ANTIMICROBIALS

Microrganism classification

Prions lack nucleic acids and appear to only have protenaecius infectious particles

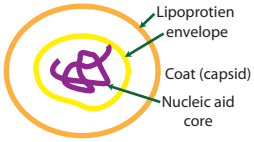
Viruses lack the cell membranes, cytoplasm, and machinery for synthesizing macromolecules

Prokaryotes are the **bacteria** (and archaea) which have ribsomes and a cell wall but not a membrane bound nucleus

Eukaryotes are the remainder of all organisms characterised by a membrane bound nucleus. Including; **fungi, protozoa** and **helminths** up to **mammals**

Prions are small protienaceous particles, thought to be modified forms of a normal cellular protien, and cause disease by converting normal protien into further abnormal forms. There are characterised by their small size (<100nm, therefore filterable), lack of nucleic acid genome, extreme resistance to heat, disinfectnats and irradiation (but susceptible to high concentrations of phenol, periodate, sodium hydroxide and sodium hypochlorite), slow replication with indubation periods of up to 35 yrs, their inability to be cultured, and the fact that they do not elict known inflammatory or immune responses. Prion diseases are difficult to diagnos and are untreatable at present.

Viruses differ from all other infectious organisms in their structure and biology, particularly their reproduction. Although they carry conventional genetic material in the form of single or double stranded DNA or RNA, they lack to cellular machinery to process new virus material and therefore are dependent on the cells of the host for reproduction. They range in size from very small such as the polio virus at 30nm to the large such as vaccinia at 400nm. The difference between viruses in terms of their outer surface has important survival and virulence consequences. Encapulated viruses are less tolerant ot environental factors such as drying, and survival in gastric acid when compared to viruses without an external surface. Following infection with a virus the result may be cell lysis, persistant infection or latent infection. Viruses are classified by whether their nucleic acid in the genome (DNA or RNA), number of nucleic acid strands (single or double), mode of replication, and the size, structure and symmetry of the virus particle.



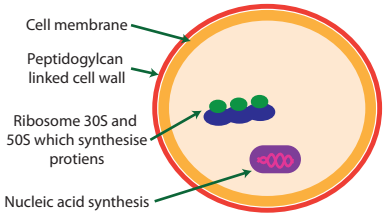
1 Prevent penetration
amantidine
2 Inhibit nucleic acid production
NNRTIs, NRTIs, Acyclovir
3 Inhibit protien synthesis
Protease inhibitors
4 Prevent viral release
osteltamivir
5 Modify immune response
immunoglobulins, interferon, MAbs

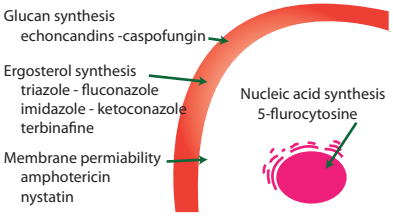
Antiviral medications are classified by their spectrum of activity and they mechanism of action. It is the later which is the most common method of classification. The mechanism of action is conceptulaised with relation to the process of viral invasion, survival and replication within the host cell. Amantidine prevents penetration of the virus into the cell and is used in the treatment of influenza. Acyclovir and ganacyclovir inhibit viral DNA synthesis. Nucleoside reverse transcriptase inhibitors such as zidovudine act as a substrate during reverse transcriptase and subsequent terminate DNA chain formation. Non nucleoside reverse transcriptase inhibitors such as nerviapine bind to the reverse transcriptase near the catalytic site and denature it. Protease inhibitors such as ritonovir stop the synthesis of new protiens. Finallly neuroaminidase inibitors such as osteltamivir block the release of virus for infected cells and is used in the treatment of influenza. The last main type of antivirals are the immunological medications such as immunoglobulin and interferon which modulate immune responses and the monoclonal antibodies which attack specific viruses.

