum and Meropenum → broadest spectrum coverage (Gram +ve and Gram –ve; aerobics and anaerobics), but does not cover MRSA or E. faecalis
  - *Mechanism* – Similar to penicillins
  - *Pharmacokinetics* – Imipenum is metabolised by Dehydropeptidase I (given with "cilastatin" to prevent extensive metabolism); Meropenum is entirely excreted renally

- *Side-effects/Issues* – Well-tolerated, but can cause (i) GI upset (N/V, diarrhoea), (ii) allergic reactions, (iii) seizures (esp if underlying CNS disorder), and (iv) +ve Coombs test

(II) Aminoglycosides (Eg. gentamicin)
- *Overview* – Used to treat Gram –ve (and some Gram +ve) bacterial infections
- *Mechanism* – Bactericidal → irreversibly binds to bacterial 30S ribosomal RNA subunit → (i) blocks initiation of peptide bonds and translocation of protein (Ie. inhibits protein synthesis, (ii) causes mRNA to be misread (Ie. produce non-functional proteins)

> Important to note – Aminoglycosides are large polar molecules → taken up by an active O_2-dependent polyamine carrier (this transporter is inhibited by (i) hypoxia, (ii) acidosis and (iii) divalent cations (Ca^{2+}/Mg^{2+}))

- *Pharmacokinetics* – Given IV only; poor lipid solubility with low protein-binding (20%) and distributed in ECF (poor IC and CSF penetration); 100% renally excreted
- *Side-effects/Issues*:
  - (i) Narrow therapeutic index → need to check blood levels pre-dose to adjust dose to ensure therapeutic efficacy but minimise toxicity
  - (ii) Ototoxicity → due to accumulation of drug in inner ear perilymph. This is permanent and related to peak plasma [ ]. ↑ risk with use of other ototoxic drugs
  - (iii) Nephrotoxicity → due to accumulation in renal cortex (causing ATN). This is reversible and related to peak plasma [ ]. ↑ risk with frusemide use and preexisting renal failure
  - (iv) Muscle weakness (and potentiates ND NMDR blockade) → due to ↓ prejunctional ACh release and ↓ post-junctional nAChR sensitivity

(III) Glycopeptides (Eg. vancomycin)
- *Overview* – Used to treat Gram +ve bacteria (MSSA and MRSA), coagulase –ve staphylococcus, and Gram +ve anaerobes (Clostridia) → minimal Gram -ve activity as it cannot penetrate outer lipid layer of bacteria
- *Mechanism* – Bactericidal → inhibit glycopeptide synthetase, thus preventing peptidoglycan formation in bacterial cell wall → cell lysis due to weakened cell wall
- *Pharmacokinetics* – Given PO or IV; variable protein-binding (10-80%) and distributes to serous fluids well (but poorly into CSF/bone); 90% renal excretion
- *Side-effects/Issues*:
  - (i) Narrow therapeutic index → need to check blood levels pre-dose to adjust dose to ensure therapeutic efficacy but minimise toxicity
  - (ii) Histamine release (esp if too rapid IVI > 10 mg/min) → causes hypotension, tachycardia and rash ("Red man syndrome")
  - (iii) Nephrotoxicity → rare and reversible; ↑ risk with concurrent use of aminoglycosides or underlying renal dysfunction
  - (iv) Ototoxicity → very rare; ↑ risk with preexisting hearing loss or use of other ototoxic agent
  - (v) Phlebitis → thus, needs to be diluted if given peripherally
  - (vi) Haematological effects (esp neutropaenia and thrombocytopaenia) → rare and reversible

