MICROBIOLOGY

2009-2010

NOTE: NO SECTION E
↳ Use Lect. for those Answers.

DEVANGNA BHATIA

Microbiology Questions

General microbiology

1) Bacterial cell (morphology, staining reactions, classification of bacteria)

Morphology: the form and structure of an organism. It includes shape and size.

Shape: this can be of 3 main types:

- round (**cocci**) – regular (staphylococci)
  flattened (meningococci) – diplococci
  lancet shaped (pneumococci)

- elongated (**rods**) – straight (majority of them are like this; e.g. E.coli),
  short (coccobacilli; e.g acinetobacters)
  long (fibres) – these are mainly found in OLD cultures
  slender – mycobacterium tuberculosis
  robust – lactobacilli, bacillus
  with split ends - bifidobacteria
  branching - nocardiae, actinomycetes
  curved - campylobacters
  with flat ends – bacillus anthracis
  spindle-shaped - fusobacteria
  club-shaped - corynebacteria
  pleomorphic – haemophili
  spiral – helicobacter, spirilium

- Spiral bacteria (spirochetes): these are different to the spiral bacteria mentioned above! They are tightly coiled bacteria.
  - Uneven: borrelia
  - Delicate, regular: Treponema
  - Slender with bent ends: Leptospira

Size: pathogenic bacteria are generally between **1-5µm**
Rods—the fibres can be upto **50 µm** long
Some can be very large, e.g bacillus and clostridium **(1x10 µm)**
Others can be small, e.g. haemophilus **(0.3 µm x 0.6 µm)**

COCCI ARE NEVER FOUND SINGLY!

Cocci can be found in:

- Clumps, e.g. Staphylococcus aureus
- Chains, e.g. Streptococcus pyogenes
- Diplococci (lancet-like) e.g. Strep. Pneumoniae
- Diplococci (flattened) e.g. Neisseria gonorrhoeae
- Cocci in tetrads e.g. Micrococcus luteus

Rods can be found in:

- Most of rods are found singly, e.g. E.coli
- Delicate streptobacilli, e.g. haemophilus ducreyi
- Diplobacilli (in pairs) e.g. moraxella lacunata
- Robust rods with rounded ends e.g. clostridium perfringens
- Robust rods which are flat, with concave ends, found in bamboo cane-like chains, e.g. Bacillus anthracis
- club-like in palisades: Corynebacterium diphtheriae
- slender, hinted palisades: Mycobacterium tuberculosis
- branched and fragmented: Nocardia asteroides
- spindle-like: Fusobacterium fusiforme
- pleomorphic and small: Haemophilus influenza

Curved or Spiral rods:

- curved rods, crescent-shaped: Vibrio cholerae
- thick spirals: Spirillum minus
- uneven spirals: Borrelia recurrentis
- delicate, regular spirals : Treponema pallidum
- very fine spirals with bent ends : Leptospira icterohaemorrhagiae

Staining Reactions and Classification of bacteria: this depends on their morphology (above) and staining reactions (either G+ or G-).

Gram + bacteria have thick a peptidoglycan layer in their cell wall, which is able to retain the crystal violet stain. This results in dark blue or violet staining by Gram staining. Also these bacteria, lack the outer membrane which is found in G- bacteria.
E.g. Staphylococcus, Streptococcus, Bacillus, Lactobacillus, Corynebacterium…

Due to the lack of this thick peptidoglycan layer in the G- bacteria cell wall, these bacteria can't retain the crystal violet stain, so it gets washed out and the counter stain, Safranin, colours all the G- bacteria red or pink. More lipids can be found in these cell walls. E.g. Escherichia, Salmonella, Vibrio, Haemophilus, Pseudomonas, mycoplasma…

↳ Capsules surrounding bacterial cells ⇒ India Ink (Negative staining)
↳ Acid-fast organisms ⇒ Ziehl-Neelsen method – TB blue-green

2) Anatomy of bacterial cell – I (contents of cytoplasm + cytoplasmic membrane)

Bacteria are prokaryotes meaning that they lack the membrane bound organelles found in eukaryotes, e.g. they **don't** have nucleus, mitochondria, Golgi apparatus or endoplasmic reticulum (ER).
Some bacteria produce nutrient granules and store them in their cytoplasm, for use later on, e.g. glycogen or sulphur.
Other cytoplasmic contents are: vacuoles, plasmids, ribosomes and the nucleoid.
The cytoplasmic (plasma/plasmatic) membrane is a phospholipid bilayer, containing fatty acids but lacking sterols. Channels called **porins**, can be found, which allow the passive transport of several ions, sugars and amino acids across the outer membrane. The function of the phospholipid bilayer is to act as a permeability barrier for most molecules and it serves as the location for the transport of molecules into the cell.

Ziehl Neelsen stain - identify mainly Mycobacteria (M.B.)

3) Anatomy of the bacterial cell – II (cell wall, capsule, flagella, fimbriae, pili)

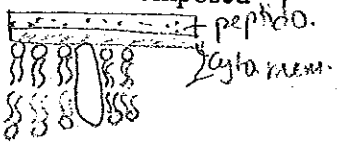
Virulence Factor: molecules produced by a pathogen that specifically cause disease

Desiccation: drying out

Cell wall: The function of the bacterial cell wall is to provide structural integrity to the cell. However, its primary function is to protect the cell from internal turgor pressure caused by the higher concentration of proteins and other molecules inside the cell compared to the outside.

The bacterial cell wall contains peptidoglycan, which is located immediately outside of the cytoplasmic membrane. This peptidoglycan is responsible for the **rigidity** of the bacterial cell wall and determines the cell shape. It is relatively permeable, especially for small substrates. There are **two** main types of bacterial cell walls, **Gram positive and Gram negative**, which are differentiated by differences in their Gram staining characteristics.

The G+ cell wall has a thicker peptidoglycan layer, meaning that the cell wall is able to retain the crystal violet dye, hence staining it **dark blue or violet.**
On the other hand, the G- cell wall has a thin peptidoglycan layer and this cannot retain the dye, hence it gets decolourised (by ethanol) during staining. This results in the cell wall, staining a **red or pink colour**, due to the counter-staining with safranin. G- cell wall contains an outer membrane composed of phospholipids and lipopolysaccharides, which face the external environment.

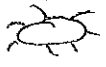
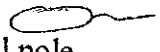


Both types of cell wall have an overall negative charge!

Capsule: They are mainly found in **G- bacteria**. Capsules are relatively impermeable layers, found outside the cell wall. They are water soluble, meaning that it is difficult to stain them, since many stains don't adhere to the capsule. A capsule is a well organised layer, which isn't easily washed off and it can be the causes of many diseases.
Their function is to help protect bacteria from phagocytosis and desiccation. Due to the fact that they help to protect bacteria against phagocytosis, they are considered a virulence factor. Capsules also contain water which protects bacteria against desiccation. Furthermore, bacterial capsules allow bacteria to adhere to surfaces and other cells.

Flagella: These are whip-like structures protruding from the bacterial cell wall and are responsible for bacterial motility (movement). The arrangement of flagella is unique to the species. Common forms include:

- **Peritrichous** - Many flagella found at numerous locations about the cell
- **Polar** - Single flagella found at one of the cell poles
- **Lophotrichous** - A bunch of flagella found at one cell pole


Flagella are complex structures, composed of many different proteins, including **flagellin**, which makes up the whip-like tube and a **protein complex** that extends through the cell wall and cell membrane to form a motor that causes the flagellum to rotate. This rotation is normally driven by proton motive force and is found in the body of the cell.

Fimbriae and Pili:

Fimbriae are protein microfibrils that extend out from the outer membrane. They are usually **short, half as thick as pili** and present in **high numbers** on the entire bacterial cell surface. The function of

fimbriae is to help the attachment of a bacterium to a surface (e.g. to form a biofilm) or to other cells (e.g. animal cells during pathogenesis). A few organisms (e.g. *Myxococcus*) use fimbriae for motility to facilitate the assembly of multicellular structures. They are found in many G- bacteria.

Pili are similar in structure to fimbriae but are much **longer** and present on the bacterial cell in **low numbers**. Pili are involved in the process of bacterial conjugation. Non-sex pili also aid bacteria in gripping surfaces.

transfer of genetic material between bac, through direct cell-cell contact

4) Anatomy of bacterial cell III – bacterial spores

Noxae: agents capable of exerting a harmful effect on the body.

A bacterial spore or endospore is a dormant, tough, and non-reproductive structure, which is produced by **G+ bacteria**. Among human pathogenic bacteria, only **Clostridium** and **Bacillus** produce spores.
The spores are spherical to oval in shape and are characterized by a thick spore wall and a high level of resistance to chemical and physical noxae. This ensures the survival of the bacterium in a dormant phase through long periods of starvation and other adverse environmental conditions. Also, they are highly **heat resistant**, meaning that during heat sterilisation procedures, very high temperatures are required to kill them effectively, i.e. 100-120°C for 10-20mins.
They are also resistant to ultraviolet and gamma radiation, desiccation, lysozyme, starvation, and chemical disinfectants. Endospores are commonly found in soil and water, where they may survive for long periods of time.
In unstained preparations, the spores are larger than lipid inclusion granules and often oval in shape.

The location of the endospore in the bacterium differs among different species and is useful in identification. The main types within the cell are

- **Terminal**: seen at the poles of cells - *C. tetani*
- **Subterminal**: those between these two extremes, usually near the poles but close enough to the centre as well, so can't be considered either terminal or central - *Bacillus subtilis*
- **Centrally placed**: more or less in the middle - *Bacillus cereus*
- **Lateral endospores**: seen occasionally

5) Microbial growth, incl. conditions required

Bacteria reproduce by **binary fission**, which is a form of asexual reproduction and cell division.

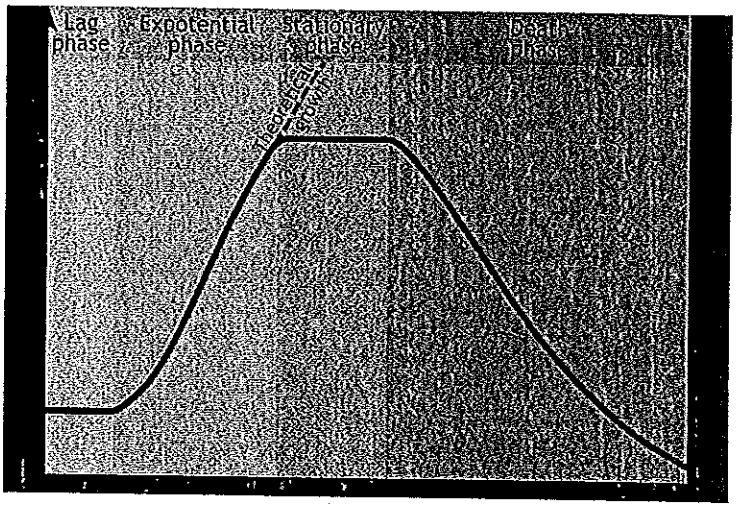
- Period **I (initiation):** the cell grows and proteins that start the next step accumulate inside it.
- Period **C (chromosome replication):** begins in one spot and diverges out in opposite directions
- Period **D (division):** a **supply of macromolecules** is formed
  The **cytoplasmic membrane** inserts between the replicated chromosomes and separates them
  The **cell wall** grows into the cell at a particular spot and forms a **septum** that ultimately divides the maternal cell into two daughter cells

Division of cocci can occur in **one plane** e.g. streptococci or in **different planes** e.g. staphylococci.
Division of rods can occur in the **transverse plane** e.g. majority of chain rods or in the **vertical plane**, e.g. corynebacteria, mycobacteria.

The **generation time** is the time taken for the number of bacteria to double OR duration of the growth cycle. On average it is usually about 30 minutes. Other examples: E.coli – 20mins, Mycobacterium tuberculosis (TBC) – about 12 hours.
Since the number of bacterium double generation time, we can say that bacteria multiply by **geometric progression.**

E.g. If the generation time is 30 min, after 24hrs theoretically one cell gives origin to $2^{48} = 2.8 \times 10^{14}$ cells. However the actual amount of cells produced, is approximately 5 orders less (i.e. around 10^9 **cells**). This amount of cells can be seen by the naked eye and in a liquid broth it appears **cloudy** or **sedimentation** occurs at the bottom or a **pellicle** is seen at the top. In a solid medium (agar), a **bacterial colony** is formed.

The result 10^9cells/24hrs applies for **stationary cultures,** in which nutrients are consumed and metabolites accumulate. The speed of multiplication changes depending on time and the growth of the bacterium can be illustrated by the use of a **growth curve.**
A growth curve depicts the number of viable cells in the logarithmic scale, depending on the age of culture.



There are 4 growth phases, and they gradually change from one to the other:

- **Lag** – microbes are growing but **not** dividing. During this phase, bacterial growth cycle, synthesis of RNA, enzymes and other molecules occurs.
- **Log (exponential)** – cells are dividing at a constant speed. The relation between the no. of living cells and time is **exponential.** There are more than enough nutrients to allow the cells to grow.
- **Stationary** – the no. of cells is stable – the no. of cells being produced = no. of cells dying. Here the growth rate slows down due to the lack of nutrients and the accumulation of metabolites.
- **Death** – no. of cells dying > no. of cells being produced. Here the bacteria have run out of nutrients and die.

Growth conditions:

① - **Temperature**: most bacteria grow optimally at human body temperature (37°C), e.g. E.coli, which is part of the normal human intestinal micro flora. Some can survive at higher/lower temperatures than the human body temperature.

② - **pH**: optimal conditions are between 6.7 – 7.5. However some other bacteria, like vibrio cholera, can survive in pH conditions as high as 9.0 and gastric helicobacter can survive in acidic pH.

③ - **NaCl concentration**: should be about 0.9% (physiological saline). Staphylococci can multiply on sweaty skin, where the concentrations are about 10%. ∴ used on BA ⇒ selective media then

④ - **Nutrients**: need to be in the correct balance of carbon, nitrogen, hydrogen, sulphur, iron etc. for synthesis of specific bacterial compounds. Some bacteria also require "**growth factors,**" i.e., organic compounds they are unable to synthesise themselves.

C, N, H, S

(5) - **Osmotic Pressure:** Bacteria are about 80-90% water; they require moisture to grow because they obtain most of their nutrients from their aqueous environment.

(6) - **Anaerobes/aerobes:** oxygen may or may not be needed, depending on the species of bacteria and the type of **metabolism** used to extract energy from food. In all cases, the initial breakdown of glucose to pyruvic acid occurs during **glycolysis**, which produces a net gain of **two molecules** of ATP.

6) Microbial metabolism

This is the way in which a microbe obtains energy and nutrients it requires, to survive and reproduce. The processes can be **anabolic** (synthesis of compounds and the consumption of energy) or **catabolic** (break down of substrates to gain energy).
Human pathogenic bacteria are always chemosynthetic, organotrophic bacteria (or chemo-organotrophs).

Catabolic Reactions:

- **Digestion** – bacterial exoenzymes split the nutrient substrates into smaller molecules outside the cell
- **Uptake** – nutrients are taken up by passive diffusion, or more usually active transport through the membrane
- **Preparation for Oxidation** – phosphorylation etc
- **Oxidation** – removal of electrons and H^+ ions. The H_2 atoms are then transferred to the hydrogen acceptor.

There are 3 types of catabolism:

1) **Fermentation** – breakdown of nutrients without the need for oxygen. Only small amounts of energy are produced. Products are lactate, ethanol etc
2) **Aerobic Respiration** – uses oxygen and a small amount of nutrient provides a large amount of energy. Products are CO_2 and H_2O
3) **Anaerobic Respiration** – another electron acceptor

The type of catabolism is related to oxygen consumption:

1) **Facultative anaerobes** – they oxidise nutrients by respiration and **fermentation**. They can grow in all conditions.
2) **Obligate (strict) aerobes** – they can only reproduce in the presence of oxygen.
3) **Obligate (strict) anaerobes** – they die in the presence of oxygen. Their vital enzymes are inhibited by oxygen.
4) **Micro-aerophile bacteria** – grow in conditions with traces of oxygen.
5) **Aerotolerant anaerobes** – they don't utilise oxygen for growth but can survive in its' presence.
6) **Capnophile bacteria** – they need higher amounts of CO_2

7) Media for microbial growth – examples

Microbes can be grown on a **solid medium** or in a liquid medium, usually called a **liquid broth.**
There are 2 types of liquid media:

- **Multiplying media**: the most common and universal one, e.g. broth for aerobic culture and VL broth (Viande-Levure) – strictly anaerobes
- **Selectively multiplying media**: only some bacteria can grow in this, e.g. selenite broth for salmonella

4) **Micro-aerophile bacteria** – grow in conditions with traces of oxygen.
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Liquid broths are used when there is only a small amount of microbes in the specimen and when they multiply quickly.

Solid media: there are several types of this as well:

- **Selective solid media**: similar to the liquid broth, only certain bacteria can grow in this, from a mixture of several bacteria, e.g. blood agar with 10% NaCl is used for staphylococci.

Sometimes antibiotics are also added for selectivity, e.g. blood agar with amikacin is selective for streptococci and enterococci.

- **Diagnostic media**: they don't selectively grow any bacteria, since they don't suppress the growth of any microbe. Their contents allow microbes to grow and they can be differentiated according to some properties, e.g. blood agar to observe haemolytic properties.

Special kinds of diagnostic media are chromogenic and fluorogenic media.

- **Chromogenic media**: they contain a dye with bound specific substrate. The dye loses colour and is no longer a dye but a chromogen.
  Bacteria are able to break down this specific substrate and change the specific substrate to the original dye. The media can contain more chromogens, depending on the number of species you want to differentiate. It is used for yeast cultures.
- **Fluorogenic media**: works in the same way but uses a fluorescent dye instead.

Blood Agar: on this you can see haemolysis of RBCs, whether it is absent, partial or total. It is also possible to see viridation (goes green). Total haemolysis shows up due to β-hemolytic activity, whereas partial haemolysis is due to α-hemolysis activity and it appears green. γ-hemolysis refers to the lack of haemolytic activity.
BA is an enriched medium, although it can also be classed as a diagnostic medium, therefore it can be classed as both (sometimes).
Endo Agar: it is a selective and diagnostic medium, used to grow some G- bacteria (not all!). The growing bacteria can be divided into or . Lactose positive bacteria are usually milder pathogens that lactose negative ones!
Other selective media: McConkey media, XLD and MAL– these ones are selective and diagnostic media used to grow Salmonella.
Hajna medium is grown in test tubes, even though it is a solid medium. This is because it is used for biochemical testing and to see the difference between the lower part (no oxygen access) and the upper part (surface of the medium).

Name	Class	Colour	Type	For
Broth	Liquid media	yellowish	multiplying	aerobes
VL-broth		darker		anaerobes
Selenite broth		pinkish	selective multiplying	Salmonella
Sabouraud Agar	solid media in test tubes!	white	selective (only with antibiotics)	Fungi
Lowentein-Jensen		green	enriched	TBC
Blood Agar	Solid media on Petri Dish	red	enriched + diagnostic	majority of bacteria
Endo Agar		pink	selective diagnostic	mostly enterobacteria
Müller-Hinton (MH) agar		white	special	antibiotic susceptibility
NaCl		[illegible]	selective	staphylococci
VL-Agar		red	enriched + diagnostic	anaerobes
XLD (and MAL)			selective diagnostic	Salmonella
Chocolate Agar		[illegible]	enriched	Haemophili, Niesseriae
Levinthal Agar		yellowish	enriched	Haemophili
Slanetz-Bartley		pink	selective diagnostic	Enterococci

8) Sterilisation

Sterilisation refers to any process that effectively kills or eliminates transmissible agents (such as fungi, bacteria, viruses, spore forms, etc.) from a biological culture medium. It doesn't, remove prions. It can be done in various ways, such as use of heat, chemicals, irradiation, high pressure or filtration.