Bacteria are prokaryotic organisms (simple single celled structures which do not have a membrane bound nucleus). They consist of a outer cell wall and a cell membrane which contains ribosomes for protien synthesis and DNA material often in a circular molecule. They must duplicate their DNA before they can divide which is their means of replication (asexual). They can change by mutation and conjugation. They may be classified in a range of different ways, most commonly according to whether their cell wall stains and the shape of the bacterial. They may also be classified in terms of virulence, response to antibiotics, and their viability in aerobic and anaerobic conditions. Gram staining results in the binding of a blue/violet stain to the thick peptidoglycan cell wall of gram positive bacteria, this may be washed away in gram negative bacteria which have a much thinner peptidoglycan wall and are usually then stained a pink/violet colour. Decribing the shape and the gram stain of an orgnaism is a rapid identification process, which guides management choices such as antibiotic coverage while the culture and sensitivites are pending.

Antibacterial agents Successful antimicrobial therapy of an infection ultimately depends on the concentration of the antibiotic at the site of infection, which must be sufficient to inhibit growth of the offending microorganisms. If host defenses are intact, agents that interfere with growth or replication of the microorganism but do not kill it (i.e., bacteriostatic agents) may suffice. If host defenses are impaired, antibiotic-mediated killing (i.e., a bactericidal effect) may be required. The drug concetration at the site of infection must inhibit the organism but also must remain below the level that is toxic to human cells. If this can be achieved, the microorganism is considered sensitive; if not, the microorganism is considered resistant to the drug. Antibacterial agents may be classified by their chemical structure, such as the location of amino groups as in aminoglycosides or the presence of a beta lactam group as in the penicillins and cephalosporins, by their spectrum of action (gram negative verses gram poisitive, broad spectrum versus narrow spectrum) or most commonly by their mechanism of action. There are a range of methods to classify according to mechanism of action, one of the more simple systems divides antibacterials into four categories, agents which inhibit nucleic acid synthesis, inhibit cell wall synthesis, inhibit mebrane function and inhibit protien synthesis intracellularly. This is shown below with the main categories for each category.

MECHANISM OF ACTION			
Inhibit membrane function	Inhibit cell wall synthesis	Inhibit protien synthesis	Inhibit nucleic acid synthesis
Colistin Daptomycin	Penicillins Cephalosporins Carbapenums (Meropenum) Glycopeptides (Vancomycin) Oxazolidinones (Linezolid)	Macolides Aminogylcosides Tetracyclines Phenicols (Chloramphenicol) Lincosomides	Quinolones Sulphinomides Metronidazole





Fungi and Antifungals Fungi are eurkaryotes with unique cell walls containing glucans and chitin. Systemic infection is rare and is generally limited to patients with immunocomprimise. There are a limited range of antifungals available. Antifungals may be classified according to whether they are given systemically or topically and by their mechanism of action. Available agents have effects on the synthesis of membrane and cell wall components, on membrane permiability, on the synthesis of nucleic acids and on microtubule mitotic spindle function. Amphotericin is one of the better known antifungals and its action through binding to ergosterol in the fungal cell membrane which it forms pores and causing increased permiability loss of the internal cell contents. Nystatin has a similar action. The drug is selectively toxic because in human cell was the sterol is usually cholesterol, however it does have both common and serious side effects. Imidazoles (ketaconazole, miconazole and clotrimazole) and triazoles (fluconazole, itraconazole and voriconazole) also act on ergosterol however they block its synthesis rather than change permiability. Echinocandins (caspofungin) block glucan formation synthesis in the cell wall.

Helminths (paracytic worms) and Antihelmintics Worms that are pathogenic for humans are metazoa and can be classified into roundworms (nematodes) and two types of flatworms, flukes (trematodes) and tapeworms (cesrodes). They are biologically diverse eurkaryotes which invade via the skin or GI tract and evolve into well-differentiated adult worms with characteristic tissue distributions. With few exceptions (strongoloides and echinococcus) they cannot complete their life cycle in the host. Antihelmintics are drugs which act locally within the gut lumen to cause the explusion of worms from the GI tract or systemically against the helminths residing outside the GI tract. Safe and effective broad spectrum antihelmintics are available but some strains such a filarial parasites are only partially susceptible. Benzimidazoles are broad sectrum antihelminthics, their mechanism of action is via inhibition of microtubule polymerisation by binding to beta-tubulin.

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