(IV) Nitroimidazoles (Eg. metronidazole)
- *Overview* – Used to treat obligate anaerobes, protozoa, clostridia, bacteroides, campylobacter
- *Mechanism* – Bactericidal → Nitro-group reduced (and charged) in anaerobic conditions causing it to be trapped within anaerobe → causes bacterial DNA strand breakage and cell death
- *Pharmacokinetics* – Given PO or IV; widely distributed (abscess, CSF, serous fluids); metabolised to an active metabolite, then excreted in urine
- *Side-effects/Issues* – Well-tolerated (mainly causes N/V and metallic taste) → rarely causes rash, peripheral neuropathy, pancreatitis. Can cause "disulfuram-like reaction" (Ie. flushing, hypotension, dysphoria) when combined with EtOH

(V) Macrolides (Eg. erythromycin, azithromycin)

- *Overview* – Used to treat Gram +ve organisms, Gram +ve/-ve anaerobes, Neisseria, Haemophilius, Mycoplasma and Legionella
- *Mechanism* – Bactericidal or bacteriostatic (depending on plasma [ ]) → inhibits bacterial protein synthesis by binding to 50S ribosomal subunit → inhibits protein translocation
- *Pharmacokinetics* – Given PO or IV; penetrates lung/sputum well (but not CSF); hepatic metabolism (CYP3A4) and excreted renally unchanged
- *Side-effects/Issues:*
    - (i) Several drug interactions (as it is metabolised by CYP3A4) → esp inhibits metabolism of warfarin, digoxin, theophylline GI → ↑ drug levels
    - (ii) Trigger of acute porphyria
    - (iii) Prolongs QTc → torsades de Pointes
    - (iv) GI effects → N/V, diarrhoea, reversible hepatic dysfunction

(VI) Quinolones (Eg. ciprofloxacin, norfloxacin)

- *Overview* – Wide Gram –ve spectrum (and some Gram +ve cover also), Legionella, Mycoplasma, Chlamydia, Rickettsia
- *Mechanism* – Bactericidal → inhibits DNA-gyrase and prevents -ve supercoiling of bacterial DNA → causes cell death
- *Pharmacokinetics* – Given PO or IV; widely distributed (incl CSF and tissues); excreted via urine/faeces (minimal metabolism)
- *Side-effects/Issues* – CNS effects (esp confusion and seizures (esp epileptic pts)), GI effects (N/V, abdominal pain, hepatic dysfunction), allergic reactions, G6PDH deficiency causes haemolytic anaemia

(VII) Lincosamides (Eg. lincomycin, clindamycin)

- *Overview* – Used against Gram +ve aerobes mainly, but also anaerobes, MRSA, Toxoplasma and P. falciparum
- *Mechanism* – Bacteriostatic → inhibits bacterial protein synthesis by disrupting 50S ribosomal subunit
- *Pharmacokinetics* – Given PO or IV; widely distributed (esp bones/joints) but poor CSF penetration; metabolised to active metabolites with some excreted in urine
- *Side-effects/Issues* – Well-tolerated , but can cause GI upset (incl pseudomembranous colitis), fevers, rash, haematological issues (esp transient ↓ platelets and neutrophils)

(VIII) Sulphamide/Trimethoprim:

- *Overview* – Commonly combined to treat Gram +ve/-ve bacterial infections
- *Mechanism* – Bacteriostatic → competitive and reversible inhibition of dihydropteroate synthase (sulphonamide) and dihydrofolate reductase (trimethoprim) → ↓ bacterial folate synthesis and ↓ DNA synthesis
- *Side-effects/Issues* – Allergic reactions (incl anaphylaxis), haemolytic anaemia (esp those with G6PDH deficiency), and urinary tract obstruction (ppt in renal tubules)

(IX) Tetracycline

- *Overview* – Used to treat Mycoplasma, Chlamydia, rickettsial, Lyme disease
- *Mechanism* – Bacteriostatic → reversible binding to bacterial 30S ribosome → blocks t-RNA binding to it, thus preventing addition of a.a. to peptide chain
- *Side-effects/Issues* – (i) Impairs bone growth and discolours teeth, (ii) Crosses placenta and breast milk (can impair bone growth and discolour teeth of neonate also), (iii) Forms insoluble complex with divalent cations (Ca^{2+} in antacids/milk)