In microbiology, sterilisation is done in the following ways:

1) **Hot steam under pressure**: it should be saturated steam, which is only suitable for objects made of glass, metal, ceramics, china, textile, rubber and some plastics. Temperature ranges from 121-134°C
2) **Hot air sterilisation**: in apparatus with artificial air circulation: 180°C for 20mins, or 170°C for 30mins, or 160°C for 1hour. Used for glass, china and metal
3) **Hot water sterilisation under pressure**: NOT USED ANY MORE!
4) **Gamma-ray sterilisation**: in industrial production, e.g. single use gloves
5) **Plasma sterilisation**: in a high frequency electromagnetic field. This is a new method
6) **Chemical sterilisation using formaldehyde vapours or ethylenoxide**: in situations disabling the use of physical methods.
7) **Fire sterilisation**: for microbiological loops only. Incineration of waste

The method to use for sterilisation depends on the resistance of the materials to various temperatures, humidity, chemicals etc. Also, the temperature and time has to be sufficient enough to kill the microbes.
To check how effect the sterilisation was, indicators that change colour can be used at certain temperatures. This is the chemical method. There is a biological one as well, which consists of using resistant strains of ***Bacillus*** genus. Since they are resistant, their survival is assessed at the end of the sterilisation cycle.

9) Disinfection

This means cleaning of surfaces by destroying all harmful microbes, i.e. all pathogenic organisms, which may cause an infection.
Disinfectants are anti-microbial agents that can be used to destroy microorganisms. Some are suitable for surfaces or tools whereas others are suitable for the skin only.
Disinfection can be done by various methods:

- Physical methods: by **boiling**
  - At normal pressure for at least 30mins (in medicine)
  - In pressure vessels but for a shorter period of time
- Other physical methods such as **filtration, sunrays, UV rays etc**
- Chemical disinfectants:
  - Oxidation reagents: **peroxides**, e.g. peracetic acid, it can be used for spores, fungi and TBC. Disadvantages – it is highly aggressive, causes decolourisation of textiles and instability of solutions
  - Hydrogen peroxide: similar to the above, but less effective and aggressive.
  - Halogen preparations: **hypochlorite**, e.g. Sodium hypochlorite (bleach), calcium hypochlorite
  - Chloramine
  - Iodine Solutions

The effectivity of various disinfectants to various organisms, can be found in booklets where they are divided into different groups, which are alphabetically arranged, e.g. **A = effective to yeasts and bacteria, B = effective against viruses, C = bacterial endospores, T = TB mycobacterium, M= atypical mycobacterium and V = filamentous fungi.**

10) Mechanism of antimicrobial drug action

"IDEALLY THE ANTIMICROBIAL AGENT SHOULD ACT AT A TARGET SITE PRESENT ON THE PATHOGEN, AND NOT ON THE HOST CELL".

Many microbial agents are today derived from natural products of fermentation (and they are usually also chemically modified for its improvement). Some antimicrobial agents are synthetic as well, e.g. sulfonamides, quinolones . . .

An antimicrobial drug which is **bactericidal** means that it kills the cells and the process is, hence, irreversible. An antimicrobial drug which is **bacteriostatic** stops bacterial cell growth and is reversible. Bacteriostatic drugs are good to use in patients with normal immune defense, which then can take care of the infection by normal immune response. However, it's not suitable for immunocompromised patients (lowered immune response).

E.g. CLORAMPHENICOL inhibits growth of Escherichia coli (bacteriostatic) and kills Haemophilus influenza (bactericidal).

Types of antimicrobial agents:

- Antiparasital agents against parasites
- Antimycotics against yeasts and molds
- Antivirotics against viruses
- Antituberculotics against mycobacteria
- Antibiotics against bacteria

(10) Mechanisms of antimicrobial drug action

↳ Bactericidal: kills all the cells + irreversible

↳ Bacteriostatic: stops bac. cell growth + reversible

↳ good in ppl w/ a func/normal immune defense

e.g. chloramphenicol: inhibits growth of E. coli (bistatic) + kills haemophilus influenzae (bactericidal)

Types: Antiparasital

Antimycotics - fungi, yeasts + moulds

Antivirotic

Antituberculotics - mycobac. TB

Antibiotics (incl. antibacterial chemotherapeutics against bac, but synth.

Antiseptics - act locally

1° resistance: bac. have innate resistance; all strains of a given species are resistant

2° resistance: Some bac. " acquired resistance - non-susceptible mutants arise & due to selection pressure - their no ↑↑ PBP = penicillin binding proteins

Mechanism of resistance: 4: antibiotic

① Block entrance of atb into the cell: by alteration of target site eg. alteration of PBP in MRSA

② Active efflux of an atb from a cell: (access to the target site maybe altered ↓ amount of drug reaching the microbe)

↳ ↓ drug accum by ↓ drug permeability & /or ↑ active efflux

③ ↑ false receptor is offered to the atb: target site maybe altered → ↓ affinity

④ Alteration of metabolic pathway: e.g. enzymes that modify/destroy the atb

e.g. β-lactamases split β-lactamic atb

* other side

Site of action + mechanism

④ Metabolic pathways - bacteriostatic ⇒ sulfonamid

⑤ Cytoplasmic mem ⇒ bacstatic ⇒ polypep

① cell wall synthesis: bactericidal - β-lactames atb

② protein synthesis: ~~bactericidal~~ (macrolides, tetracyclines → bacteriostatic)

③ Nucleic Acid " : bactericidal - quinolones

(11) Inhibitors of bac. cell wall synthesis

↳ they act on the peptidoglycan layer (it is a crucial layer for bac. cell wall synthesis)

↳ Mycoplasmas – NO CELL WALL ∴ RESISTANT to these agents

↳ e.g. Penicillin + Cephalosporins

↳ have a β-lactam ring in their struc ⇒ inhibits peptidoglycan synthesis

↳ Penicillin: staphy, (MRSA) strep, Neiss, spirochetes – some strains are resistant!

↳ Cephalosporins: only differ in 1 chemical ring

↳ stable against staphylococcal penicillinase (less susceptible)

↳ don't work against enterococci

↳ advantage: ↓ hypersensitivity reactions

Others:

Sulphones: β-lactamase inhibitor, used in combination w/ ampicillin (e.g.).

Glycopeptides: only for Gr+ bac (cocci) cos vankomycin (etc) cannot penetrate the cell wall of Gr- bac!

Vancomycin Resistant Enterococci (VRE)!

* There are 4 organelles in bacterial cell that are different from human cells where these drugs act:

(1) Cell Wall of Bacteria – inhibition of cell wall synthesis (Pen, Vancomicin)
(2) Ribosomes: Inhibition of protein synthesis (ex: tetracyclins, clindamicin)
(3) Nucleic acids: Inhibition of Nucleic acid synthesis (ex: Sulfonamides, Quinolones)
(4) Cell membrane: alteration of cell membrane function

Drugs: (1) Broad Spectrum → tetracyclins (G- rods)
(2) Narrow Spectrum → Glycopeptides Vancomicin (G+ cocci)

(12) Inhibitors of bact protein synthesis

↳ some diff between eukaryotic + prokaryotic protein synthesis (eg. 70S rRNA (pro) & 80S rRNA (euk)) => allows selective toxicity of inhibitors

(1) Aminoglycosides: Bactericidal activity; bind to specific proteins in the 30S ribosomal subunit + interfere w/ fmet-tRNA (formylmethionyl-transfer RNA) + inhibit initiation of protein synthesis, only against aerobes, susceptible organisms have O_2 dependent system that transports the antibiotic across the cell membrane

↳ Intravenously; excreted into urine

↳ Gentamicin, Amikacin, streptomycin => Serious G- infec

↳ NOT active against anaerobes + strep. but STAPHY!

(2) Tetracyclines: Inhibit aminoacyl ~~dea~~ tRNA from attaching to its receptor = INHIBIT PROTEIN SYNTHESIS, doxycycline

↳ mycoplasma, chlamydiae, rickettsiae; other infec = RESISTANCE

↳ Cause a ↓ in gut flora ∴ DON'T use in preg + < 8yrs age.

↳ orally; bile + urine

(3) Macrolides: contain ↳ Macrocyclic lactone (cyclic ester) ring + BACTERIOSTATIC

↳ erythromycin - binds to 23S rRNA in the 50S subunit, blocking the translocation in protein synthesis

↳ orally + intravenously; bile; when allergic to penicillin

↳ G+ cocci => atypical pneumonia + chlamydial infec of urogen. tract

(4) Lincosamides - Clindamycin

↳ inhibits 50S ribosomal subunit

↳ G+ & G- anaerobes

↳ orally, intravenously or intramuscular

(5) Oxazolidinones = new, synthetic, bacteriostatic => LINEZOLID

↳ G+ bac - targets 23S rRNA in the 50S subunit => prevents form of 70Sa

↳ orally or intravenously

(13) Inhibitors of bact nucleic acid synthesis

① Quinolones: Synthetic, bactericidal; inhibit DNA replication by inhibiting the bac. DNA gyrase + topoisomerases (remove supercoils + separate newly formed DNA daughter strands) ↑ Selective toxicity

↳ these enzymes are needed for bac DNA replication; don't affect mammalian cells!

↳ Some microbes have chromosomally mediated resistance:

↳ ① mutations on the target enzymes fr quinolones - changes in binding

② changes in cell wall permeability

↳ G- rods; systemic G- infec, intracellula chlamydial + rickettsial infec.

↳ orally but GIT disturbances

② Rifamycin: inhibitor of RNA polymerase; RIFAMPICIN- blocks m RNA synthesis by binding to DNA-dependent RNA polymerase ⇒ BACTERICIDAL

↳ Mycobacteria; staphy resis ↑

↳ orally; crosses BBB; Metabolised in the liver + excreted in bile

③ Sulfonamides: synthetic; inhibits ~~precursor~~ precursor nl. acid syn. w/ BACTERIOSTATICa

↳ compete w/ PABA fr the active site of dihydropteroate synthetase (catalyses the formation of tetrahydrofolic A, THFA)

↳ selective toxicity ensured on the fact that bacteria like to synthesise their own THFA, whereas mammalian cells receive it exogeneously

↳ G- orgs, except PSEUDOMONAS ⇒ UTI ! WIDESPREAD ACQUIRED RESIST.

↳ orally; liver metabolises → urine

④ Trimethoprim (+ co-trimoxazole): anti-metabolite; prevents THFA synthesis

↳ trimethoprim often given w/

↳ G- rods, treatment of ~~Chlamydia~~ UTI

↳ orally, intravenously → urine

⑤ Nitroimidazoles: eg metronidazole - interfere w/ + breakage of DNA

↳ anaerobes

↳ reduced chemically in the body to become active

14. The strategy of antimicrobial chemotherapy

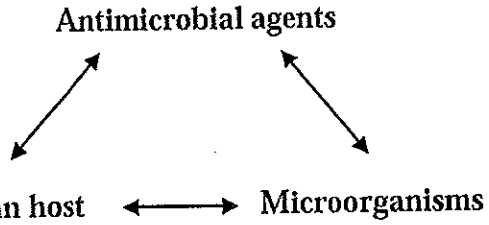
Antimicrobial chemotherapy is the use of chemical agents for antimicrobial action, which work by either killing it (bactericidal) or stopping its growth (bacteriostatic).
The strategy of the antimicrobial agents is to have a target site exclusively present on the microbe and not on the host cell → **SELECTIVE TOXICITY**.

Selective toxicity with desired properties of a new antimicrobial agent:

- Selectivity for microbes rather than mammalian cells.
- Cidal activity.
- Slow emergence of resistance.
- Narrow spectrum of activity.
- Non-toxic side effects to the host.
- Long plasma half-life (so, low dosage is possible).
- Good body distribution.
- Decrease in plasma protein-binding.
- No interference with other drugs.
- Easy administration.

The antimicrobial agents target cell wall, protein, and nucleic acid synthesis; metabolic pathways, and cell membrane functions.

Triangle relationship:



(Interfering with one side of the triangle will affect the other parts).

15. Bacterial genetics

Bacteria can have **primary resistance** (i.e. innate resistance), and some bacteria can acquire it (**secondary resistance**).
Bacteria can rapidly develop secondary resistance, as seen in many cases, e.g. Staphylococcus aureus.

Resistance can become present because of:

1) Single chromosomal mutation in one bacterial cell → change in one protein. Although, this is rare.
2) Series of mutations.

When there is an antibiotic present, these mutations within the microbe become more probable, and hence, the risk of acquiring secondary resistance increases.
Secondary resistance is acquired by genes on transmissible **plasmids** (the cell can even acquire multiple resistance in this manner, so-called *infectious resistance*).
Resistance genes may also occur on **transposons** ('jumping genes') → these genes can integrate into chromosome (more stable location for the genes but slower spreading of genes than plasmids) or into plasmids.
An integron = site of multiple resistances (cassettes of resistance), It is found in plasmids, chromosomes and transposons.

Resistance gene cassette
↓
Integrons
↓
Transposons
↓
Chromosome/plasmid

Mechanism of resistance:

- The target site may be altered – lowered affinity.
- Access to the target site may be altered (altered uptake, efflux mechanism, decreased cell wall permeability).
- Enzymes that modify or destroy the antimicrobial agent may be produced e.g. beta-lactamases, amino-glycoside modifying enzymes, chloramphenicol acetyl transferases.

Epidemiologically important resistances:

- MRSA (methicillin resistant staphylococci) – oxacillin or other beta-lactams cannot enter the cells. Many MRSAs are also resistant to other drugs, e.g. macrolides, lincosamides etc.
- VISA, VRSA (vancomycin-intermediate Staphylococcus aureus, vancomycin-resistant Staphylococcus aureus) – staphylococci partially or fully resistant to glycopeptides (e.g. vancomycin).
- VRE (vancomycin resistant enterococci) – they spread easily. Enterococci are found in many people's intestine.

16. Pathogenicity and virulence

Pathogenicity = the ability of a microbe to be harmful and cause disease (alter the state of health).

Infectiousness = the ability to cause infection.

In a disease, symptoms are present i.e. ***disease x symptoms***. The relation between infection and symptoms is following, ***infection x no symptoms (inapparent) or symptoms***.

Microbes can also cause food poisoning apart from infections.

Three forms of symbiosis:

1. **Mutualism** - when both parts are benefitting from each other (☺,☺).
2. **Commensalism** – when only one part benefits from the symbiosis, the other part remains unaffected (☺,-).
3. **Parasitism** – when one part benefits from the other part but at the same time negatively affecting it (☺,☹).

Microbe ↔ Host
↕ ↕
Environment

Illness is not a rule – peaceful co-existence is usually better for parasitism!

Pathogenicity depens on:

1. **Microbial species** – pathogenic x nonpathogenic.
2. **Host species** – susceptible x resistant.

- **Primary obligate pathogens:** they cause infections in healthy individuals → classical infections, e.g. diphtheria, typhoid fever, plague, gonorrhoeae, tetanus, influenza, etc.
- **Opportunistic (facultative) pathogens:** members of normal flora reach other parts of the body, where they shouldn't be present. They can also spread to other locations when the person has decreased immunity. E.g. of facultative pathogens are *E.coli* (1% of normal colonic flora), *Staphylococcus epidermidis* (normal in skin and mucosal flora).

Virulence = the degree or measure of pathogenicity. It defines the property of a certain strain which could be highly virulent or almost avirulent. It is the relative ability of a pathogen to cause disease.

Indicator of strain virulence: (ability to kill)

- **LD_{50} (50% lethal dose)** - it is the amount of microbe that is able to kill 50% of experimental animals.

Attenuation: it's a method causing artificial weakening of virulence (e.g. to produce attenuated vaccines → BCG vaccine against TBC).

Three elements of pathogenicity and virulence:

1) **Communicability (transmissibility)** – ability to be transmitted between hosts.

2) **Invasiveness** – ability to:
   - a) Enter the host.
   - b) Multiply in it.
   - c) Spread inside it.

   } Ability to overcome the immune defense of the host.

3) **Toxicity** – ability to do harm to the host.

17. Colonization and invasion

presence of bacteria on a body surface without causing disease in the person

Colonization means the colonization of a nonpathogenic microbe (or by a pathogen which does not cause pathological symptoms at that area) on a bodily surface. It is the establishment of a stable population of bacteria on the host.
Invasion is when the microbe enters the host, and it is usually through the mucosae. It is also commonly preceded by colonization (overcoming the possibility of commensalism (= symbiosis: ☺,-)). For successful entry of the microbe it needs to adhere to the epithelium by means of *adherence factors*, and penetrate through the epith. by means of *penetration factors.*

Adherence factors: of pathogens

1) **Fimbriae (pili)** – their end reacts with a receptor on the epithelial surface.
2) **Nonfimbrial adhesions** –hemagglutinins of yersinae, bordetellae, F protein of streptococcus pyogenes.
3) **Viruses** – they can envelope projections (hemagglutinin) of influenza virus. Glycoprotein gp120 of HIV is also an adherence factor.
4) **Parasites** – suck themselves to the mucosae.
5) **Micromyocetes** – glucans and mannans of yeasts, & keratophilia of dermatophytes (skin moulds).

Penetration factors:

- **Direct penetration:**
  - Small cracks in skin.
  - Small cracks in mucosa.
  - Animal bite.
  - Arthropod bite.
  - Enzymes.
- **Forced penetration:**
  - Changing cellular framework (invasines).
  - Ruffling (trouble) of epithelial surface (e.g. Salmonellae)
  - Unknown mechanisms.

Multiplication:

- **Intracellular multiplication** – better because of good nutrient supply, & defense against host immunity. E.g. of intracellular parasites are mycobacteria, rickettsiae, chlamydiae, usteriae, salmonellae.
- **Extracellular multiplication** – stopped by antibacterial substances (e.g. complement, lysozym, antibodies) but mostly because of shortage of free iron (lactoferrin, transferin), and also high temperature.

Spreading of the microbe in the body:

- **Localized infections** (common cold, salmonellosis, gonorrhea).
- **Systemic infections** (influenza, meningitis).
- **Generalized infections** (morbilli, typhoid fever, and even localized and systemic infections). ↳ Measles
  - **Way of spreading:**
    - Lymph
    - Blood
    - Per continuitatem along nerves

Invasion by transmission:

- **The way of transmission** - exit point of the body, and entry point of the host.
- **Microbe tenacity** – degree of resistance to the external environment. E.g. Clostridium tetani, Giardi lamblia, and Helminth eggs (Taenia saginata) are all spore forming, so, that they can survive in the external environment.
- **Minimum infectious dose** - amount of microbes required to start infection. An immune person has a high infectious dose Coxiella burnetii, which causes Q fever, has an extremely low infectious dose of only 10^0 cells.
- **Behvaiour of the host** – immune defense reflexes (cough, sneezing, diarrhea).
- **Way of elimination** – every biological substance is infectious.
- **Amount of eliminated substance.**
- **Portal of entry** – better penetration through mucosa than skin. Some requires direct transmission (sexual contact, e.g. gonococci, treponemae), biological vector (tick, mosquitos → arboviruses, borreliae), and transmission by water (leptospirae, shigellae).

