3012NSC Infectious Disease

complete summary 2019

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Highlighted text indicates content **VERY USEFUL** for the exams.

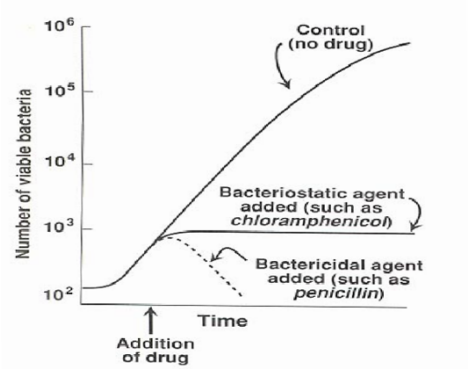
Module 2A – Parasites I

- DALY = YLL + YLD → measure of disease burden in a population
- Infection vs disease – why measure infection? → reservoir size, epidemic risk
- Reservoir vs Source vs Vector
- Elimination (local) vs Eradication (global) – @ incidence = 0
- **Protozoa:** unicellular eukaryotes
- **Malaria:**
    - **Transmission:** female anopheles mosquito vector
    - **Organism:** *Plasmodium spp.*
        - *P. falciparum* (Sub-Saharn Africa) – most severe, due to **clonal antigenic variation of the *Pf*EMP1 cytoadhesion protein** (encoded by ~60 copies of *var* gene) → cause circulatory thrombosis (autoagglutination, rosetting) + cytoadhesion (**avoid spleen**)
        - *P. vivax* (Asia) & *P. ovale* – hypozoite stages can become dormant in the liver → relapsing malaria
        - *P. knowlesi* – zoonotic from macaques
    - **Tropisms:** hepatocytes (asymptomatic stage), erythrocytes (symptomatic stage)
        - **CM (young children):** high risk due to immune naivety, and waning maternal passive IgG immunity from breastmilk → neurological symptoms, coma, death
        - **PAM (pregnant women):** Novel placental antigen (**chondroitin sulphate A**) able to be adhered to by *P. falciparum*'s *Pf*EMP1 → cause malaria even in mothers who have survived it previously
    - **Diagnosis:**
        - **Light microscopy** – training
        - **RDTs** – stability, storage
        - **PCR** – expertise, electricity
    - **Immunity:**
        - Partial acquired immunity follows repeat infection
        - *P. falciparum* – heterozygote sickle-cell anaemia carriers
        - *P. vivax* – Duffy -ve blood group – explains why *P. vivax* isn't found in Africa
    - **Vaccine: Mosquirix** (40% effective) – *P.falciparum* protein conjugated to HBV antigen – not long-lasting, given to travellers mostly
    - **Treatment:**
        - **Prevention in pregnant women, control mosquito reservoir**
        - **Gold-standard: ACTs** – Artemisinin + Piperaquine *(resistance is building)*
    - **At most risk:**
        - Children from 3months → 5yrs (naivety + waning maternal passive IgG)
        - Travellers (naivety)
        - Pregnant women (even those who have fought it off before)

ANTIMICROBIALS

- **Antimicrobial agent:** chemical, chemotherapeutic agent (CTA) or medicine which targets pathogenic microorganisms while causing minimal damage to host tissues (**selective toxicity**)
- **Prophylaxis:** preventative administration of a CTA to control infection/disease severity of progression early on

- **Pharmacokinetics (PK):** the study of the time course of drug absorption, distribution, metabolism and excretion. "What the body does to the drug".
- **Pharmacodynamics (PD):** the relationship between drug concentration at the site of action, and the resulting physiological effect (time course, intensity, adverse effects). "What the drug does to the body/target".
- **The perfect antimicrobial:**
  - High selective toxicity
  - Minimal side-effects
  - Low (potential for) microbial resistance
  - Generally fast, long-$t_{1/2}$, readily available (easily complied with)
  - Inexpensive
  - Long shelf-life (stability)
  - **Cidal** over static activity

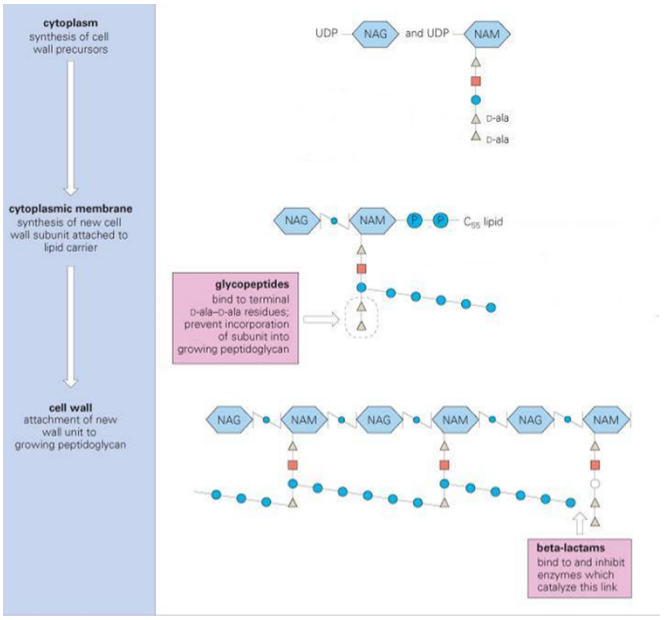


- **Bactericidal:** kills the susceptible microbe (e.g. **penicillin**)
  - Key @ dangerous infections: **meningitis, endocarditis** (host defences ineffective @ these sites)
- **Bacteriostatic:** inhibits growth of the susceptible microbe, which is then able to be removed by immune system
  - Therapy duration needs to be long enough to allow for full eradication

ANTIBACTERIAL AGENTS

BACTERIAL CELL WALL SYNTHESIS INHIBITORS

*Binds **PBP** (transpeptidase enzyme)*
*→ Autolysin also involved – stimulated by **β-Lactam binding***



β-Lactam antibiotics (contain β-Lactam ring):

- Penicillins
  - Natural: **Penicillins G** and **V** (**V** is acid stable)
  - Semi-synthetic: **ampicillin**, **amoxicillin**
  - Most GRAM– aren't susceptible
  - **Bactericidal** (cell lyses)
  - **Resistance:** β-Lactamase, transpeptidase mutations
- Cephalosporins
  - More active against GRAM–
  - More resistant to β-Lactamase
  - Semisynthetic (2, 3, 4 generations)
  - Some have good CNS penetration (for GRAM– meningitis)
  - **Resistance:** β-Lactamase, transpeptidase mutations, GRAM– permeability issues
- Carbapenems
  - Fully synthetic β-Lactams
  - **Imipenem** has severe neuro side-effects, **meropenem → drug of choice for** melioidosis
  - Parenteral admin only – hospital-only
  - **Resistance:** increasing concern @ METALLO-β-Lactamase development
- Monobactams – not widely used