(c) ***To explain the principles of antibiotic prophylaxis.***

Decision of antibiotic prophylaxis depends on a risk-benefit evaluation:

- (i) Risk of infection from indigenous flora in tissue planes penetrated during surgery → depends on nature of operative procedure
- (ii) Risks of antibiotics → drug toxicity (Eg. anaphylaxis), superinfections (Eg. pseudomembranous colitis), selection of resistant bacteria, cost

> Important to note → surgical procedures that benefit from antibiotic prophylaxis:
> - (i) O&G – LSCS, hysterectomy
> - (ii) Orthopaedic – Joint arthroplasty/replacements, ORIFs
> - (iii) General surgery – Cholecystectomy, appendectomy, colonic surgery, Etc.
> - (iv) Urological surgery
> - (v) ENT/head/neck surgery
> - (vi) Cardiothoracic and vascular surgery
> - (vii) Neurosurgery

Antibiotic should be delivered to the site of probable infection at an appropriate time (and for a limited time) → generally given as a single dose via IV route no more than > 2 hrs pre-surgical incision, (with the infusion completed before induction of anaesthesia) +/- repeated doses for up to 48 hrs post-procedure

Types of antibiotics used:

- (i) 1st generation cephalosporins (cephazolin) is the 1st line agent used in which normal skin, GI or GU flora are most likely pathogens → provides broad antimicrobial spectrum with minimal allergic risk and cost
- (ii) Metronidazole is appropriate when anaerobes are likely pathogens (Ie. colorectal procedures)
- (iii) Vancomycin or lincomycin can be used for resistant-bacteria or patients allergic to penicillins

(d) ***To outline the pharmacology of antiseptics and disinfectants.***

"Antispetic" → agent applied topically to living tissues to kill or prevent growth of microorganisms

(1) Alcohols (Eg. ethyl alcohol, isopropyl alcohol)
- *Mechanism* – Bactericidal only (NOT fungicidal or virucidal) → ↑ effect with prior mechanical cleansing with H_2O/detergent
- *Clinical uses* – Used to prep skin for needle puncture or surgical skin prep → Ethyl alcohol (70%) can kill 90% of cutaneous bacteria in 2 mins, while isopropyl alcohol has ↑ bactericidal activity
- *Side-effects/Issues* – (i) Flammable in presence of heat source, until all liquid evaporated, and (ii) Corneal toxicity if contacts eyes

(2) Chlorhexidine
- *Mechanism* – Bactericidal activity (both Gram +ve and –ve) by disrupting bacterial cell membranes
- *Clinical uses* – 2% chlorhexidine is used as hand wash, surgical scrub, surgical skin prep and to treat wounds → rapid antibacterial action that persists over time due to residual adherence to skin

> Important to note:
> - Initial bactericidal effect of chlorhexidine is more effective cf. povidine-iodine or hexachlorophene, while persistent bactericidal action is the same or greater cf. hexachlorophene
> - Chlorhexidine is superior to povidine-iodine for surgical skin prep and prevention of CVC-related line sepsis

- *Side-effects/Issues* – (i) ↓ incidence of contact sensitivity and photosensitivity, (ii) poor absorbed through skin (even with repeated use), (iii) Corneal toxicity if contacts eyes, (iv) Deafness if enters middle ear