18. Aviodance of host defense mechanisms

Ability to overcome the innate immunity by:

① - Resisting complement.
② - Inhibiting complement activation.
③ - Protecting one's own surface.
④ - Resisting phagocytosis by not getting engulfed, or by surving inside the phagocyte.
⑤ - Interfering with the cytokine functions.

① **Resisting complement system:**
It's achievable by:

- **Formation of capsule** (shielding surface molecules), e.g. seen in meningococci, pneumococci.
- **Activation of inhibitors**, e.g. gonococci add sialic acid to terminal saccharides.
- **Production and regulation of factor H** (= regulates the alternative pathway of the complement system), e.g. many viruses, E.coli, Strept. Pyogenes. (inhibits)
- **Production of enzymes** splitting C3b and C5a, e.g. Strept. Pyogenes and Pseudomonas aeruginosa. Blocking Complement System.
- **Protection of the surface**, e.g. Salmonellae and E.coli in S phase, and flagellae of motile bacteria.

The ability to resist the complement system leads to **seroresistance.**

④ **Resisting phagocytosis:**

- **Not allowing to become engulfed**
  - **Inhibiting chemotaxis** - e.g. bordetellae, vaginal anaerobes, pseudomonads.
  - **Leukocidins and lecithinase** (causes myonecrosis and hemolysis) – produced by staphylococci, streptococci, pseudomonads, & clostridia.
  - **Formation of capsule** – by agents of meningitis and pneumonia, e.g. Neisseria meningitidis, Haemophilus, Influenzae, E.coli, Streptococcus pneumoniae, Klebsiella pneumoniae.
- **Surviving inside the phagocyte**
  - **Blocking phagolysosome formation**, e.g. Chlamydia, Mycobacterium, Legionella, Toxoplasma.
  - **Escaping phagosome** – e.g. Rickettsia, Shigella, Listeria, Leishmania, Trypanosoma.
  - **Production of antioxidants** – e.g. staphylococci gonococci, meningococci.
  - **Marked tenacity** (i.e. persistency) – seen in Coxiella and Ehrlichia.

Overcoming acquired immunity:
The microbe attempts to avoid antibodies or lymphocytes by:

- **Reproducing quickly**, e.g. respiratory viruses, diarrheal agents, malarial plasmodia.
- **Deceiving the immune system**
  1. **Hiding:**
     - Inside ganglions – HSV, VZV (Varicella zoster virus – one of the eight herpes viruses → chicken-pox in children).
     - On intracellular membranes – HSV, adenoviruses.
     - In infectious focuses – Mycobacterium tuberculosis, Echinococci.

- At privileged sites – agents of mucosal infections, Toxoplasma gondii in eye, retroviruses in cellular genome.

2. **Changing one's own antigens:**
   - Antigenic mimicry – Strept. pyogenes, Treponema pallidum, Mycoplasma pneumoniae.
   - Antigenic camouflage – Schistosomes (= blood proteins), Staphylococci → protein A; Streptococci → protein G; cytomegalovirus → βmG.
   - Antigenic variability – trypanosomes, borreliae, gonococci, influenza virus.
3. **Inducing tolerance** – cytomegalovirus (CMV - a herpes virus), rubella virus, leishmaniae, cryptococci, maybe HIV.

➢ **Suppressing immune response**
- Invading the immune system – HIV, measles virus.
- Interference of cytokine formation – Mycobacterium leprae, protozoa.
- Production of superantigens – staphylococci, streptococci.
- Production of proteases – meningococci, gonococci, haemophili, pneuomococci.
- Binding of Fc fragment (= fragment crystallizable region → activates the immune system) – staphylocooci, streptococci, HSV.

19.Bacterial toxins and aggressins

Bacterial toxins is one of the stages of Bacterial pathogenesis.

- Entry into the host
- Adherence of the microorganism to the host cell
- propagation of organism
- Damage to the host cell by bacterial toxins
- Evasion of host secondary Defenses

Bacterial toxins are two type:

- Endotoxins
- Exotoxins

Exotoxins: are proteins secreted by both gram-negative and gram-positive.They are the most poisonous substances known.
Exotoxins have 2 polypeptide components:

- one is responsible for binding to cell membrane
- and one is responsible for the toxic effect

Such as **Diphtheria toxin**:is an exotoxin secreted by Corynebacterium diphtheriae. It is an enzyme that block protein synthesis.**Cholera toxins**: result in ionic imbalance and loss of water.

Treatment: most antigens are inactivated by moderate heating(60 degree). In addition treatment with dilute formaldehyde destroys the toxic activity of most exotoxins ---> toxoids(are usful in preparing vaccines).

Gram⊖

Endotoxins: are heat stable, lipopolysaccharides (LPC), which are not secreted but instead are integral components of the cell wall of gram-negative bacteria (not the gram-positive). G−
They are released into the host's circulation following bacterial cell lysis.

Main effect is fever, shock, hypotension and thrombosis, result to septic shock. These effects are produced indirectly by activation of complement, and activation of the coagulation cascade. Death can result from multiple organ failure.

Aggressins: invasive bacteria are those that can enter host cells or pentrate mucosal surfaces, spreading from the initial site of infections. Invasiveness is facilitated by several bacterial enzymes, most important are collagenase and hyaluronidase. There enzymes degrade components of the extracellular matrix, providing the bacteria with easier access to host cell surface. Invasion is followed by inflammation, which can be either pyogenic(involving pus formation) or granulomatous (having nodular inflammatory lesions), depending on the organism.

Aggressins: Substances like toxins and tissue damaging enzymes like collagenase and hyaluronidase that facilitate Invasiveness. These substances facilitate penetration in mucosal surfaces and entrance in host cells

↳ subs. formed in the body by bacteria which enhance the bacteria's virulence. Incl. capsular material, enzymes + toxins

Aka- virulin

20. Antigens, incl. antigen recognition and examples of bacterial antigens.

Antigen: is a substance capable of provoking the lymphoid tissues of an animal to respond by generating an immune reaction directed specifically at the inducing substance.
It need to be foreign to the body, molecular weight that is higher then 5000 Da , chemical complex.
The reaction of an animal to contact with an antigen, called :
acquired immune response:

- **humoral response**
- **cell mediated response**

Antigen Determinants:
A response to antigen involves the specific interaction of components of immune system, antibodies and lymphocytes, with epitopes on the antigen. The lymphocytes have receptors on their surface that function as the recognition units, on **B lymphocytes surface-bound immunoglobulin** is the receptor and on the **T lymphocytes** the recognition unit is known as **T cell receptor.**
The better the fit between the epitope and the paratope the stronger the non-covalant bonds formed and consequently the higher the affinity of the interaction.
Antigenic determinants can be formed in two ways:

- Sequential epitopes
- Conformational epitopes

Epitope = Antigenic determinant
↳ Part of a macromolecule that is recognized by the Immune system.

Antigen Recognition:
Two separate recognition systems:

- humoral immunity
- cell-mediated immunity

Humoral immunity: Antibody is the recognition molecule. This glycoprotein is produced by plasma cells and circulates in the blood and other body fluid. Antibody is also present on the surface of the B lymphocytes. The interaction of this surface immunoglobulin with its specific antigen is responsible for the differentiation of these cells into plasma cells. Antibody molecules, whether free or on the surface of a B cell, will recognize free native antigen.

Cell-mediated immunity: ~~The lymphocytes~~ T-lymphocytes antigen receptor will only bind to fragments of antigen thatare associated with products of the major histocompatibility complex (MHC). T cell recognition of antigen is said to be MHC-restricted. This MHC-restricted recognition mechanism has evolved because of the functions carried out by T lymphocytes.
The joint recognition of MHC molecules and antigen ensure that T cell makes contact with antigen on the surface of the appropriate target cell.

B cell receptor: antigen is found free in body fluids and as a transmembrane protein on the surface of B lymphocytes, i.e. surface immunoglobulin, where it acts as the B cell antigen receptor.

T cell receptor: the T cell antigen receptors heterodimer composed of an alpha and beta or a gamma and a delta chain, mostly used is the alpha/beta heterodimer. the T cell receptor is the molecule that is responsible for the recognition of specific MHC- antigen complexes and will be different for every T cell.

Examples of bacterial antigens:

- Somatic or O-antigen: composed of repeating oligosaccharides. Such as gram negative bacteria E. coli
- flagellar protein or H-antigen: structure protein which make up flagella then enter in the organism with motility. Enteric bacilli
- Capsular or K-antigens: acidic polysaccharide, external to cell wall such as Salmonella.

21. Immunoglobulins. = DAMAGE 6 Rastiles.

Antibodies:

- Glycoproteins.
- Presenting the serum and body fluids
- Induced when immunogenic molecules are introduced into the host's lymphoid system
- Reactive with, and bind specifically to, the antigen that induced their formation

There are five distinct classes or isotypes of immunoglobulins: IgG, IgA, IgM, IgD and IgE. They differ from each other in size, charge, carbohydrate content and amino acid composition.

Antibody structure: all antibody molecules have the same basic four chain structure, composed of two light chains and two heavy chains. DAMAGE

IgG: = Mature response

- Monomer
- major immunoglobulin of serum 75%
- exist as : IgG1, IgG2, IgG3, IgG4
- IgG is the major antibody of secondary response and is found in both serum and tissue fluid. and colostrum
- It is the only antibody that is capable of crossing the placenta and giving passive immunity to fetus

IgA:

- Dimmer
- Found in breast milk, mucosal areas, respiratory tract, urogenital tract. → Seromucous secretions → Mucosal epithelial surf
- Subclasses: IgA1, IgA2

IgM: = Immune response in action

- Pentamer
- Large size hence confined to intravascular pool
- First antibody type to be produced during immune response.

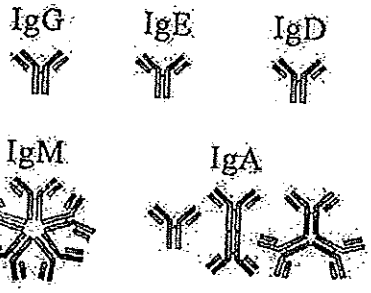
IgD:

- Monomer
- Many circulating B cells have IgD present on their surface. 1% of circulating Ab's

↳ Begin of Ig production together with IgM

IgE:

- Monomer
- Present in very low levels
- Found on the surface of mast cells and basophiles.
- Triggers histamine release from mast cells and basophiles, involve in allergy.



22. Antibody function in Infection:

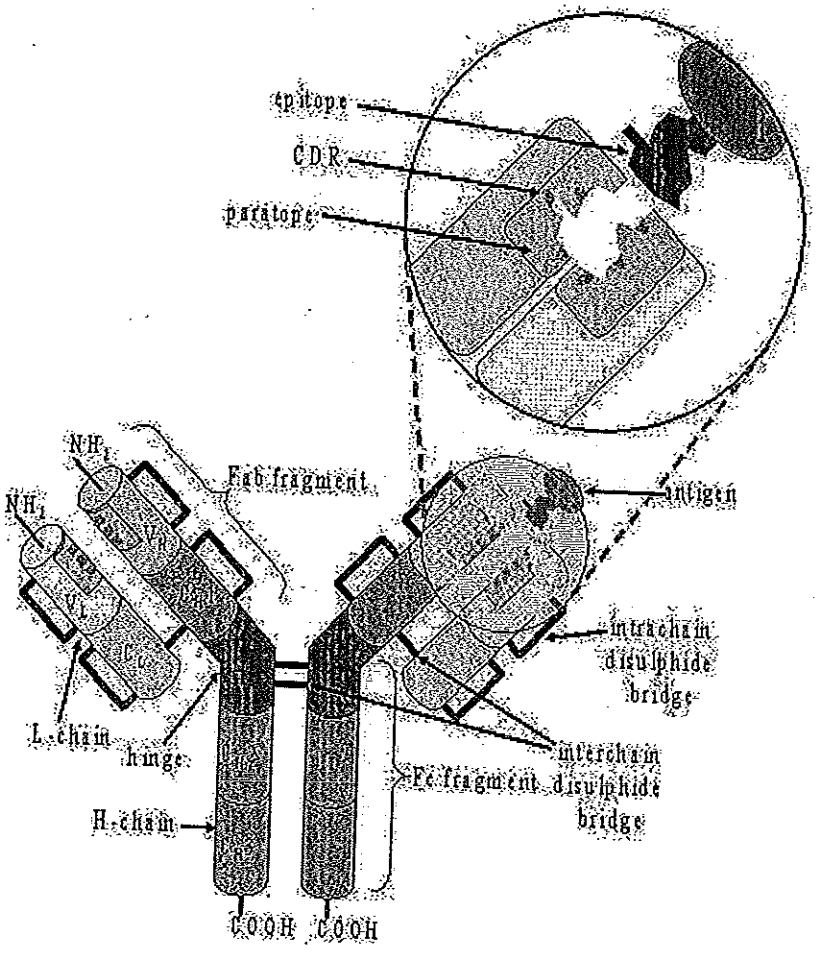
Primary function of an antibody is to bind the antigen that induced its formation. The binding of the antigen is mediated by the **Fab portion** and **Fs region** controls the biological defence mechanisms. For every antibody the paratope is different.

Neutralization:
Because antibodies are at least divalent they can form a complex with multivalent antigens. Depending on the physical nature of the antigen these innate complexes exist in various forms: Antibody excess, equivalence, antigen excess, monovalent antigen.

Complement activation:
Activation of the complement system is one of the most important antibody effecter mechanisms. Complement cascade is a complex group of serum proteins that mediate inflammatory reactions and cell lysis.

Cell binding and opsonisation:
Antibodies specific for particular antigens, such as bacteria, play a valuable role by binding to the surface and making the antigen more susceptible to phagocytosis and subsequent elimination. process know as opsonisation and is mediated by the **Fc portion** of the antibody
The important residues are in the C_H2 domain near the hinge region, composed of disulphide bond.

↳ The higher the amount of opsonized antigens by ↑ no. of Ig ⇒ ↑↑↑ the signal for phagocytosis is ~~sent~~ emited!!!



23) Immune System

It is one of the homeostatic mechanisms of the body. It is a system of biological structures and processes within an organism. His main functions are the recognition of foreign or dangerous substances, the triggering complex reactions that eliminates, or attack to tumour or viral infected cells. In order to accomplish that he needs to detect and distinguish them from their onw healthy cells and tissues.

The immune system is divided in: just generalised reactions

Innate, non specif immunity: is the first line of defence against infectious agents, and most potentials pathogens are checked before they establish an overt infection. Is quick (min-hours), recognizes foreign substance, eliminates them, has no memory.

Adaptative/ Specific immunity acquired immunity: produces a specific response to each infectious agent, and the effector mechanisms generated normally eradicate the offending material. It makes the distintion between self and non-self. Longer (requires several days), but has immune memory.

Innate => Granulocyte (BEN), macrofag + NK

The immune system consists of a number of organs and several different cell types. All cells of the immune system – tissue cells and white blood cells or leukocytes- develop from pluripotent stem cells in the bone marrow. The production of leucocytes is through two main pathways of differentiation:

Specific => T & B cells

Lymphoid lineage- T/lymphocytes, b/lymphocytes and (NK) natural killer cells.

Myeloid pathways- mononuclear phagocytes, monocytes and macrophages and granulocytes, basophils, eosinophils and neutrophils

24) Innate immunity Characteristics and humoral mechanisms

Innate Immunity

This kind of immunity doesn't depend on prior exposure to any particular organism. The innate defence mechanisms are nonspecific in the sense that they are effective against a wide range of potentially infectious agents.

The components of the innate immune system recognize structures that are unique to microbes like complex of lipids and carbohydrates such as peptidoglycan of bacteria, lipopolysacharides of gram/negative bacteria, lipoteichoic acid in gram/positive bacteria and mannose containing oligosaccharides found in many microbial molecules. Therefore the innate immune system is able to recognize non/self structures and react appropriately but does not recognize self structure, so the potential autoimmunity is avoided. The microbial products recognized by the innate immune system (PAMPs- pathogen/associated molecular patterns) are essential for survival of the microorganisms and cannot be easily be discarded or mutated. Different classes of microorganisms express different PAMPs that are recognized by different pattern recognition receptors (PRRs). On host cells and circulating molecules.

can diff between self + nonself Structures but doesn't harm self!

Innate defences act as the initial response to microbial challenge and can eliminate the microorganisms from the host. When it is insufficient, it plays a critical role in the generation of an effective acquired immune response. Cytokine produced by the innate immune system signal that infectious agents are present and influence the type of acquired immune response that develops.

Humoral defence mechanisms

Lysozyme

Basic protein of low molecular weight found in relatively high concentrations in neutrophils as well in most tissue fluids (except CSF, sweat and urine). Functions as a muccolytic enzyme, splitting sugars of the structural pepdidoglycan of the cell wall of many gram-positive bacteria causing their lysis. In many pathogenic bacteria the peptidoglycan of the cell wall appears to be protected by other wall components (lipopolysacharides), requiring the use of other enzymes to remove this protection.

might not be enough

Basic polypeptides

A variety of basic proteins, derived from tissues and blood cells, have antibacterial properties, that depends on their ability to react non-specifically with acid polysaccharides at the bacterial cell surface. In this group, spermine and spermidine, which can kill tubercle bacilli and some staphylococci. Protamine and histone (lysine and arginine proteins) are also included.

Acute/phase proteins

Their concentration rises dramatically in case of infection. Microbial products aas endotoxin stimulate macrophages to release IL-1. which stimulates liver to produce increased amounts of these proteins.

C/reactive protein binds phosphorylcholine residues in the cell wall of microorganisms, activating the classical complement pathway.

α1-antitrypsin, α2-macroglobulin, fibrinogen and serum amyloid A protein act to limit the spread of the infectious agent or to stimulate the host response.

Interferon – α and β

Antiviral agents α- and β participate in innate immunity in the way that stop the processes that permit virus to spread.

Complement

is composed of a large number (about 30) of different serum proteins present in low concentrations in normal serum;some of them are enzymes, other control molecules and other structural proteins with no enzymatic activity.. Normally these proteins are inactivated but can be activated to form a an enzyme cascade. There are two pathways of complement activation, the alternative and the classical, that lead to the same consequences:

Opsononization

Cellular activation

Lysis

The 2 pathways use different initiation processes. Component C3 forms the connection between both pathways, the binding of this molecule to a surface is the key process in complement activation.

Classic Pathway ⟹ Page 113

The classical pathway is triggered by activation of the C1-complex (C1q, two molecules of C1r, and two molecules of C1s thus forming C1qr2s2), which occurs when C1q binds to IgM or IgG complexed with antigens (a single IgM can initiate the pathway, while multiple IgGs

are needed), or when C1q binds directly to the surface of the pathogen. Such binding leads to conformational changes in the C1q molecule, which leads to the activation of two C1r (a serine protease) molecules. They then cleave C1s (another serine protease). The C1r2s2 component now splits C4 and then C2, producing C4a,C4b,C2a,and C2b. C4b and C2a bind to form the classical pathway C3-convertase (C4b2a complex), which promotes cleavage of C3 into C3a and C3b; C3b later joins with C4b2a (the C3 convertase) to make C5 convertase (C4b2a3b complex).

Alternative pathway => Page 113

The alternative pathway is triggered by spontaneous C3 hydrolysis directly due to the breakdown of the thioester bond via condensation reaction (C3 is mildly unstable in aqueous environment) to form C3a and C3b. It does not rely on a pathogen-binding antibodies like the other pathways.[1]. C3b is then capable of covalently binding to a pathogenic membrane surface if it is near enough. If there is no pathogen in the blood, the C3a and C3b protein fragments will be deactivated by rejoining with each other. Upon binding with a cellular membrane C3b is bound by factor B to form C3bB. This complex in presence of factor D will be cleaved into Ba and Bb. Bb will remain covalently bonded to C3b to form C3bBb which is the alternative pathway C3-convertase. The protein C3 is produced in the liver.

The C3bBb complex, which is "hooked" onto the surface of the pathogen, will then act like a "chain saw," catalyzing the hydrolysis of C3 in the blood into C3a and C3b, which positively affects the number of C3bBb hooked onto a pathogen. After hydrolysis of C3, C3b complexes to become C3bBbC3b, which cleaves C5 into C5a and C5b. C5b with C6, C7, C8, and C9 (C5b6789) complex to form the membrane attack complex, also known as MAC, which is inserted into the cell membrane, "punches a hole," and initiates cells lysis. C5a and C3a are known to trigger mast cell degranulation.

IgA is associated with activating the alternative path.

25) Innate immunity- barriers & cell-mediated mechanisms

Non Specific barriers: Anatomical/Physiological

The skin is a resistant barrier because of its outer horny layer consisting mainly of keratin; indigestible for most micro/organisms; the drycondition of the skin and the high concentration of salt of sweat are inhibitory or lethal to many other microorganisms. The sebaceous secretions and sweat contain also bactericidal and fungicidal fatty acids.
The sticky mucous covering the respiratory tract act as a trapping mechanism for inhaled particles, the cilia push the secretions to oropharynx so that they are swalloed and the acidic secretions of stomach destroy most of the microorganisms.
Nasal secretions and saliva contain mucopolysacharides capable of blocking virus.
The washing action of tears and the flushing of urine are effective in stoping invasion by microorganisms.
The natural bacterial flora covering epithelial surface are protective in a number of ways:
Their presence uses a niche that cannot be used by a pathogen
Compete for nutrients

They produce by-products that inhibit the growth of other organisms.

Cell mediated mechanisms

Phagocytes- cells actively phagocitic (solid particles) and pinocytic (soluble material), contain enzymes to degrade ingested material intracelularly in specialised vacuoles, are an important link between the innate and the acquired immune mechanism.

Neutrophils and mononuclear phagocytes engulf rapidly microorganisms Mononuclear phagocytes are named monocytes in the blood stream or macrophages in the tissues. (In connective tissue- histiocytes, kidney- mesangial cells, liver- kupfer cells, bone- osteoclasts, brain- microglia and in spleen, lymph node and thymus as the sinus-linning macrophages).

The phagocytes are attracted by a process- chemotaxis. The chemotaxic factors include:

Products of the injured tissue

Factors from blood (C5a)

Substances produced by neutrophils and mast cells (leukotrienes and histamine) .

Bacterial products (formyl/methionine peptides)

Phagocytosis involves 3 stages: recognition and binding; ingestion and digestion.

Phagocytes have receptors on their surface that mediate the attachment of particles coated with the correct ligand - Fc portion of certain Immmunoglobulins isotypes and some of the components of the complement cascade- opsonins, this enhances the ingestion process where the particle is surrounded by cell membrane, which then invaginates and produces an endossome or phagosome within the cell. The microbicidal particles of the phagocyte are contained in lysosomes preventing the autodestruction of the cells by so toxic compounds. The phagosome and lysosome fuse forming a phagolysosome in which the ingested material is digested by a enzymatic complex. This is accompanied by increase in production of oxygen/dependent killing mechanisms (superoxides and peroxides) and the digestion.

Natural killer cells recognize changes in virus infected cell, cancer cells and destroy them by extracellular killing mechanism, damaging the membrane of the infected cell. They are enhanced by interferons that appear to stimulate their production and rate of killing.

Eosinophils polymorphonuclerar leucocytes with bilobated nucleus and granules, in very low levels. They increase their number in parasitic infections and allergies, they are not efficient in phagocytosis but their granules contain susbstances toxic to parasites, that are to big to be internalized

26) <u>Acquired immunity- general characteristics</u>

This kind of immunity can be acquired in two ways:

Induced by overt clinical infection or unapparent

Deliberate artificial immunization

Is dependent of exposure of the antigens of the invading microorganism to the cells of the immune system (macrophages and lymphocytes) to start a specific immune response to the material. This cells are pre-committed because of their surface receptors, to respond to a particular epitope on the antigen.

This response is divided in two that usually develop in parallel: Humoral and cell mediated.

Humoral immunity depends on the appearance in the blood of antibodies produced by plasma cells. Cell mediated immunity refers to any response in which the antibody plays a

L> Mature B- lymphocytes that are responsible for Ig production after Ag presentation.

Cellular immunity

subordinate role. Depends mainly on the development of T cells that are specifically responsive to the inducing agent and is generally active against intracellular organisms.
So we can say that acquired immunity is adaptive and has a high degree of specificity in distinction between self and non-self. The reaction requires several days to be effectively triggered. There is immune memory.

27) Acquired immunity – humoral immunity

This kind of immunity is named like humoral because is found in the humours (body fluids), is mediated by secreted antibodies, which are produced in the cells of B lymphocytes. B cells with co-stimulation (anthem antigen presented cell for example) transform into plasma cells which secrete antibodies. In this processes also co-operate CD4+ T-helper2 cell. The antibodies will bind to the antigens presented in the surface of the invading microorganisms, acting like a marker for their destruction recognition of antigens associated with microorganisms or foreign substances. This recognition is coupled with the ability to initiate appropriate actions (e.g., antibody production) against these microorganisms or foreign substances.

CD4+

Besides antibody production, also includes: functions of the antibody pathogen and toxin neutralization, classical complement activation, opsonin promotion of phagocytosis and pathogen elimination.

28) Acquired immunity – cell mediated immunity

Macrophages engulf antigens, process them internally, then display parts of them on their surface together with some of their own proteins. This sensitizes the T cells to recognize these antigens. All cells are coated with various substances. CD (cluster of differentiation) and there are more than one hundred and sixty clusters, each of which is a different chemical molecule that coats the surface." Every T and B cell has about 105 = 100,000 molecules on its surface. B cells are coated with CD21, CD35, CD40, and CD45 in addition to other non-CD molecules. T cells have CD2, CD3, CD4, CD28, CD45R, and other non-CD molecules on their surfaces.

The large number of molecules on the surfaces of lymphocytes allows huge variability in the forms of the receptors. They are produced with random configurations on their surfaces. There are some 1018 different structurally different receptors. Essentially, an antigen may find a near-perfect fit with a very small number of lymphocytes, perhaps as few as one.

T cells are primed in the thymus, where they undergo two selection processes. The first positive selection process weeds out only those T cells with the correct set of receptors that can recognize the MHC molecules responsible for self-recognition. Then a negative selection process begins whereby T cells that can recognize MHC molecules complexed with foreign peptides are allowed to pass out of the thymus.

Cytotoxic or killer T cells (CD8+) do their work by releasing lymphotoxins, which cause cell lysis. Helper T cells (CD4+) serve as managers, directing the immune response. They secrete chemicals called lymphokines that stimulate cytotoxic T cells and B cells to grow and divide,

attract neutrophils, and enhance the ability of macrophages to engulf and destroy microbes. Suppressor T cells inhibit the production of cytotoxic T cells once they are unneeded, lest they cause more damage than necessary. Memory T cells are programmed to recognize and respond to a pathogen once it has invaded and been repelled.

29) Immunodeficiency

Immunodeficiency refers to a group of disorders in which the immune system does not function normally. Our bodies' immune cells attack and kill what they see as foreign invaders, usually bacteria, viruses, and fungi. When the immune system does not work properly, a person is more likely to suffer from frequent and longer lasting infections, often from organisms that don't normally make most people sick. Congenital immunodeficiency is present at birth. Another type of immunodeficiency disorder is called acquired immunodeficiency, which develops later in life.

The deficiency states seen are either due to defects in one of the components of the system itself or secondary to some other disease process affecting the normal functioning of some part of lymphoid tissues. This can be inherited, developmental or acquired. The individual affected is said to be immune compromised.

Defective innate defence mechanisms can be presented in 2 forms:

-Where there is a quantitative deficiency in neutrophils that may be congenital (infantile agranulosis) or acquired as a result of replacement of bone marrow by tumour cells or the toxic effect of drugs or chemicals. ↓↓ in no.

-Where there is a qualitative deficiency in the functioning neutrophils which, while intestinal bacteria normally, fail to digest them by an enzymatic defect. Susceptibility to bacterial and fungal diseases is common, but not to viral or protozoan. ↓↓ in func.

Defective acquired immune defence mechanisms

- Primary immunodeficiencies Caused by defined genetic defects, usually rare, but severe

Can arise from failure of any developmental procesessfrom stem cell to functional end cell. A complete lack of all leukocytes is seen in reticular dysgenesis due to a defect in bone marrow stem cells in the foetus, normally leading to death of baby in one year due to recurrent intractable infections. Defects in the development of the common lymphoid stem cell give rise to severe combined immunodeficiency (both T and B cells fail to develop, but functional phagocytes are present). B cell defects give rise to several hypogammaglobulinaemias, low levels of gamma globulins (antibodies) in blood. Deficiencies of immunoglobulin synthesis is almost complete in x-linked Bruton's disease (cell mediated mechanisms function normally). Partial defects in immunoglobulin synthesis:

-wiskott-aldrich syndrome (low IgM, but high IgA and IgE) pyogenic infections, bleeding and eczema

-dysgammaglobulinaemia- deficiency in one antybody class reduced IgA rest is normal increased infections of upper and lower respiratory tracts.

T cells defects lead to more severe and persistent infections. Lack of t cells is normally associated to rise in levels of antibodies. Patients with this defect are prone to viral, intracellular bacterial, fungal and protozoan infections rather than acute bacterial infections (Digeorge syndrome)

Secondary immunodeficiencies: Consequence of some other disease (viral diseases are often immunosuppressive- measles, human immunodeficiency), treatment (irradiation citotoxic drugs and steroids), environmental factors like exposure to drugs or chemicals. Usually frequent, but usually clinically mild (exceptions: HIV disease, secondary aganulocytosis). Deficiency in immunoglobulins can be caused by deficiency in proteins due to renal disease or intestine in protein losing entheropaty. Malnutrition and iron deficiency can lead to depressed immuno-responsiveness, particularly in cell-mediated immunity. In contrast to the deficiency states raised immunoglobulins levels are found in certain disorders of the plasma cells due to malignant proliferation of a particular clone group of plasma cells (chronic lymphocytic leukaemia or multiple myeloma) malignant clones each produces a particular type of antibody. Usually with low synthesis of normal immunoglobulins and associated decrease of immune system to acute bacterial infections.

30) Immunity in bacterial infections

Inflammation

After breaking the mechanical barriers, bacterial substances and phagocytosis, the bacteria starts to proliferate in the tissues.

The presence of bacteria specific molecules are recognized by pattern recognition receptors, leading to cytokine release. These, along with tissue damaging bacterial products, trigger an inflammatory reaction. The resulting increase in permeability leads to exudation of serum proteins, including complement components, antibodies, and clotting factors as well as phagocytic cells. By chemotaxis the phagocytes are attracted to the site of inflammation. Anaphylatoxins generated by complement increase the vascular permeability and encourage exudation. These mediators also cause vasodilatation, increasing blood flow in the area. The attack is primarily directed to the external components and secreted molecules. Bacteria are surrounded by a cytoplasmic membrane and peptidoglycan cell wall (lysosomal enzymes and the outer lipid layer of Gram/negative bacteria by cationic proteins and complement). Associated to them can be a variety of other components such as proteins, capsules, liposacharides or teichoic acids. There are also structures associated with the motility (flagella or fimbriae usually attacked by specific antibodies also responsible for inactivating bacterial enzymes and toxins) or adherence to the cells of the host. Ultimately in some situations cell mediated responses are required.

31) Passive Immunization

w/o harm

The objectives in immunization are, to produce, without arm the recipient, a degree of resistance sufficient to prevent clinical attack of the natural infection and to prevent the spread of the infection to susceptible in the community. In other words, the gains are both personal and also for the population. The degree of resistance conferred may not protect against an overwhelming challenge, but exposure may help to boost immunity.

Passive immunization is where pre-synthesized elements of the immune system are transferred to a person so that the body does not need to produce these elements itself. Antibodies are used in this kind of immunization begins to work very quickly, but it is short lasting, because the antibodies are naturally broken down, and if there are no B cells to produce more antibodies, they will disappear. Passive immunization occurs physiologically in pregnancy in transfer of antibodies from mother to fetus

Artificial passive immunization is used in clinical practice when it's necessary to protect a patient at a short notice and for a limited period. Antibodies, which may be antitoxic, antibacterial or antiviral, in preparations of human (homologous) or animal (heterologous) serum are injected to give temporary protection. Homologous antisera are much less likely to produce adverse reactions, and their protection last longer (3-6 months) against heterologous (few weeks).

Treatment of diphtheria is made with antiserum raised in horse against diphtheria toxin (equine diphtheria antitoxin), also a similar serum is used in botulism, and still some countries used equine tetanus antitoxin, that is being replaced by human tetanus immunoglobulin.

Pooled immunoglobulins

Protective levels of antibody to a range of diseases are present in pooled normal human serum. Human normal immunoglobulin (HNIG) is short term prophylaxis of hepatitis (A) and agammaglobulinaemia.

Specific immunoglobulins
Tetanus (human tetanus immunoglobulin HTIG);
Hepatitis B (HBIG)
Rabies (HRIG)
Varicella-zoster (ZIG)

32) Active immunization

Active immunization entails the introduction of a foreign molecule into the body, which causes the body itself to generate immunity against the target. This immunity comes from the.T cells and the B cells with their antibodies.

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Active immunization can occur naturally when a person comes in contact with, for example, a microbe. If the person has not yet come into contact with the microbe and has no pre-made antibodies for defense (like in passive immunization), the person becomes immunized. The immune system will eventually create antibodies and other defenses against the microbe. The next time, the immune response against this microbe can be very efficient; this is the case in many of the childhood infections that a person only contracts once, but then is immune.

Artificial active immunization is where the microbe, or parts of it, are injected into the person before they are able to take it in naturally. If whole microbes are used, they are pre-treated, attenuated vaccine.

Depending on the type of disease, this technique also works with dead microbes, parts of the microbe, or treated toxins from the microbe.

Types of vaccine

Toxoids, when the signs and symptoms of a disease can be attributed essentially to the effects of a single toxin, a modified form of toxin, that preserves his antigenicity but has lost his toxicity, like in case of tetanus and diphtheria.

Inactivated vaccines - If the disease is not mediated by a single toxin, it may be possible to stimulate the production of protective antibodies by using killed (inactivated organisms) this is donne in vaccines against Pertussis (whooping cough), Influenza and inactivated Polio (Salk) vaccine.

Attenuated live vaccines

When the inactivation procedure to make an inactivated vaccine destroys or modifies the protective antigenicity (immunogenicty) of the organisms, the solution is to use suspensions of living organisms that are reduced in their virulence (attenuated) but still immunogenic. Mumps, Measles and Rubella vaccines (combined), the live-virus Polio (Sabin) vaccine and the Yellow fever vaccine.

Other aerobic	5%
Anaerobes	1%

Monomicrobial etiology, agents originate in community

Etiology of respiratory	late VAP
G- non-fermenting rods	40%
Enteric bacteria	30%
Staphs, mainly aureus	20%
Yeasts	5%

Polymicrobial origin – hospital origin

Etiology Aspiration pneumonia

same as in VAP but more G- rods, non-fermenting rather than enteric

Pneumonia in febrile neutropenia

Initial drug: G+ cocci/staphs and pneumococci occurs 2x more than G rods/enteric bacteria 8

Penicillin G given to all G+ except Staph aureus and pneumoniae

① S. aureus "Golden Staphylococcus"

- G+ coccus ; bunches like grapes
- non sporing ; non-capsulated ; non-motile
- large, round golden/whitish colonies => BA + 10% NaCl
- part of skin flora in the nose + on the skin (mucous mem)
- pyogenic infec of skin, hair + nails etc. => wound infec ; impetigo ; bacteriemia ; pneumonia, endocarditis
- facultative anaerobe
- produces (some strains) enterotoxins => act as Superantigens
  - ↳ Toxic Shock Syndrome toxin (TSST-1) => toxic shock in tampon users
- Coag +ve staphy
- produces enzyme => coagulase => plasma fibrinogen => fibrin
- " clumping factor/bound coagulase that reacts with fibrinogen => Agglutination
- Catalase +ve (∵ produces enzyme "catalase") - bubbles => $H_2O_2 \rightarrow H_2O + O_2$
- Coagulase +ve
- Hyaluronidase +ve (produces hyaluronidase => breaks the capsule of encapsulated bacteria)
- β-haemolytic - lysis + complete digestion of RBCs surrounding the colonies
- Oxidase -ve (α, β + γ)

Atb

- ↳ Staph => oxacilin
- ↳ UTI => Cefalosporins of 1st gen
- ↳ Allergic ppl => macrolides
- ↳ locomotor system infec => lincosamids
- ↳ Combination => Aminoglycosides
- ↳ MRSA => glycopeptides => VANKOMYCIN + TEIKOPLANIN
- ↳ LAST resort => LINEZOID

Septicemia
Necrotising pneumonia
Acute infective endocarditis
TSS

MRSA => methicilin resistant S. aureus
- ↳ caused by a change of mem. - Penicilin Binding Proteins (PBP)
- ↳ detected when => small zone in oxacilin + cefoxitin

Sinusitis + Otitis Media => NO need for swabs, if no puncture coz it can lead to false outcomes - misleading
- ↳ u can find other bacteria, which are just part of normal flora or ppl are carriers

② Coag -ve Staphy (CONS)

- Most common ones: *S. epidermidis* ~75%.
  - *S. hominis*
  - *S. haemolyticus*
  - *S. saprophyticus* - vaginal flora
- all part of common skin microflora
- G+ cocci, clusters, facultative anaerobes
- Non-spoing, non-motile + non-capsulated
- less pathogenic
- imp. causative agents in weakend ppl (immunocompromised) => hosp. infec. (nosocomial)
- forms biofilms on venous catheters (*S. epidermidis*)
- UTI, wound infx, catheter sepsis, bacteraemia
- Coag. -ve
- Catalase +ve
- Oxidase -ve
- Hyaluronidase -ve
- delta haemolysin → haemolysis occurs

Atb

- multiple resistance (penicillin, gentamicin, erythromycin)
- ① Oxacilin
- Vaulcomycin, Rifampicin

- Use staphylo-test for diagnostics!

vii.