(3) Iodine compounds (Eg. iodine, povidine-iodine)
- *Mechanism*:
  - Iodine has bactericidal, virucidal and sporicidal activities → efficacy ↓ in presence of organic material (as iodine binds covalently to it)
  - "Iodophor" (Eg. povidine-iodine) → loose complex of elemental iodine with organic carrier (Eg. polyvinylpyrrolidone) that ↑ solubility of iodine and also forms a reservoir for sustained iodine release
- *Clinical uses*:
  - 1% and 5% iodine used for surgical skin prep or to treat wounds → rapid effect and most effective antiseptic with 90% cutaneous bacterial killed in 60-90 secs
  - 10% povidine-iodine (has 1% iodine only) is used as hand-wash, surgical scrub, surgical skin prep, skin prep for needle puncture and to treat wounds → kills 90% of cutaneous bacteria
- *Side-effect/Issues* – (i) Skin staining and allergic reactions (skin eruptions, fever) → esp if ↑ [ ] used (> 7%), (ii) Lowest risk of corneal toxicity with povidine-iodine (cf. other antiseptics)

(4) Quaternary ammonium compounds (Eg. Benzalkonium)
- Mechanism – Bactericidal (both Gram +ve and –ve), funcidal and virucidal activities
- Clinical uses – Used a surgical skin prep or sterilisation of instruments → rapid onset of action but less effective cf. other commonly used antiseptics

(5) Hexachlorophene:
- *Mechanism* – Bacteriostatic against Gram +ve organisms only

- *Clinical uses* – 3% hexachlorophene is used for hand cleaning and surgical skin prep → ↓ cutaneous bacterial count by 50% initially (cf. > 90% with iodine) BUT by 96% after 1 minute (cf. 84% with iodine)
- *Side-effect/Issues* – (i) Absorbed through skin → neurotoxicity, (ii) Corneal toxicity if contacts eyes

"Disinfectant" → agent applied topically to an inanimate object to destroy pathogenic microorganisms, thus preventing transmission of infections

(1) Aldehydes (Eg. formaldehyde, glutaraldehyde)
- Kills bacteria, fungi and viruses by precipitating protein in inanimate objects
- Glutaraldehyde is superior cf. formaldehyde → b/c more rapid effect (Ie. 10 hrs to kill dried spores vs 2-4 days) and less volatile (Ie. ↓ odour/fumes)

(2) Phenolic compound cresol → kills common pathogens (including M. tuberculosis) BUT can cause burns if tissue contact

(3) Elemental chlorine

(e) ***To outline the pharmacology of antiviral agents.***

(I) Inhibitors of viral genome transcription
- (1) DNA polymerase inhibitors (Eg. acyclovir)
    - *Clinical uses* – Treat HSV I/II and VZV
    - *Mechanism* – Acyclovir is converted to a monophosphate by viral thymidine kinase, and then to an active triphosphate by host cell kinases → triphosphate acyclovir competes with deoxy-GTP for viral DNA polymerase (30x ↑ affinity cf. host DNA polymerase) → incorporation of triphosphate in viral DNA causes chain termination → blocks viral genome transcription
    - *Pharmacokinetics* – Poor GI absorption 2° to ↓ bioavailability; widely distributed 2° to ↓ protein binding; mainly excreted renally, but partly metabolised into inactive compounds
    - *Side-effects/Issues* – Renal impairment, thromboplebitis, CNS effects (esp tremors, confusion, seizures, coma)
- (2) Reverse transcriptase inhibitors (Eg. zidovudine, lamivudine)
    - *Clinical uses* – Treat HIV
    - *Mechanism of action* – Drug is converted to an active triphosphate by host cell kinases → this then competitively inhibits HIV reverse transcriptase to cause provirus DNA chain termination → blocks viral genome transcription
    - *Pharmacokinetics* – Given PO or IV; widely distributed (incl CSF); hepatic metabolism and renal excretion
    - *Side-effects/Issues* – Haematological effects (anaemia, neutropaenia), GI effects (anorexia, GI upset, deranged LFTs, steatorrhoea), myalgias, headaches

(II) Protease inhibitors (Eg. saquinavir)
- *Clinical uses* – Treat HIV
- *Mechanism* – Viral structural proteins/enzymes are synthesised as polyproteins that require cleavage by viral protease → these drugs inhibit viral proteases, thus impairing production of mature virus
- *Pharmacokinetics* – Given PO → hepatic metabolism by CYP3A4
- *Side-effects/Issues* – Several drug interactions due to inhibition of CYP3A4 → ↑ drug levels

(III) Inhibition of viral attachment/penetration (Eg. amantadine)
- *Clinical uses* – Treat influenza
- *Mechanism* – Inhibits viral membrane protein M2 → ↓ fusion of viral membrane with endosome membrane, ↓ release into cytoplasm, and ↓ assembly/release of new virus

(IV) Immunomodulators (Eg. interferons)
- *Clinical uses* – Treat HCV
- *Mechanism* – Induce host cell enzymes that inhibit translation of viral mRNA into viral protein

(f) ***To outline the pharmacology of antifungal agents.***

(I) Amphotericin B:

- *Clinical uses* – Wide-spectrum antifungal used to treat serious systemic fungal infections (incl aspergillus, candida, cryptococcus)
- *Mechanism* – Reacts with ergosterol in fungal cell membrane → creates pores and cell damage
- *Pharmacokinetics* – Given IV; ↑ protein-binding with poor tissue penetration (esp CSF and urine); undergoes hepatic metabolism; liposomal rep (allow HD with less renal toxicity)
- *Side-effects/Issues* – 1°ly renal impairment (reversible if ceased early), blood dyscrasia, deranged LFTs, anaphylaxis, GI upset, seizures, febrile reactions, myalgias, visual/hearing disturbances

(II) Azoles:

- *Types* – (i) Triazoles (Eg. fluconazole) and (ii) Imidazoles (Eg. ketoconazole)
- *Clinical uses* – Treats wide range of fungi and yeast infections (incl candida and cryptococcus)
- *Mechanism* – Disrupt ergosterol synthesis → ↓ fungal membrane function and cell death
- *Pharmacokinetics* – Given PO and IV; variable protein-binding and CSF penetration; undergoes hepatic metabolism and biliary excretion
- *Side-effects/Issues* – Adrenal insufficiency (as it inhibits steroid synthesis), cardiac arrhythmias (esp rapid IVI), thrombophlebitis, GI upset, hepatitis (rare), several drug interactions (Ie. inhibits metabolism of warfarin, cisapride, Etc.)

(g) ***To outline the pharmacology of cancer chemotherapeutic agents with particular reference to problems in the peri-operative period.***

(I) Tumour antibiotics:

- (i) Bleomycin
  - Used to treat advanced germ cell tumours
  - Adverse effects → interstitial pneumonitis, myelosuppression, alopecia and N/V

> Important to note → "Bleomycin-induced pneumonitis"
> - Hypersensitivity-like syndrome (fever, tachyponea, pleuritic chest pains, ↓ DLCO)
> - Risk factors:
>   - (i) Prolonged O_2 exposure ($FiO_2 > 0.3$), esp in pts with bleomycin exposure in last 1-2 months or preexisting bleomycin-lung injury
>   - (ii) ↑ total cumulative dose
>   - (iii) IV bleomycin (cf. IM)
>   - (iv) Prior lung radiation
>   - (v) Advanced age
>   - (vi) Renal impairment
> - Mechanism of injury unknown → "idiosyncratic"
> - Treated with high-dose steroids → fatalities are rare

- (ii) Mitomycin C/Actinomycin D → adverse effects include myelosuppression, TCP, pulmonary fibrosis

(II) Anthracyclines:

- Examples – Doxorubicin, daunorubicin, epirubicin, mitoxantrone
- Mechanism – Topoisomerase II dependent DNA cleavage and subsequent intercalation with dsDNA
- Adverse effects → myelosuppression, cardiotoxicity (denoted by various ECG changes) and dose-dependent cardiomyopathy with chronic use

> Important to note → Risk factors for cardiomyopathy include:
> - (i) ↑ cumulative dose
> - (ii) Prior or current mediastinal radiotherapy
> - (iii) Preexisting heart disease
> - (iv) Concurrent cyclophosphamide or mitomycin use
> - (v) Extreme age

> Important to note → Despite normal resting LV function, past exposure to anthracycliens can enhance myocardial depressive effects of GA agents!