③ S. pyogenes - Group A Strep (GAS)
- part of normal flora of s/cm and anterior nares.
- β-haemolytical on BA - completely breaks RBCs. => partial/complete lysis
- G+ cocci - chains ; grey in mitis ph colonies on BA
- Catalase -ve ; Oxidase -ve
- Non spoulating ; non-capsulated & non-granulated
- Facultative anaerobe - *
- Hyaluronic acid capsule present in some strains - grow as mucoid colonies on BA
  ↳ capsule has anti-phagocytic effect
- PYR +ve (only strep that is +ve)
- Bacitracin +ve (more sensitive to this than other strep). BACITRACIN DISK TEST
- CAMP -ve
- Produce 2 diff haemolysins - Streptlysin O+S => destroy membranes of RBCs + platelets (holes in the mem)
  ↳ Streptolysin O can act like an antigen!
- Latex agglutination
- Resist phagocytosis due to M-protein in the wall - varies among strains
- Diseases : pharyngitis ; acute tonsilitis
  Scarlet fever - bright red tongue w/ "strawberry appearance" ; fever
  Skin infec, e.g impetigo
  necrotising fasciitis
  erysipelas (inflam / infec of the dermis)
- If antibodies remain + circulate in the blood & bind to structures in the organs => Rheumatic fever +
  acute glomerulonephritis

Surgical Implants

Atb
Penicillin
Macrolids / erythromycin / Clindamycin

ASO test : Anti-Streptlysin-O (o) +ve
Neutralisation test ; atb blocks the effect of the toxin ∴ NO HAEM

PYR test : +ve => yellow → red PYR- Pyrrolidonyl arylamidase

④ Other β-haemo. strep

- S. agalactiae (Group B strep) - urogenital infec w/ risk of newborn infec (Pneumonia + meningitis)
  ↳ damages milk production in cattle
  ↳ normal flora of female genital tract
- Non Non B Strep
  ↳ pharyngitis
  ↳ found in healthy person's throat

Throat Swab!

- G+ cocci ; chains
- BA = grey-whitish colonies
- Catalase -ve ; Coag -ve
- Oxidase -ve
- PYR -ve
- S. agalactiae ⇒ +ve CAMP test = means stronger haemolysis in the areas around the inoculated area - butterfly like
  ↳ Bacitrain -ve
- latex agglutination ⇒ detailed diagnostics
- Non-sporing
- Capsulated - antiphagocytic

? Osteomyelitis
Conjunctivitis, sinusitis, otitis media

⇒ & Neonatal septicemia, Meningitis (w/ non-specific symp)
⇒ Adults, sepsis, pneumonia

S. agalactiae: when 2 bacteria produce haemolysins, their co-operation maybe synergic or antagonistic
↳ e.g. synergisms of CAMP of s. agalactiae + β-lysins of S. aureus

Baby - mother / baby - baby spread in wards...
↳ transmission from pregnant mother to fetus

Atb
Penicillin
Macrolides
Glycopeptides (e.g. vancomycin)

- Resistant to aminoglycosides (BA + amikacin) : amikacin can be a selective medium
  ↳ hydrolyze Sodium hippurate

CAMP test ⇒ based on formation of CAMP factor
↳ used to identify S. agalactiae ⇒ not strongly β-haemolytic on its own but wedge shaped growth in presence of S. aureus

⑤ <u>S. pneumoniae</u> – "<u>Pneumococcus / Diplococcus pneumoniae</u>"

- α-haemolytical / viridating ⇒ BA goes [GREEN!] oxidation of $Fe^{2+} \Rightarrow Fe^{3+}$
- G+ cocci – couples not chains – PAIRS!
- lancet shaped
- Capsulated – thick ⇒ protects from phagocytosis
- Non-sporulating ; non-granulated
- grey colonies ; mucoid ; green zone arnd colonies ⇒ due to α-haemolysis
  ↳ small colonies
- Catalase <u>-ve</u>
- Oxidase <u>-ve</u>
- Optochin sensitivity test – diff. pneumococci & other cocci (α-haemo). ("oral" strep)
  ↳ pneumococci from oral strept.
- Diseases : Pneumonia
  Sinusitis
  Otitis Media
  Sepsis
  Meningitis – Adults
- 40-70% of healthy adults are carriers of pneumococci
  ↳ mucosa of URT

<u>Atb</u>
Penicillin
Macrolides
Cephalosporins

- Growth on Slanetz-Bartley (SB) + Bile-Aesculin (BE) differentiates them frm enterococ

!! Prevention: Vaccine w/ Anti-Pneumococcal Capsular Polysaccharyde.

Identification: Microscopy ① encapsulated
② lancet shaped
③ occur in Pairs

Quellung Reaction: pneumococci treated w/ specific anti-sera that forms capsular swelling.

⑥ Enterococci + other strep

Diagnosis:

- "Oral" strep ⇒ Streaking / X-haemo on BA ⇒ GREEN!
  - ↳ normal oral + pharyngeal flora
  - ↳ G+ cocci - chains
  - ↳ Oxidase & catalase -ve
  - ↳ normal conditions ⇒ some enter bloodstream in small amounts
- S. mutans ⇒ dental caries
- S. mitis ⇒ found in cheek region
- S. sanguinis ⇒ ~~chest~~ oral cavity ⇒ bloodstream ⇒ endocarditis - mitral + aortic valves
- S. salivarius
- S. constellatus

Atb

Penicillin G, Macrolids, Vankomycin - 100% effective: reserve

- Müller-Hinton (MH) Agar + blood / BA ⇒ for atb susceptibility

Slanetz-Bartley - selective for Enterococci

Enterococci ⇒ E. faecalis + faecium

E. faecalis - UTI + biliary tract infect

- ↳ G+ cocci; short chains; greyish colonies
- ↳ Non-sporing; Non-cap + Non-gran
- ↳ facultative anaerobe
- ↳ Catalase -ve
- ↳ norm in intestine BUT more of a pathogen ⇒ (UTI) pathogen ⇒ need a urine sample then
- ↳ u. bladder, vagina, wounds + bloodstream
- ↳ Oxidase -ve

E. faecium

- ↳ G+ cocci; short chains; greyish colo
- ↳ Non-sporing; non-cap + non-gran
- ↳ facultative anaerobe
- ↳ Catalase -ve
- ↳ Norm. intestinal flora (GIT) + stool
- ↳ Oxidase -ve

↳ Both grow on SB Agar but ARABINOSE test used to diff them ⇒ faecalis = doesn't split - stays green = -ve

faecium = splits - yellow = +ve

↳ Atb testing on MH agar

Atb ⇒ NO CEPHALOSPORINS!

faecalis ⇒ Ampicillin

faecium ⇒ Co-trimoxazol; doxycyklin

VANKOMYCIN / LINEZOLID

(7) Corynebacterium

↳ mainly C. diphtheriae but others aswell - C. jejkeium

↳ G+ rods, pleomorphic

↳ Non-sporing, granulating

↳ in palisades; clubbed shaped appearance

↳ Aerobic + facultative anaerobe

↳ Blackish colonies after 24hours - BA - tiny colonies

↳ soil, water, plants + food products

↳ produces diphtheria toxin → harmful for target tissues ⇒ Diphtheria

↳ toxin has 2 fragments — A (active) B (binding)

↳ person-person transmission - sneeze, cough, talk (respiratory droplets) - direct contact w/ skin lesions

↳ vaccination possible - antitoxin - DPT - diphtheria, pertussis + tetanus. (triple vaccine)

↳ Catalase +ve

↳ ELK test ⇒ detection of diphtheria toxin

↳ paper w/ specific antitoxin - put on agar surface - tested strains are inoculated

↳ +ve result ⇒ ppt lines (no 2)

Found on: skin, nose, throat + nasopharynx of patients

Clinical: Hypocalcaemia

URT infection: mucus, pseudo on tonsils, pharynx, fatigue, fever

incubation period 2-5 days

Atb

Penicillin

erythromycin / rifampin / clindamycin (allergic ppl)

Non-diphtheria coryneform:

↳ normal flora of skin

↳ pathogens in wounds

Toxin produced when C. diphtheria infected w/ a bacteriophage (virus)

C. jejkeium: aerobic, cat +ve, opportunistic infx in ppl w/ bone marrow transplants

↳ Vancomycin + tetracyclines

↳ Nosocomial!

⑧ Listeria monocytogenes

cheese and meat.

- Gram +ve rods in short chains ; bacilli ; palisade arrangement
- non-sporing ; reposited after intracellular existence INTRACELLULAR
- non-granulated ; motile — not like Corynebacterium Diphtheriae
- facultative anaerobe
- enters phagocytic + non-phagocytic cells Also cat ①
- 13 serotypes
- Diseases : Intra-uterine infections Listeriosis → newborns, elderly, immunocomp.
  - Meningitis + stiff neck, headache, convulsions fever, muscle aches; 7-10 days
  - Septicaemia
  - bacteraemia + endocarditis + gastro-enteritis
- contaminated foods ; man-man (rare)
- low temp + high [NaCl] - BA 4°C - grey / colourless colonies → tiny + short chains
- grows on bile aesculin (BE) agar
- if CNS infc → need CSF + blood for culture

Atb

Penicillin

Ampicillin (+ gentamicin) → synergistic effects

Vankomycin

Co-trimoxazol

Prevention : no vaccine

proper food preparation

Detection : Tumbling motility in Liquid Media

⑨ Mycobacterium tuberculosis → TB

- Acid-fast bacteria ; straight / slightly curved rods
- lives inside cells ; single / clumps & in liquid cultures
- opportune infec of HIV
- not only pulmonary TB → brain+menings, bone, liver, spleen, peritoneum, urogenital sys, intestin
- highly hydrophobic cell wall due to mycolic acids → DON'T Gram stain
- grows slowly - long generation period → special media
  - Löwenstein-Jensen media, liquid Sula or Bantic media eggs ogawa
  - solid media in test tubes - firmly closed to prevent drying + less dangerous to personnel → 6 weeks = +ve result
  - read after 3, 6 (for sure) + 9 weeks of culture
- resistant to disinfectants - esp class A ; needs class T (against TB) & (atypical myco bac.)
- resistant to anti-microbial drugs
- non-motile ; non-sporulating ; non-capsulated
- highly aerobic
- man-man ⇒ coughing
- vaccination = BCG - live attenuated vaccine of m. bovis strain
- Ziehl-Neelsen staining = carbolfuchsine, hot temp
  - decolourise acid alcohol (HCl + ethanol)
  - counterstain - malachite green / methylene blue
  - red acidoresistant rods on blue/green background
- NaOH used before culture to kill all other bacteria
- PCR - for TB diagnostics
- Anti-tuberculotics are used, in combination, e.g. Isoniazid, Rifampicin, Streptomycin, → resistance develops easily & some only have intra/extra cellular effect
- fluorescence microscopy

- Tuberculin test

⑩ Mycobacterium leprae → Leprosy!

↳ Rod shaped (bacillus) bacterium – straight / slightly curved
↳ Acid-fast " – mycolic acids cell wall ∴ Don't gram stain } just like TB.
↳ non-sporulating; non-capsulated; non-granulated
↳ clumps, rounded masses or in groups of bacilli side by side
↳ aerobic bacterium like TB
↳ man-man transmission ⇒ nasal secretions
↳ longer generation period than TB.
↳ Ziehl-Neelsen (ZN) staining
↳ Flourescence micro
↳ Lepromin test - Mycobacterium leprae (inactivated) injected into skin
↳ produced by 9 banded armadillo
↳ (OH) used before culture ⇒ to kill other bacteria

Atb
↳ multi drug therapy for 24 months - rifampicin, clofazimine & dapsone

Leprosy ⇒ granulomatous disease of the skin + mucosa of URT
↳ skin lesions

2 Forms of the disease: ∘ tuberculoid leprosy: treated w/ Rifampicin, Lepromin (+)
∘ lepromatous leprosy: " " clofazemine, Lepromin (−)

Diagnostic

Prevention: some effects by BCG.

(1) Atypical Mycobacterium

- nontuberculous mycobacteria (NTM) / environmental mycobacteria
- divided into 3 main groups for diagnosis/treatment
- cause pulmonary disease resembling TB, lymphadenitis, skin disease, or disseminated
- small rod-shaped bacili, strictly aerobic, also not coloured by Gram staining
- natural environment - soil, water
- also part of human + animal mucosal flora (e.g. M. smegmatis)
- most of them - resistant to main TB drugs
- Diagnosis: need a culture & +ve identification
  - detected microscopically & grow on Löwenstein-Jensen medium
- infections are rare in healthy ppl
- Immunosupp. ppl - 80% of cases = M. avium or M. intercellulare
- causes pulmonary diseases resembling TB etc.
- Treatment: removal of the infection focus
  Chemotherapy - depending on the pathogen species
  Combination anti-TB drugs (ethambutol, rifampicin) - 4/5 of them

M. kansasii → Pulmonary infec, susceptible to anti-TB drugs.
M. ulcerans → chronic skin ulcers w/ necrotic centres
M. marinum → Skin granulomas (swimming pool/fish tank granulomas) wound infec + other problems
M. scrofulaceum → cervical lymphadenitis (1° in children) → SCROFULA

↓ can be caused by M. TB or Non TB Myc. in children.

Treatment of scrofula: Surgical excision of affected lymph nodes

M avium - intracellulare - pulmonary disease - T: Rifampicin

(12) Actinomycetes + Nocardiae

ACTINOMYCETES (Actinomyces israelii)

Diagnostic: ↳ filamentous bacteria - G+ rods but hydrophobic cell wall w/ mycolic acids ∴ don't Stain well; like M. tub, leprae, Non TB mycobacterium

↳ Actinomyces ; fungi-like bacteria

↳ found in the oral cavity of healthy ppl + (colon) GIT & vagina

↳ Culture: ↳ agar in anaerobic jar, T = 25-37°C ; 5-10% CO_2 for 1-2 weeks

↳ Micro: "Sulphur granules" are seen. ⇒ microcolonies of actinomycetes + cellular debris

↳ infec. can occur if they enter bloodstream after tooth extraction

↳ Clinical: eroding abscesses of the mouth, lung or GITs

↳ Cervicofacial actinomycosis — actinomycosis

↳ Thoracic "

↳ Abdominal "

↳ Treatment: Penicillin G ; surgery (drainage of pus)

NOCARDIAE (Nocardia asteroides)

↳ Similar to actinomycetes - G+ rod ; fungi-like bacteria BUT strictly aerobic

↳ mycolic cell wall ⇒ partially acid-fast ⇒ resistant to decolorization by acids in staining procedure

↳ grow as branching chains or beaded filaments

↳ Culture: ↳ - characteristic smell ∴ of soil

↳ part of normal flora

↳ respiratory transmission

↳ Clinical: same disease process + acid-fast: Pneumonia

↳ formation of abscesses in the lung, kidney + CNS

↳ Treatment: Sulphamethoxazole / Trimethoprim

↳ Nocardiosis - infectious disease - affects lungs / whole body - night sweats, fever, cough, headache, CT = cerebral abscess

↳ immunocomp. ppl (esp. men)

Atb susceptibility of actinomycetes + nocardiae

↳ disc tests — MH agar

↳ grow slowly + badly

(13) Bacillus - usually harmless microbes fm ext. environment

↳ G+ robust rods ; large, flat colonies, sm times intensive shaom lysis

↳ Spore forming ; non-motile

↳ chains + no branching

↳ facultative anaerobes / or strictly aerobes

↳ Catalase +ve

↳ PCR of nasal swab

↳ usually found in the soil - fr decades ; herbivores - cattle, sheep, goats

↳ pathogenicity due to its anti-phagocytic capsule + toxin (→ oedema + necrosis)

↳ very stable bacteria - survives drying, heat, UV light, disinfectants

↳ animal → human - cutaneous, inhalation or digestion

↳ Treatment: β-lactam atb ⇒ Penicillin,

↳ Ciprofloxacin + doxycycline

Vaccination: fr high risk individuals ⇒ vaccine composed of protective antigen

B. anthracis → anthrax (above) → leads to fatal septicemia (cutaneous), inhalation spores - haemorrhagic pneumonia, ingestion of spores.

B. cereus → intoxication from cereals (food borne illness)

B. stearothermophilus + B. subtilis ⇒ survive hot temps

↳ control orgs. for indicator + steam sterilizers → AUTOCLAVE

B. cereus

↳ motile ; aerobic ; non-encapsulated ; penicillin resistant

↳ from infected food (endospores)

↳ food poisoning: vomiting, nausea + diarrhea

↳ culture specimen from suspected food source

↳ Treatment: Vancomycin,

Clindamycin

No treatment for food poisoning

Micro: central / subterminal spores ⇒ larger than ∅ of rod

Lab id: large grey, non-hemolytic colonies on BA.

(14) Clostridium botulinum → Botulism

↳ G+ sporulating rod – ∴ gram stain (spores remain colourless)

↳ motile (has a flagella)

↳ Obligate Anaerobes – for culture anaerobic conditions (like all Clostridium)

↳ soil, blood, eggs, smoked fish, fresh honey, uncooked meats

↳ produces Neurotoxin → inhibits the release of ACh fm pre-synaptic N. terminals in ANS + motor end plates → flaccid muscle paralysis

↳ transmitted by endospores (heat resistant)

↳ 3 types of botulism:

1) food borne
2) Infant (Floppy baby syndrome -
3) Wound

↳ Treatment: Antitoxin (for food borne + wound botulism)

Penicillin

Hyperbaric chamber

Human botulism Ig (for infant botulism)

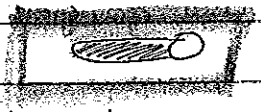
↳ Catalase –ve

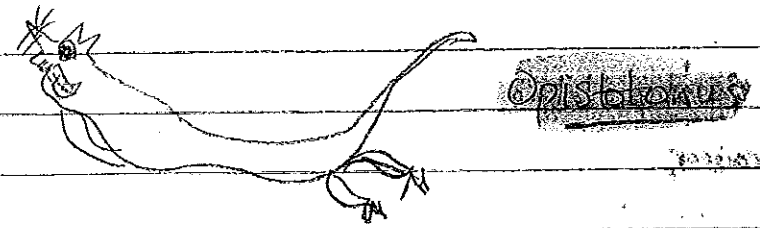
↳ Oxidase –ve

↳ NL agar + paraffin layer → anaerobic conditions / "Viande-Levure"

↳ used as botox → blocks ACh release, muscle contraction + wrinkles

(13) Clostridium tetani → Tetanus

- G+ obligate anaerobe - rod
- Sporulating → endospores at the end 
- gram stain but spore doesn't - remains colourless
- motile
- Catalase -ve
- Oxidase -ve
- soil + animal feces
- releases a toxin - causes spasms - neurotoxin → blocks neurotransmission from S-C-F-B-S. → Tetanospasmin
  - GABA (inhibitor N.T.)
  - inhibits GABA release + glycine release → ↑ freq. of impulses to muscle cells → tetanic contraction
- endospores - enter through wounds
- Tetanus: muscle spasms, lockjaw, resp muscle paralysis
- Vaccine: DPT: Diphtheria, Pertussis + Tetanus
- Treatment: Penicillin G
  - if vaccinated >10yrs ago → booster
  - never " → booster + preformed antibodies
- Diagnosis: toxin detection in wound material in an animal (mouse) test based on either neutralisation or detection of the toxin gene w/ PCR.
  - difficult to culture

Tetanic Mouse 

(16) Other clostridium

C. perfringens ⇒ Gas gangrene (war disease)

- ↳ G+ sporulating rod
- ↳ strictly anaerobe
- ↳ BA ⇒ double haemolysis
- ↳ in liquids ⇒ gas forming
- ↳ Non-motile (C. botulin and tetani are motile) and C. difficile
- ↳ Polysaccharide capsules
- ↳ soil + GIT flora + Vagina
- ↳ transmission via endospores ⇒ deep wounds with ↑ necrotising tissue
- ↳ Enterotoxins are intestinal pathogens

T: gas gangrene - amputation / Pen G

Prevention: Appropriate food practices.

Diseases:
- Gas gangrene = myonecrosis
- Cellulitis
- necrotising enterocolitis

Treatment ⇒ Penicillin

Lab Id: Fm Anaerobe culture, produces unique double zone of β-hemolysis.

C. difficile ⇒ pseudomembranous colitis ⇒ characterized by watery explosive diarrhea

- ↳ G+ sporulating rod
- ↳ strictly anaerobe
- ↳ motile (flagella)
- ↳ found in the intestine flora - toxin is produced while the clostridia multiply
- ↳ endospores, found in hospitals + nursing homes
- ↳ fecal-oral transmission
- ↳ Immunoassay for C. difficile toxin
- ↳ colonoscopy examination
- ↳ antibiotic associated diarrhea (AAD)
  - ↳ stop taking Atb

T: ↳ Vancomycin, metronidazole,
- replace fluids

(17) Neisseria Gonorrhoeae → Gonococcus → Gonorrhoea

- G- diplococcal bacteria "PAIR OF BEANS"
- coffee-bean shaped; within WBCs ∞
- facultative anaerobe or aerobe
- Catalase +ve no capsule unlike meningococcus
- Oxidase +ve
- Splits glucose only – Neisseria test → ferments glucose but not maltose like meningococcus
- culture on Choc Agar only (5–10% CO_2)
- Sexual transmission only
- purulent discharge from genitals: inflam, redness, swelling, dysuria
- conjunctivitis, pharyngitis, urethritis & cervicitis (females)
- symptomatic or asymptomatic
- females = NOT colpitis (vag. inflam) ∴ no need for vaginal swabs
  - cervical + urethral ones preferred
- Treatment: Penicillin

  Macrolids, quinolones or ceftriaxone

Pili confers resistance to phagocytosis.
Conjunctivitis in New born.

No vaccine, prevented by condom.

(18) Neisseria Meningitides → Meningococcus → Meningitis

- G- diplococcal bacteria
- coffee-bean shaped (both) - pleomorphic
- non-motile + polysaccharide capsule → antiphagocytic
- grows on nutrient rich variants of BA

Lab:
- Neisseria test - meningococcus splits glc + maltose
- latex agglutination ⇒ direct antigen detection in CSF

- transmission by droplet infection
- usually found in the throat of ~10% of the pop.
- virulence is related w/ protein antigens
- invasive infection occurs when strain is highly virulent + host is weak
  - transmitted by narrow contact ∴ when mucous mem. are damaged e.g. by smoking / prev viral infection
- can occur after large amount of physical activity after a long time of inactivity
- Penicillin G
  Macrolids, ceftriaxone, quinolones
- Men. serotype B ⇒ not preventable by vaccination, A, C ex have vaccine.
  - antibodies don't form against this serotype

Lab: Oxidative (+) (both) on CA
aerobic (both)

allow attachment to nasopharynx mucosa.

Antigens detected at CSF antigen analysis:
- N. meningitidis A, B, C + Y/W135 ⇒ Teens + children (Young adults)
- h. influenzae B ⇒ children
- S. pneumoniae ⇒ elderly
- S. agalactiae ⇒ newborns

Meningitis: if lining of Nasopharynx is penetrated → blood → crosses BBB → infection
- Symptoms: rigid neck, vomiting, sensitivity to bright light → Sepsis

(19) Salmonella Typhi → Salmonella, Typhoid fever

↳ G- rods and fac. anaerobe

↳ Motile; Aerobic; intracellular – macrophages in CN gallbladder

Lab: ↳ Glc fermenter – does not ferment lactose.

↳ Catalase +ve

↳ Oxidase –ve

↳ produces H_2S; asplenic ppl – 1 risk

↳ need stool / blood or urine sample

Lab: ↳ Culture: XLD ⇒ pale colonies + black centres

HAL ⇒ " " " "

Hajna medium ⇒ change from RED!

↳ fecal-oral transmission - contamination of food/water w/ animal feces

↳ Clinical: Typhoid fever - systemic disease w/ fever and abdominal pain, bloody diarrhea

Cavitation

Sepsis

Endocarditis

Osteomyelitis

↳ Treatment: Ciprofloxacin

Ceftriaxone

Vaccine available, prevention is proper hygiene and well cooked food.

Lab: can be cultured in MacConkey Agar: colorless non-fermenting colonies.

(20) Other Salmonella

S. choleraesuis + S. enteritidis (S. enteritis ⇒ Salmonellosis)

↳ similar to S. typhii but zoonotic ⇒ chicken + uncooked eggs

↳ Paratyphoid fever - caused by non-typhoid Salmonella

↳ Sepsis ⇒ lung, brain, bone

↳ Diarrhoea - gastroenteritis

↳ they are encapsulated + immune system reacts by opsonisation of them w/ antibodies (enhancer for the process of phagocytosis) ↓ macrophages + neutrophils in spleen phagocytose opsonised bacteria.

↳ aspleen patients - can't do that ∴ risk of salmonella infection

↳ Treatment: sepsis ⇒ ciprofloxacin
ceftriaxone

Diarrhoea ⇒ electrolyte + fluid replacement

S. enterica = S. choleraesuis

Salmonellosis = Diarrhoea
fever
Vomiting
Ab. cramps

~~S. Typhi~~

S. Typhimurium:

faecal → oral transmission, contaminated food (eggs)

→ Enterocolitis

Same as S. enteritidis.

Both: Lab: MacConkey Agar produces colourless colonies.
↳ Non-lactose fermenting

No vaccine.

Produce H_2S

(21) Shigella

≠ from Salmonella:
- no H_2S production
- no spore
- non-motile

- G- non-sporing rod-shaped
- facultative ~~aerobe~~ anaerobe, ~~non-motile~~
- Catalase +ve
- Oxidase -ve

Lab:
- non-lactose fermenting
- no H_2S production L+/L-
- Culture: MacConkey Agar - bright colour => White/colourless colonies

Lab: Endo Agar => L+ (Shigella) => clear/colourless

- found in humans only - only pathologically active in humans
- 4 serotypes: *S. dysenteriae* -> Dysentry (severe diarrhoea containing mucous &/or blood in the faeces)
  - *S. flexneri* -> diarrhoea
  - *S. boydii* -> dysentry, Indian subcontinent
  - *S. sonnei* -> "
- transmitted: ~~faecal-orally~~
- releases Shiga toxin -> causes cell destruction
  - released after invasion of intestinal epi cells - A & B subunits
  - B = binds to microvillus membrane, allows A to enter cells
  - A = inactivates the 60s ribosome, inhibiting protein synthesis -> killing intestinal epi cells
- Treatment: Fluoroquindones -> Ciprofloxacin
  - Azithromycin
  - Sulphamethoxazole
  - ~~oral rehydration therapy~~
  - Ampicillin (β-lactam)

No vaccine

Lab: serological w/ Anti-O Ab in Ags test
Endo Agar = L- colourless

(22) Escherichia coli

↳ Gr- rod

↳ facultative anaerobe ; opportune pathogen

↳ Catalase +ve

↳ Oxidase -ve

Lab: ↳ ferments lactose + glc

↳ part of intestinal microbiota, colonizes vagina/urethra and ascends to urinary tract

↳ non-pathogenic E.coli + virulence factor ⇒ disease!

Lab: ↳ Red/Pink on Mac-Conkey agar

Yellow on Hajna medium

Methylene green on EMB (eosin methylene blue) agar - inhibits growth of Gr+ bac & distinguishes lactose + non-lactose fermenters

↳ harmful if one of the following:

↳ intestinal: EPEC (enteropathogenous E.coli)

ETEC (enterotoxic ") - watery diarrhea

EIEC (enteroinvasive ") "bloody"

STEC (Shiga-like toxigenous ")

↳ extraintestinal: UPEC (uropathogenous ")

↳ Transmission: faecal-oral

migration up the urethra

colonisation of catheters in hospitalised patients

aspiration of oral E.coli

↳ Diseases: newborn meningitis

UTI

Hosp. acquired sepsis

Diarrhoea

Pneumonia

↳ Treatment: Aminoglycosides - gentamicin, amikacin, streptomycin

Cephalosporins (Meningitis)

Sulfamethoxazole & Trimethoprim

Fluoroquinolones

UTI - Ciprofloxacin.

(23) Facultative pathogen enterobac

KLEBSIELLA

↳ G- rods

↳ capsulated ; non-motile ≠ from Proteus Mirabilis.

↳ lactose fumenting - ∴ grows [illegible] on MacConkey Agar

↳ facultative anaerobe - strictly anaerobic growth = poor

↳ capsular media is produced in greater amounts on media rich in carbs

↳ Diseases : Pneumonia - in individuals compromised w/ DM., alcoholism.

UTI

Sepsis

↳ on BA => more mucoid + white than E.coli ≠ from E. Coli

↳ Sometimes haemolysis of escherchia on BA

↳ Treatment : Ciprofloxacin

3rd gen cephalosporins - Ceftriaxone

≠ from Klebsiella and E. coli

PROTEUS MIRABILIS → Doesn't grows on MacConkey Agar = colourless/clear

Non-lactose fermenter ; G- facultative anaerobe ; rod shaped

↳ Characteristic smell ; motile ; produces H_2S ; Catalase +ve

↳ urease +ve ; found in the intestinal tract Oxidase -ve

↳ don't grow only on inoculation plate but spread on agar surface. => SWARMING PHENOMENON

↳ urine exam. = high pH (splitting of urea → $NH_3 + CO_2$) UREASE (+)

↳ Diseases : UTI

bladder stones

Sepsis, wound inf + pneumonia in hosp. patients NOSOCOMIAL INF

↳ Treatment : Ampicillin

Sulfamethoxazole + Trimethoprim

(24) Pseudomonas Aeruginosa

↳ colonies + infects sick + immunocompromised hosp. patients
↳ resistant to almost every atb
↳ G- non fermenter; rod -:. colourless colonies on MacConkey Agar
↳ strict aerobe, encapsulated :; [illegible]
↳ motile ; Pleomorphical
Lab: ↳ oxidase +ve ; Catalase +ve
Lab: ↳ green on MH (Mueller-Hinton) Agar ; grows on Endo Agar (colourless)
Lab: MacConkey ↑ non-fermenter
↳ from soil, water, skin flora, intestine
↳ infects immunocomp. ppl / ppl w/ burns / A&E / transplant centres
↳ opportunistic human pathogen
↳ ~~grows on endo agar~~
Transmission: Water w/ faecal matter, faeces.
↳ Diseases: Pneumonia
↳ Cystic fibrosis patients → chronic pneumonia
↳ Immunocomp. patients
Osteomyelitis
Soft tissue infec.
Sepsis
UTI
Endocarditis (IV drug users)
↳ Treatment: resistant to most Atb
Aminoglycosides ⇒ gentamicin, amikacin
Cephalosporins ⇒ ceftazidime
Quinolones ⇒ Ciprofloxacin
w/ anti-pseudomonal activity

Most Common Cause of Nosocomial Infections

(25) Pseudomonas mallei & Pseudomonas pseudomallei

aka Burkholderia mallei

- G- aerobic
- non motile
- bipolar staining ?

Disease : Incubation period of 1-14 days

Appears in 3 forms :

- Chronic pulmonary - w/ cough + mucopurulent discharge
- Farcy form - multiple abcesses in the skin, subcutaneous tissue + lymph
- Acute septicemic - w/ fever, chills, prostration & death 7-10 days

Mainly in horses ; humans = accidental hosts

Transmission : direct contact w/ nasal secretion of equines ?
inhalation of aerosols ; enter humans via microtraumas in skin/mucosa
survives in water at room temp. for 30 days

Treatment : ~~Resistant to Tetracycline~~

- gentamicin (Aminoglycoside)
- Ciprofloxacin (Fluoroquinolone)
- Doxycycline (tetracycline)

aka Burkholderia pseudomallei ~~→ melioidosis~~

- G- rod ; aerobic
- motile ≠ from Mallei (non-motile)
- bipolar staining
- wrinkled colonies on agar media
- culture fm sputum, blood or pus
- water, soil, sheep, horses, swine, monkey & rodents
- enters via injuries of skin/mucosa

Transmission : contact w/ mucous mem w/ lesion discharge of infected animals
acquired by ingestion, inhalation or contact of wounded/burned skin w/ contaminated soil/wat

Disease : Melioidosis - Acute - fever, bloody purulent sputum → sepsis + death
(Thailand + Australia) - Chronic - pneumonia/lung abscess

Treatment : Ceftazidime

(26) Campylobacter

↳ 1 of 3 most common causes of diarrhoea (watery, sometimes bloody) in the world (E.coli + rotavirus)

↳ C. jejuni (Gastroenteritis)

↳ G- curved rods

↳ Catalase +ve

↳ Oxidase +ve

↳ Microaerophilic (needs O_2 to survive, but can manage w/ ↓$[O_2]$)

↳ motile

↳ Culture : needs 4 special conditions

↳ special selective media, enriched w/ charcoal, Atb/anti-mycotics

↳ ↓ pO_2

↳ temp ~ 42°C (coz it is a bird pathogen)

↳ prolonged culture period ~ 48hours (BA)

↳ zoonotic disease (poultry) ; animal feaces

↳ faecal-oral - contaminated water, unpasteurised milk & undercooked meat

↳ person-person - sexual contact

↳ Enterotoxin - similar to cholera's toxin + E.Coli

Cytotoxin - destroys mucosal cells in S.intestine

↳ Treatment : Fluoroquinolone

erythromycin

↳ Anal swab! - Cotton swab + transport medium

(27) Helicobacter pylori ⇒ peptic / gastric / duodenal ulcers + gastritis
↳ G- curved rod
↳ urease +ve
↳ microaerophilic (90% N_2, 5% CO_2 & 5% O_2)
like Campylobacter { ↳ Catalase +ve
↳ Oxidase +ve
↳ Can form biofilms ; motile
↳ found in the stomach of healthy ppl
↳ survives at low pH by alkalinising the environment + splits urea: UREASE (+)
$NH_2CONH_2 + 3H_2O \rightarrow CO_2 + 2NH_4OH$
CO_2 exhaled; NH_4OH ammonia - remains + alkalises
↳ Culture: from stomach biopsies are grown on enriched media + selective media under microaerobic conditions
↳ ~5 days before any growth is visible
↳ ELISA / Western blotting
↳ Urea breath test: patient gets a mixture of urea w/ heavy carbon isotope (^{13}C) or radioactive isotope (^{14}C)
↳ healthy ppl ⇒ urea → bowel → stool → out of body
↳ presence of h. pylori ⇒ split in the stomach - labelled CO_2 in air
↳ ↑ CO_2 = ↑ helicobacter
Urea ~~labelled~~ breath test
↳ Zoonotic (wild/domestic animals + poultry)
↳ fecal-oral, unpasteurised milk + uncooked meat (like Campylobacter)
↳ ~~Vacuolating~~ vacuolising cytotoxin A - destroys epi cells (VaCA) vacuolising cytotoxin A
↳ Treatment: Ampicillin
Tetracycline
Bismuth
Clarithromycin + omeprazole → both reduce duodenal ulcer relapse

(28) Vibrio + Vibrio cholerae: → Cholera

- Gr- Curved rod ; Comma shaped
- Oxidase +ve - distinguishes from enterobacteria
- motile - flagella
- Glc fermenter ; grows on endo agar
- Aerobic - facultative anaerobe Hajna medium = +ve = yellow NOT RED!
- halophilic (likes salt) ; enterotest 16 - biochem identification
- Capsulated

- Culture: special media - alkaline peptone water = liquid media
  37°C TCBS + thioglycolate, cystein, bile salts = solid media
- contaminated water ; raw / undercooked seafood
- produces toxin = Cholera toxin
- Watery diarrhoea - subtropic + tropic countries
- Antigen analysis to find out major serotypes of v. cholerae : O1 + O139
- Treatment: Fluoroquinolone + doxycycline
  replacement of fluids + electrolytes

- other members of vibrio genus => cause diarrhoea + wound infec.
- ~~opportunistic~~

V. vulnificus - Gr- motile curved rod
- estuaries, ponds, costal areas
- after eating seafood
- Septicaemia (food or wounds)
  - Vomiting
    diarrhoea
    Ab. pain
    blistering dermatitis

Lab: • Quellung • CA w/ NAD+ • Ag detection from capsule.

Penicillin

- Gram ⊖
- C.A
- Hemophilus < Influenza / Parainfluenza; • Ducreyi

(29) Haemophilus

↳ belongs to Pasteurellaceae family
↳ haemophilus influenzae:
  ↳ capsular type B (Hib) → epiglottitis, meningitis + sepsis
  ↳ " " " A, c, d, e, f
  ↳ Non-encapsulated strains
↳ haemophilus parainfluenzae → needs factor V fm blood – more common + less pathogenous
↳ " ducreyi ⇒ sexually transmitted ⇒ ULCUS MOLLE + Chancroid
  ↳ subtropic + tropic regions – genital ulcers!

Hib:
↳ G– short rods
↳ Doesn't grow on Endo Agar / BA – can't get inside RBCs for nutrients.
↳ Quellung test +ve – has a capsule (anticapsular antibodies bind to the capsule → it swells + visible)
↳ Culture: Choc Agar – ↑pCO₂ + T~32°C
  ↳ [redacted]
SATELLITE PHENOMENON, e.g. [redacted] – tiny colonies; need factors X & V fm blc
  ↳ grows on Levinthal agar
  ↳ Antigen analysis – Ag's from capsule
↳ human–human via resp. route
↳ Diseases: epiglottitis, meningitis – newborns, sepsis, pneumonia, COPD – Chronic obstructive pulmonary disease, Sinusitis, Otitis media
↳ Treatment: resistant to ampicillin + vancomycin BUT suscep. to PENICILLIN
  ↳ vaccination = Hib; amoxicilin; 3rd gen cephalosporins ⇒ Cefotaxime

H. Ducreyi ⇒ STD causing chancroids (ulcus molle)
  ↳ Use PCR to rule out syphilis, herpes...
  ↳ only needs factor X fm blood to grow
  ↳ Treatment: erythromycin; Azithromycin, cefatriaxone

Choc Agar!
opportunistic microorg

H. vaginalis ⇒ STD causing vaginitis
  ↳ clue cells ⇒ vag. epi cells contain tiny polymorphic bacili w/ cyto
  ↳ Doesn't need factor X or V

30) Bordetella → Whooping cough (pertussis) · production of mucous
phases: Catarrhal (dry)
Paroxysmal (wet)

↳ Gr- rod ; small coccobacilli

↳ Oxidase +ve capsulated colonize in resp. tract.

↳ aerobic

↳ Culture: special media: BG-(Bordet-Gengou) 🍚.

ELISA, PCR

↳ B. pertussis + B. parapertussis ⇒ whooping cough

↳ rare due to vaccination

↳ nasal swab - nasopharyngeal swabs ✗ calcium alginate swabs NOT cotton

↳ pertussis toxin

↳ humans - humans - inhalation

↳ Treatment: erythromycin (like N. gonorrhoeae)

vaccination - DPT (diphtheria, pertussis + tetanus)

↓

diphtheria + tetanus toxoids & killed whole cells of B. pertussis (=W.P.)