(III) Alkylating agents:

- (i) Cyclophosphamide
  - Mechanism – Alkylate DNA and interfere with mitosis
  - Adverse effects → Tumour-lysis syndrome (↑ K^+, ↑ PO_4^{3-}, ↓ Ca^{2+}, uric acid nephropathy), interstitial pneumonitis (esp with concurrent bleomycin use), haemorrhagic cystitis (↓ with MESNA) and ADH-like renal effects

> Important to note → Cyclophosphaamide inhibit PC activity → prolong effects of SCh, mivacurium and ester LAs

- (ii) Metal salts (Eg. cis-platin, carboplatin)
  - Mechanism – Intra-strand and inter-strand cross linkage of DNA → impairs mitosis
  - Adverse effects – Nephrotoxicity, myelosuppression, ototoxicity and peripheral neuropathy
- (iii) Busulphan, chlorambulin, melphalan → can cause interstitial pneumonitis (esp with chest radiotherapy)

- (iv) Nitrosurea (Eg. carmustine) → can cause myelosuppression, interstitial pneumonitis (esp with ↑ cumulative doses, smokers, concurrent chest radiotherapy or cyclophosphamide use)

(IV) Antimetabolites:
- Mechanism – Similar structures to metabolites involved in nuclei acid synthesis → critical enzyme inhibition or incorporation of wrong DNA code during cell synthesis
- Types:
    - (i) Folic acid (Eg. MTX) → causes renal impairment, hepatic impairment, and interstitial pneumonitis

> Important to note → N_2O potentiates MTX-toxicity!

    - (ii) Pyrimidine and purine analogues (Eg. 5-FU) → causes mucositis, hand-foot syndrome, myelosuppression, GI disturbances

(V) Mitotic agents:
- (i) Mitotic inhibitors (Eg. vincristine/vinblastine)
    - Mechanism – Inhibit formation of microtubule complexes within cytoplasm → arrest cell growth in metaphase
    - Adverse effects → peripheral neuropathy, myelosuppression, ADH release, constipation
- (ii) Mitotic stabilisers (Eg. paclitaxel, docetaxel)
    - Mechanism – Stabilise microtubule assembly when formed → prevents mitosis form proceeding
    - Adverse effects → peripheral neuropathy, myelosuppression, hypersentivity-reactions

(VI) Topoisomerase inhibitors:
- Types – (i) Topo II inhibitors (Eg. etoposide) and (ii) Topo I inhibitors (Eg. irinotecan)
- Mechanism – Inhibit unwinding of DNA during replication
- Adverse effects – Myelosuppression, GI disturbance (N/V, diarrhoea, anorexia)

(VII) Hormonal agents:
- (i) Corticosteroids
- (ii) LHRH analogues → cause mood/personality/cognitive changes and fatigue
- (iii) Tamoxifen → causes vascular thromboembolic events
- (iv) Aromatase inhibitors → well tolerated but issues with osteoporosis

(VIII) Antibody therapy:
- (i) Trastuzumab (Herceptin) – Ab against HER2 receptor (used in breast Ca) → minimal adverse effects, except cardiomyopathy esp with anthracyclines
- (ii) Retiuximab – Used in NHL → well- tolerated but causes flu-like symptoms
- (iii) Bevacizumab – Used in colorectal Ca → issues with major GI and pulmonary bleeding

(IX) Tyrosine kinase inhibitors:
- Imatinib → used to treat CML
- Mechanism – Inhibit errant constitutive TK receptor activation which promotes cell survival and proliferation
- Adverse effects – Skin rash, GI disturbances, myelosuppression, hepatic dysfunction, skin rash