Bordetella pertussis

(31) Legionella ⇒ Legionaire's disease

↳ Legionella Pneumophilia

↳ G- rod ; aerobic ; ubiquitous aquatic organism

↳ facultative, intracellular parasite, monotrichous flagella 

↳ severe disease

↳ bacteria reservoir in water pipes, air conditioning etc ; human-human inhalation

↳ Culture : special media - Buffered Charcoal yeast extract

↳ ~~blood agar or chocolate media~~

↳ can survive by going into a low metabolic state + survives in biofilms

↳ Diseases : Pontiac fever ⇒ milder + resembles acute influenza + NO Pneumonia

Legionaire's disease ⇒ Pneumonia

↳ Treatment : erythromycin (as B. Pertussis and H. Fb)

Rifampin

Macrolids, tetracyclines + quinolones

immunocomp = ↑risk (smokers, COPD sufferers) ⇒ Legionaire's.

Pontiac Fever - usually in healthy ppl.

2D : Pontiac Fever : like influenza

Legionaire's disease : Pneumonia, watery diarrhea, malaise, vomiting

No vaccine.

(32) Brucella → Brucellosis

↳ G- rod, small coccobacilli

↳ obligatory aerobe;

↳ non-motile;

↳ non-encapsulated; facultative, ~~intracellular parasite~~ of RES

↳ several species - names for animals they come from

↳ penetrates the skin, conjunctiva, lungs + GIT ⇒ lymphatic spread

↳ incubation period of 10→30 days

↳ Chronic infec. in animals, life long.

↳ to humans via direct contact w/ animal tissue — occupational disease

animal products - milk or urine

↳ B. abortus ⇒ bovine pathogen

↳ humans = Bang disease

↳ Reservoir / transmission: B. militensis (goats) — headache + fever

B. abortus (cattle) — night sweats

B. canis (dogs) — fatigue + anorexia

B. suis (pigs)

↳ Treatment: Doxycyclin + rifampin

Gentamicin / Streptomycin / rifampin

Prevention: Immunisation of cattle

Pasteurisation of milk

D: Brucellosis: malaise, sweats, fever, neurological disturbances.

Labo Id: Smear / culture on B.A.

(33) Yersinia → Bubonic Plague

↳ G- rods w/ bipolar staining pattern
↳ facultative anaerobe
↳ Oxidase -ve
↳ enterobacteriaceae
↳ Glc fermenter
↳ Non-motile, encapsulated
↳ facultative intracellular
↳ Culture: CIN agar - tiny dark pink colonies (Cefsulodin, Irgasan, Novobiocin)
↳ endo agar (since it is G-)
↳ Hajna medium - NOT red ∴ ferments it
↳ Antigen analysis - slide agglutination (for confirmation)
↳ Y. pestis - found in rodents (+ fleas) → transmition
↳ Diseases: Bubonic plague - painful, swollen lymph glands ⇒ buboes → lead to septic shock and death.
Sepsis
Pneumonic plague
↳ Treatment: Streptomycin
Gentamicin
Doxycycline

Y. enterocolitica - enteric bacterium
↳ G- rod, motile (≠ from Y pestis - non motile)
↳ blood/stool cultures
↳ colonoscopy of terminal ileum
↳ zootic - pigs
↳ indigestion of contaminated food/water
↳ unpasteurised milk
↳ Disease: Acute gastroenteritis
↳ Treatment: Abx like above (but doesn't affect diarrhoea)
Doxycycline
↳ rehydration + electrolytes

(34) Francisella Tularensis → Tularemia

↳ G- rod
- ↳ Obligate aerobe
- ↳ facultative intracellular parasite
- ↳ Non-motile
- ↳ Anti-phagocytic capsule

↳ Culture: BA w/ cysteine → very dangerous; 10 orgs can cause the disease
↳ agglutination test - highest dilution giving a +ve reaction
↳ tick bite; direct contact w/ infected animal - microtrauma or mucosa
↳ inhalation, ingestion → Gamekeepers + cooks at risk

↳ Diseases: Tularemia ⇒ "hare plague"
Pneumonia

↳ Treatment: Gentamicin / Streptomycin, doxycycline
vaccination for high risk individuals (live attenuated)

Ulcer at the site of entry (lesion)

needs BCYE for cultivation

Fever
lethargy
Anorexia
Signs of septicemia
poss. death!

Tularemia:
- flu-like symptoms
- GIT troubles
- Ulcers from tick contact
- Lymph adenopathy.

(35) Bacteriodes + other non-sporing anaerobes

BACTERIODES (3) D: bacteremia, peritonitis, ab. abcesses.

↳ mainly anaerobes found in the human colon
↳ part of normal flora; cause disease when they enter tissues/blood-surgery/trauma
↳ most common cause of serious infx caused by anaerobes
↳ Rods / cocobacilli – G- rods.
↳ polysaccharide capsule => resistance to phagocytosis
↳ after trauma: from colon -> blood/peritoneum => endogenous infx & doesn't spread person-person
↳ Major disease causing one: B. fragilis => from colon -> blood; multiplies: - bacteremia
↳ if into ab. cavity => peritonitis / ab. abcesses
↳ foul smelling; large amount of exudate
↳ on BA w/ anaerobic conditions.
↳ Treatment: Drug resistance! Aminoglycans = ineffective (β-lactams aswell)
B. fragilis => ~~metr~~ metronidazole / ampicillin-sulbactam
Surgical drainage of any abcesses
pre-op atb => cefoxitin

OTHER NON-SPORING ANAEROBES: Gut, oral biofilm, Vagina

↳ part of common microflora:
↳ L. bowel = 99.9% of total microorgs
↳ oral cavity = survive in the biofilm (no air!)
↳ vagina = ~ 70% of females have it => overmultiplication – treatment
↳ in inflam => usually no single pathogen but a mixture => "Veillonella flora"

G+ cocci: Peptococcus / Peptostreptococcus (4) D: dental infx, ulcers, cellulitis, aspiration pneumonia
↳ normal flora of mouth, GIT, genital tract + skin
↳ only endogenous infx
↳ Site of infection: usually part of mixed infx; all abcessesses; dental infx; musculoskeletal ulcers; cellulitis; lung: aspiration pneumonia

G- Cocci: Veillonella (2) D:
↳ lactate fermenting abilities
↳ norm. bac in intestines + oral mucosa
↳ rare cases of osteomyelitis + endocarditis

Gr+ bacilli : Eubacterium / Propionibacterium

↳ norm skin flora ; rare cases => endocarditis of plastic implants

↳ P. acnes ⇒ acne

Gr- bacilli : Leptotrichia, Bacteroides, Fusobacterium, Prevotella, Porphyromonas

Fusobacterium

↳ can adhere w/ both Gr- + Gr+ plaque micro-orgs in biofilms ∴ highly invasive

↳ gain energy via fermenting carbs + certain A.A.

↳ F. nucleatum => typical subgingival plaque

involved in periodontal diseases

invasive human infec of head, neck, chest, lung, liver + pelvic abdomen.

Prevotella

↳ non-motile ; rod-shaped ; singular cells.

↳ host-associated - colonising the human mouth

↳ colonise by binding/attaching to other bac + epi cells ∴ creating a larger infec

↳ natural atb resistance

↳ Infections : abscesses ; bac. wound infec, bite infec ; genital tract infec + periodontitis

↳ Atb : Metronidazole

Amoxicillin

Clindamycin

Chloramphenicol

↳ Anaerobiose needed :

↳ anaerobic box - air is replaced by a mixture of anaerobic gases

↳ VL broth + paraffin

↳ grow on VL blood agar

(36) Treponema Pallidum → Syphilis

↳ G- Spirochete bac. → cell wall too thin to stain (similar to G-)

↳ highly motile - helical structure ∴ moves in corkscrew motion thru mucus (e.g.)

↳ Doesn't grow in culture

↳ Sexually transmitted; vertical transmission → mother-fetus; horizontal → person-person

↳ enters via break in the skin or by penetrating mucous mem.

↳ secrete hyaluronidase → breaks ground subs. ∴ spreads infec.

↳ classic Sexual disease

↳ systemic disease - later stages: whole body is affected

↳ can be latent for upto 30 years!

Lab: ↳ Micro using dark-field, flourescence or immunoflourescence microscopy — antigen detection but diff

↳ wet mount dark field → treponema shines (immersion is used)

↳ Indirect methods: Non-treponema test → cardiolipin from bovine hearts (Antigen)

↳ RPR - Rapid Reagin Test → turbidity = +ve

↳ less specific; false +ves but gd fr screening + monitoring

Lab: ↳ Treponema tests - real antigen from T. pallidum

↳ agglutination of carrier (RBCs) - potato shaped = +ve ; dot = -ve (≡) +ve

↳ TPHA → Tr. passive haemagglutination test

TPPA → same but RBCs replaced by polycellulose

↳ for confirmation of results: ELISA + Western blotting (→ highly specific)

↳ exam. of IgG + IgM antibodies = imp → IgG +ve = proof of prev. infec.

↳ Animal exp: Rabbit Infectivity Test (RIT) - minimised due to ethics (NZ rabbit)

↳ Syphilis → 3 stages: ① genital/oral chancre (ulcus durum) ~ 3 weeks to occur

② red, maculopapular rash on any body part

③ - 40% of infected ppl - this stage occurs → degeneration of NS, CVS lesions → aneurysms, gummas, aortal dissection

↳ Treatment: P+2 Syphilis → Penicillin G injection (allergic - erythromycin/tetracycline)

late " → benzathin penicillin (3 times after 7 days)

Congenital syphilis: pregnant woman can transmit it through placenta → can cause Abortion.

G⁻ spinal rods 2 Lab Tests: • Giemsa - Wright stain • PCR

37) Borrelia → all 3 cause Lyme disease; just diff. parts of the world

B. burgdorferi → G⁻ bacteria but stain poorly

USA ↳ contains B. garinii, B. afzelii & B. Burgdoferi

↳ vector borne diseases, transmitted by ticks (deer, rodents, mammals) ← Europe →

↳ endoflagella : highly motile

↳ linear plasmid + chromosomal DNA ; no person-person!

B. afzelii → Lyme disease

↳ cultured using blood samples w/ Giemsa/Wright stain → diff + 6-8 weeks!

↳ PCR

Lab: ↳ Serological: IgG + IgM antibodies using ELISA ; +ve result → Western blotting confirmation

↳ Treatment: Amoxicillin + doxycycline → early stages

vaccination ~ 90% effective

↳ 3 stages of Lyme disease: ① 3-32 days after bite → red, circular lesion ↳ erythema migrans

↳ lymphatic spread

② weeks → months - arthritis, meningitis

③ months → years - chronic arthritis, progressive CNS disease

B. recurrentis → Relapsing fever

↳ large culturable

↳ can change surface protein antigens

↳ recovery followed by relapse → new relapse → new antigenic variant arise

↳ endemic relapsing fever → Lyme disease ≠ from B. afzelii

epidemic → human-human; body lice

↳ ↑ fever, headaches, muscle pain ~ 3-5 days + spirochets in blood

↳ recovery for abt 4-10 days (+ bc spirochets) then fever again

↳ Giemsa / Wright staining → loosely coiled spirochets

↳ erythromycin + penicillin

↳ NO vaccines ≠ from Azfelii

(38) Leptospira ⟶ Leptospirosis

↳ Leptospira Interrogans

↳ cell wall similar to Gr but [illegible] : doesn't stain well

↳ Spirochete ; long ; slender ; flexible ; spiral rods.

↳ highly motile ; cultured on special medium

↳ sensitive to drying + broad range of disinfectants

↳ can survive for weeks in highly alkaline water

↳ leptospirosis → animal disease transmitted to humans via contaminated water/food w/ animal urine

↳ can also enter via small skin abrasions or conjunctiva

X D: ↳ serovar Icterohaemorrhage → jaundice + bleeding

↳ " Grippotyphosa → Field / Canefield fever

↳ flu-typhoid symptoms

Lab: ↳ Dark-field micro

↳ Serologic agglutination tests - latex agglutination

↳ viral demonstration of spirochetes in urine/blood or CSF

↳ cultured on special media

↳ early stages = Penicillin G + doxycycline

later " = nothing

↳ No vaccine available

↳ prevent exposure to contaminated water or food

3 D: • serovar Icterohaemorrhage → jaundice + haemorrhage

• " Grippotyphosa → marsh fever

• Meningitis.

T: Doxycycelin

(39) Chlamydiae — not decolorised w/ gram stain

↳ small; round/ovoid; cell wall (lipid bilayer) (structurally G-)

↳ no peptidoglycan or muramic acid

↳ obligate intracellular parasites => grows in cytoplasmic vacuoles in a limited no. of host cell types

↳ energy parasites => depend on host cell for energy: ATP + NAD+

↳ have ribosomes + synthesise proteins ∴ sensitive to atb which inhibit this process - tetracyclines (doxycycline) + macrolides (erythromycin) => TREATMENT

↳ 3 species: ① C. trachomatis => genitourinary tract infec + eye (trachoma)

↳ trachoma (eye) ↳ inclusion conjunctivitis (newborns) + Swimming Pool Conjunctivitis

3 D: Genitourinary inf. ↳ Nonspecific urogenital infec (males + females) => urethritis, cervicitis, salpingitis

↳ lymphogranuloma ↳ lymphogranuloma venereum - warm climates mainly

② C. psittaci => ornithosis or psittacosis (birds); via their faeces - LRT

③ C. pneumoniae => infec of URT + mild form of pneumonia

↳ Identification: NOT gram staining but visualised using stains that reveal architecture

↳ Direct immunofluorescence

↳ C. trachomatis => no. of serovars - each correlate w/ a clinical syndrome, e.g.

A, B, C => trachoma

D-K => inclusion conjunc + urogenital infec.

↳ Identification: C. trachomatis: fluorescent antibody staining; DNA amplification (PCR)

↳ Culture: McCoy cells (tissue culture of several human cell lines) - 2-7 incubation days

↳ serovars can be detected using immunofluorescence staining w/ monoclonal atbodies

↳ C. psittaci => 4fold ↑ in antibody titre w/ either complement fixation or indirect immunofluorescence tests

No vaccine.

C. trichomonas: most common sexual transmitted disease in U.S.A. => Sterility

T: Doxycyclin for all 3.

G⁻ rods

(40) Rickettsia, Coxiella + Ehrlichia

↳ all 3 species belong to group = RICKETTSIALES } common features:

1) Intracellular parasites
2) the infx are transmitted by infected arthropods - ticks, fleas, mites
3) diseases are usually generalized infx

(Rickettsia Rickettsii)

RICKETTSIA ⟶ Typhus + Spotted fever

30: • Spotted Fever: fever, malaise, rash
• Louseborne Typhus:
• Murine Typhus

↳ feathers of prokaryotic cell
↳ rod-like; small; coccobacilli
↳ G- cell wall - double layered BUT stain poorly ⇒ are found inside host cells; polychrome staining ⇒ good ⇔ Giemsa / Macchiavello
↳ leaky p.mem.: easily permeable to host nutrients + coenzymes
↳ affinity for endothelial cells (circulatory system)
↳ ① Tick/flea bite ② enter host cell (similar to phagocytosis)
③ multiply in nl + cyto ④ mobilise host cell actin fibrils ⑤ host cells are killed + rickettsial spread throughout body via bloodstream / lymph. Focal thrombi formed.
↳ Diseases: ① Rocky Mountain spotted fever - R. rickettsii - tickborne
② Louseborne (epidemic) typhus - R. prowazekii - person-person by an infected human body louse (faeces) - poor sanitation; crowding
③ Murine typhus - R. typhi - milder than above - bites of infected rat fleas or urban rodents
↳ Identification: serologic procedures ⇒ detection of rickettsia-specific antibody response during the course of the infx.
↳ infected cells - immunofluorescence / histochemical procedures (biopsies on rashes)
↳ Treatment: Doxycycline - adults + children
R. rickettsii in preg women ⇒ Chloramphenicol
Prevention ⇒ vector control

COXIELLA ⟶ Q fever only Rickettsiae not transmitted by arthropods to humans.

↳ C. burnetti → Q fever (Q-query cos cause was unknown)
↳ distinguishing features:
① grows in cyto. vacuoles + stimulated by low pH of phagolysosome
② resistant to heat + drying; can live for long periods outside
③ Diseases in livestock, in humans via inhalation of infected dust in barnyards etc.
↳ aerogenic transmission

↳ reproduced in resp tract → disseminated to other organs
↳ Classical Q-fever = interstitial pneumonitis - maybe complicated w/ hepatitis, myocarditis or encephalitis
↳ self-limiting infecs.
↳ Identification : serological assays
↳ Treatment : Doxycycline or erythromycin

EHRLICHIA : ——→ Ehrlichioses
↳ infects WBCs - intracytoplasmic bacteria that infect monocytes + granulocytes
↳ G- (resembles rickettsia)
↳ they divide by binary fission - in host cell vacuoles ⇒ form morulae (large, mulberry shape
↳ 2 forms of tickborne ehrlichioses : ① human monocytic ehrlichioses (HME) -
↳ E. chaffeensis
② human granulocytic anaplasmosis (HGA) - Anaplasma Phagocytophilum
↳ Deer/dog tick bites
↳ Identification : antibody assays,
PCR
↳ Treatment : Doxycycline

not seen w/ Gram stain → NO CELL WALL
Normal flora of mouth + genitourinary tract.

(41) Mycoplasma pneumoniae → Atypical Pneumonia
- bacteria that lack cell wall ∴ unaffected by many atb
- coccoid cell body
- very small ∴ pass through biologic filters
- transmitted by resp droplets ⇒ LRT infec. (1° atypical pneumonia)
  - ↑↑ incidence ⇒ 6-20 yrs old
- attaches to the mucosa of host organism - extracts nutrients + grows + reproduces by binary fission
- atypical coz ⇒ longer course + lack of sputum prod + many extra-pulmonary symptoms
- Diseases: • pharyngitis
  • Bronchitis
  • Atypical Pneumonia ⇒ fever, chills, malaise, headache, dry cough
  • Ear infec

40

- Identification: Sputum samples / throat swabs ⇒ special media ⇒ 8-15 days
  - Serologic tests ⇒ Specific atb detected by complement fixation using an extract of mycoplasmal glycolipids (CF Tb)
- Treatment: Doxycycline or azithromycin
  - org. may remain in a recovery person in URT for weeks.

M hominis : 20: pelvic inf. disease, postpartum fever
Ureaplasma Urealyticum : non-gonococcal urethritis; endometritis (♀) T: Doxycycline

(42) Urogenital mycoplasmas

↳ M. hominis - vagina; normal flora (not always) → pelvic inflam. disease
↳ Ureaplasma urealyticum - urogenital flora (M+F) ~70% of sexually active humans.
↳ transmitted sexually, mother-neonate (during birth), or hosp acquired infxn via transplanted tissues.
↳ M. hominis: postpartum/postabortal fever
↳ isolated fm blood cultures in ~10% of women
↳ no. of serotypes → all resistant to erythromycin ∴ TETRACYCLINES.
↳ U. urealyticum: urethritis (men, where no chlam or gono).
↳ women: endometritis + vaginal secretions, premature labour / deliver low birth weight babies
↳ comes + goes : should clear up in 10 days of doxycycline treatment
↳ other Symp: gall/kidney stones, chronic fatigue, arthritis, asthma...
↳ Identification: cultures: M. hominis: degrades arginine; "Fried egg" colonies on GlcAgar medium 24-48 hrs
U. urealyticum: hydrolyses urea; G- (no cell wall)

M. genitalium: parasitic bacterium; motile - specialised tip to attach to surfaces + glide
↳ invade + adhere to epi lining of urogenital + resp tracts, sexually transmitted. across them
↳ urogenital infxn (M+F)
↳ flask-shaped + no cell wall
↳ p. mem - > 2/3 = proteins
↳ damage done by toxins + harmful metabolites → H_2O_2 + superoxide metabolites
↳ Men: urogenital tract disease
↳ Women: cervicitis + pelvic inflam. disease
↳ Identification: diff to study in vitro conditions - strict growth requirement
↳ lack genes for AA biosynthesis + few genes for nl acid, vitamins + FA synthesis
↳ get them via host or artificial medium

Resistant to β-lactams.

(1) Composition of viruses

- only proteins + nucleic Acids (DNA/RNA)
- acellular particles
- lack independent metabolic processes → ∴ no metabolic system - depend on mechanisms of a living cell ∴ need a host to reproduce in/
- can be infect animals/plants or bacteria - bacteriophages (→ virus that infect bacteria) viruses
- viral particle = "VIRION" - Mature virus particle; consists of:

① **Genome** — DNA / RNA; -ds / -ss; +(plus) / -(minus); linear or circular

DNA - usually ds. double stranded

RNA - " ss except REOVIRUSES

+ve/sense strand: if genome RNA has the same polarity as viral MRNA

② **Capsid** - made of subunits - Capsomeres

- virus coded proteins enclosing the nl. acid + determines antigenicity
- cubic (rotational), helical or complex symmetry
- protects nucleic acid from degradation
- used for viral attachment to host cell - NOT in enveloped viruses.

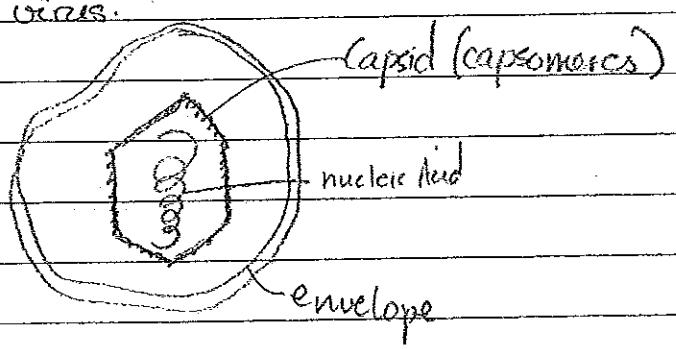
• **Nucleocapsid**: in ALL viruses

- nl acid (RNA/DNA) + protein capsid

③ **Envelope** - NOT IN ALL. — enveloped / ← unenveloped — LESS RESISTANT (more sensitive to dessication, heat + detergents ∴ easier to sterilise)

- surrounds the capsid
- from cellular membranes of host cell — ∴ lipidic bilayer w/ viral proteins inside
- enveloped cells - use this to attach to hosts
- removing this using organic solvents - ↓infectivity of the virus.

Enzymes! - e.g. neuraminidase needed for invasion + release of myxoviruses, DNA polymerase in small pox virus.



② Virus-Cell Interactions (2 interactions)

↳ quick process, ⇒ fusion of viral envelope w/ cell membrane

- ↳ PRODUCTIVE INTERACTIONS ⇒ viruses that infect + replicate within cells causing the cells to lyse when the progeny virions are released (CYTOLYTIC CYCLE)
- ↳ NON-PROD: viruses infect cells but DON'T complete the replication cycle

Cytolytic Growth Cycle: ① virus particle comes in contact w/ host cell
② capsid binds to specific receptor
③ virion enters/penetrates host
④ Partially uncoated to reveal viral genome + macromolecular synthesis of virus components occurs
⑤ mRNA - transcribed + translated into proteins (stored in inclusion bodies)
⑥ newly formed virus particles are assembled + released during cell lysis

Host cell either — • Permissive
• Non-Permissive } ↳ depends on outcome virus-cell interaction

Interaction of viruses w/ cells results in:
① prod. of new virus particles w/ or without cell lysis
② abortive infec. (non-prod. infec.)
③ Latency - virus exists w/ limited expression of viral genes, (active later on - herpes virus)

Effects of interaction:
① Lysis
② Fusion of (virus infected) cells into multinucleated cells ← ex: Herpes V., Paramyxovirus
③ Malignant transformation
④ No apparent morphologic or functional change

inhibition of host cell protein synthesis
" of DNA/RNA synthesis

CPE - Cytopathic effect - change in appearance of virus infected cells that ends in lysis or giant cell formation

③ Antiviral agents - only inhibit viral development.
↳ specific to viruses but don't destroy target pathogens; only inhibit their development!
↳ enteric, local or oral routes
↳ limited influence in therapy; some viruses only

e.g.
① Amantadine: inhibits viral uncoating
↳ blocks ion channel & prevents entry of virus in cell

② Acyclovir, Ganciclovir, Ribavirin: inhibition of viral nucleic acid synthesis
↳ inhibit herpesvirus DNA polymerase

Acyclovir - HSV & VZV (Herpes simplex virus, Varicella zoster virus)
Ganciclovir - CMV (Cytomegalovirus)
Ribavirin - Resp. Syncitial virus (RSV)

③ Saquinavir, Indinavir: cleavage of precursor polypeptides
↳ blocks action of influenza virus neuraminidase (needed for invasion + release of Ag on influenza virus surface myxoviruses)

④ Interferons - naturally occuring antiviral compounds
↳ inhibit protein synthesis ex. Papilloma virus

5 Anti-Retroviral Agents - inhibit the replicating HIV but don't eliminate integrated pro-viral DNA

Retrovirus - Viral RNA that replicates in host cell via Reverse Transcriptase into DNA of the (Pro-virus) host genome. Then it replicates as part of host cells DNA.
ARA - cannot eliminate integrated pro-virus DNA, but inhibit replication of HIV.

④ Interferons (INFs) — in response to pathogen prex

↳ heterogenous group of glycoproteins prod by humans/animals, ~~after exposure to infec~~.

↳ inhibit viral growth by blocking the translation of viral proteins

↳ belong to cytokines

↳ Divided into 3 groups:

① α - prod by leukocytes

② β - " " fibroblasts

③ γ - " " lymphocytes

Inductors of α + β INFs: Viruses + ds RNAs ⇒ strong inducers

↳ weak inducers ⇒ bacteria, protozoa

Action: ① virus enters cell; ② INF are synthesised

③ INF leave infec cell

④ They bind to the surface of infec cell + activate host defense mechanism

⑤ This induces the synthesis of enzymes, which act as antiviral proteins.

⑥ Antiviral prot block translation of viral mRNA on the uninfected cells.

• they have the ability to control immune response by induction or enhancement of Major Histocompatibility complex (MHC) encoded molecule

(5) Humoral Immunity to viral Infec

↳ Humoral Immune Response (HIR) - part of immunity that is mediated by secreted antibodies, prod. in the cells of the B-lymphocyte lineage (B cell).
↳ B cells (w/ co-stimulation) transform into plasma cells, which secrete antibodies.
↳ Comes from another antigen presenting cell, e.g. dendritic cell
↳ entire process is aided by CD4 - T-helper 2 cell
↳ Secreted antibodies bind to antigens on the surfaces of invading microbes, which flags them for destruction
↳ So named coz it involves subs found in the humours / body fluids.

↳ Antibodies CANNOT enter cells ∴ no good against latent viruses or virus that spread cell to cell.
↳ they can bind to extracellular viral epitopes - these epitopes can be on intact virions or on the surface of infec. cells

Neutralisation
↳ binding of an antibody to a free virus can inhibit a no. of processes vital for viral replicatio
① block binding to host cell mem. ∴ stopping attachment + penetration
② antibody can cause aggregation of virus particles ∴ limiting spread of infectious particles + forming a complex that is readily phagocytosed.
③ A complement can aid in the neutralisation process by opsonising the virus or directly lysing enveloped viruses

↳ in many situations, viruses are able to escape the humoral defense mech- e.g. HSV - when reactivated is passed 2 cell-cell & influenza type A =) antigenic variation

Escape: HSA: cell - cell propagation
Influenza A - drift variation

↑Th CD4 cell → ↑Macrophages, NK cells, cT cells + secretion of cytokines
HLA class II → cT cells.

(6) Cell-mediated immunity to viral infec

↳ immune response that DOESN'T involve antibodies or complement BUT involves the activation of macrophage, natural killer cells (NK), antigen-specific cytotoxic T-lymphocytes & the release of various cytokines in response to an antigen

↳ CD4 cells or helper T cells provide protection against diff pathogens

↳ Cellular immunity protects the body by:

① Activating antigen specific cytotoxic T-lymphs - induce apoptosis in cells displaying epitopes of foreign antigens on their surface, e.g virus infected cells

② Activating macrophages + NK cells - destroy intracellular pathogens

③ stimulating cells to secrete a variety of cytokines that influence the func of other cells involved in adaptive immunity responses + innate immune responses.

↳ this immunity is for microbes that survive in phagocytes + microbes that infect non-phagocytic cells

↳ most effective in removing virus infected cells but good for others as well - fungi, protozoa, cancer

↳ role in transplant rejection

→ destruction of an infected cell before progeny particles are released in an effective way to end a viral infec.

↳

↳ viral proteins are synthesised in a host cell; some of these are processed into small peptides

↳ these small antigen fragments, become associated w/ MHC Class 1 molecules + transported to the cell surface - act as recognition units for cytotoxic T (Tc) lymphs.

↳ once these Tc bind to the infected cell - they release molecules - induce apoptosis - perforins + granzyms.

(7) Immunopathology in viral infections

↳ Viruses can infect cells of the immune system – disable the norm func.

↳ Rubella, Measles + HIV

↳ some infec. can cause permanent depression of immunity, e.g. AIDS-patient becomes susceptible to otherwise harmless fungi, protozoa etc.

↳ Viruses have other mechanisms to avoid the immune system ⇒ ① Antigenic Variation, release ② of antigens + prod. of ③ antigens at sites inaccessible to the immune systems.

↳ Virus is safe fm the immune sys as long as it remains in the cell + very low / no antigenic expression on the infected cell mem ⇒ LATENT inf e.g. HSV or VZV found in dorsal root ganglions

↳ ↑ suscep. in young + elderly ppl ⇒ weaker immune responses

↳ Natural infec w/ a virus ⇒ very effective method of giving LIFELONG IMMUNI to a disease

↳ memory ensures that a 2° response can be generated before the virus can cause the disease

Lab Id (2) - tissue cultures
- CFT

4D: (1) Conjunctivitis
(2) Cold
(3) Pharyngitis
(4) GIT diseases

(8) Adenoviruses

Therapy: NO!

- medium sized 90-100nm
- non-enveloped, icosahedral viruses
- nucleocapsid + dsDNA - linear
- usually affect mucosal surfaces (resp. tract, gut + eye)
- stable to chemical + physical agents + adverse pH conditions i.e. prolonged survival outside the body + water
- NO ANTIVIRAL DRUGS AVAIL ATM
- Spread by respiratory droplets or fecal-oral route
- infants + young kids - resp. tract diseases - Acute febrile pharyngitis
  - fever, cough, sore throat, nasal congestion
- via fecal-oral route - can cause ocular/gastrointestinal diseases

- viral attaches to susceptible cells via APICAL FIBRES & taken into the cell
- passes into the nucleus + DNA is released
- Shutting down of host cell metabolism + accum. of new virions => cell lysis + death ∴ releasing the new virions!

Apical fibres → into cell → DNA released → lysis w/ release of virions.

⑨ Herpes Simplex Virus

↳ part of the herpesvirus group (CMV, VZV, EBV)

↳ large 150nm ∅ ; enveloped ; ds DNA (linear) ; icosahedral (delta) capsid

↳ 2 types:

① HSV1 : cold sores - lips ; spread by kissing + sharing utensils when sores are present (oral herpes)

↳ can also cause sores around the genitals

② HSV2 : genital sores (genital herpes: on/and vagina/penis)

↳ in babies (via vaginal birth)

↳ sexual contact

↳ can cause mouth sores; infect other body parts - eyes + brain ⇒ RARE!

↳ Sores = small, painful ; look like blisters on the skin/mucous mem of the throat, mouth, nose, urethra, rectum + vagina

↳ PATHOGENESIS: virus infects, replicates in mucoepithelial cells, cause disease at the infec site & then establish latent infec of the innervating neurons (retrogradely to ggl)

↳ HSV1 : usually above waist infec

↳ HSV2: " below " "

HSV1 - trigeminal ggl ; HSV2 - sacral ggl

↳ Tests : usually done only for genital sores:

① Herpes viral culture : most specific ; cotton swab + cells/fluid from fresh sore & place in a culture cup.

② Herpes virus antigen detection test : cells fm a fresh sore are scraped off + microscope slid

↳ test finds antigens on surface of infected cells.

③ PCR : cells/fluid fm sore or any other fluid - blood, CSF - best choice if brain infec

↳ finds DNA of HSV ; can diff. between HSV1 & HSV2 ; NO SKIN SORES!

④ Antibody tests : Blood tests can find antibodies made to fight against HSV infec.

↳ not as accurate as viral culture at finding the cause.

↳ Cant. diff. if present or past infection

↳ antibodies take time to develop after an infec ⇒ Maybe -ve antibody test after recent infection

↳ Some blood tests can diff. between HSV1 & HSV2.

↳ Treatment: Acyclovir, ~~Ganciclovir~~ Penciclovir, Valacyclovir

⑩ Varicella-Zoster Virus (VZV) ⇒ Chickenpox

↳ dsDNA ; air transmission ; contagious

↳ one of 8 herpesviruses

↳ chickenpox ⇒ children ; Adults ⇒ Shingles (zoster), postherpetic neuralgia

↳ VZV - only grown in primate cell cultures - grows slower + more cell-associated than HSV

⇒ enanthem(a) - rash on mucous membrane

↳ Initial infection: chickenpox - episodic papulous exanthem

↳ enters from: nasopharyngeal space + conjunctiva

↳ then undergoes a viremic phase - transported by blood to skin → xanthem produced.

↳ EFFECTIVE IMMUNITY

↳ Immunodef. patients: can affect other organs (lung, brain) → severe + lethal course

↳ after symptoms r gone - VZV remains in the spinal ganglion + other tissues.

↳ Reactivation causes zoster + rash on the skin (effected innervated by those Nr. → spreads neurogenically causes neuralgia

induced by internal / external influences + when cellular VZV immunity wears off (>45yrs)

Diagnosis: PCR, Isolation, EM (direct viral detection), Immunofluorescence (detection of viral antigens in tissue specimens or cell smears), antibody titre increase IgM detection (serological)

Treatment: nothing for chickenpox

↳ zoster ⇒, adults / immunocomp ppl w/ VZV infec ⇒ Acyclovir, Valacyclovir + Famciclovir

↳ Immunosup. ppl ⇒ vaccine ⇒ Varicella-Zoster Immunoglobulin (VZIG)

↳ can prevent viremic spread leading to the disease but useless if u already have the disease

(11) Epstein-Barr Virus (EBV) "Kissing Disease"

↳ part of herpesvirus group - aka human herpesvirus 4 (HHV-4)

↳ ds linear DNA ; slow replication - latent state

↳ enveloped

↳ Icosohedral symmetry

↳ intimate contact from asymptomatic shedders of EBV ⇒ infects human B-cells & transforms them

Diseases: ① Infectious mononucleosis - fever, sore throat, lethargy, enlarged LN, spleen, painful pharyngitis

② Burkitt's lymphoma (B-cell)

③ Nasopharyngeal cancers

Pathogenesis: Mononucleosis: ① EBV infects the B-cells

② Binds to the complement receptor (CD3) on it's surface

③ Then internalised, EBV changes the infected cell - so normal growth doesn't occur

④ These TRANSFORMED cells prolif + pass on copies of EBV DNA to their offspring

⑤ EBV remains in a latent state as multiple copies of circular DNA

⑥ In some cells, EBV activates + prolif + cell lysis w/ viral release occurs

⑦ until this point, transformed cells (which act like malignant cells) disappear w/ the benign appearance of mononucleosis.*

* The immune sys. destroys the infec. virus + abnorm. B cells! *

Diagnostics: ↑ heterophile antibodies (antibodies induced by ext. antigens that cross react w/ self antigens) ⇒ Heterophile Antibody Test

↳ DWCC - ↑ lymphocytes - atypical ones (large activated T-lymphs)

↳ Serology ⇒ IgM against the viral capsid antigens (VCA)

↳ Monospot test ⇒ rapid screening test for mononucleosis: blood of infec. patient has heterophile antibodies, which cross-react w/ + agglutinate sheep RBCs.

Only supportive treatment

(12) Cytomegalovirus (CMV)

↳ Human herpesvirus 5 (HHV-5)

↳ Infected cells swell ∴ the name

↳ multinucleated giant cells + intranl inclusion bodies (in all herpesviruses)

↳ can be LATENT (in all herpesviruses)

↳ ds linear DNA

↳ enveloped

↳ icosohedral symmetry

Diseases: ① Immunocomp ppl: 2 diff disease

↳ if AIDS → CMV retinitis (leading to blindness)

↳ if w/ b.marrow transplat → CMV pneumonitis

② Reactivation in immunocomp ppl: Pneumonia, Retinitis, Oesophagitis, disseminated diseases

③ Asymptomatic patients (latent phase)

④ Congenital disease- it can cross the placenta + cause congenital diseases. VIRAL CAUSE OF MENTAL RETARDATION

⑤ Young adults ⇒ CMV mononucleosis (similar to EBV)

Transmission: ① virus present in milk, saliva, urine + tears

② sexual ③ transmission occurs w/ prolonged exposure, daycare centres etc

Diagnostics: ① CMV invades WBCs ∴ culturing the buffy coat (layer of WBCs from centrifuged blood). It is cultured overnight then morning = centrifuged. This breaks WBCs, releases CMV - detected w/ monoclonal antibodies

② Serology

③ Histology: enlarged (cytomegalic) cells w/ intranuclear + cytoplasmic inclusion bodies

④ Antigen: CMV antigen in the blood - only when the virus is replicating

↳ early marker for infec. in b.marrow transplant patients

⑤ PCR: test for CMV DNA in blood - only when virus is replicating in measurable levels

Treatment: Ganciclovir, Acyclovir, Foscarnet, Cidofovir

(13) Poxviruses – Smallpox, Variola & Vaccinia viruses

↳ largest virus sizes – 230×350nm

↳ DNA viruses – only ones which replicate in a defined area within the host cell cyto – "virus factory"

↳ (4) genera – infect humans: → ds linear DNA; used to eradicate smallpox

① Orthopox – variola virus, vaccinia virus, smallpox, cowpox

② Parapox – to humans ← cows; orf virus, pseudocowpox, milker's nodule virus

③ Yatapox + tanapox virus "MOPY"

④ Molluscipox – molluscum contagiosum virus (MCV)

↳ Most common – vaccinia + molluscum contagiosum

Pathogenesis: Variola – aerogenically ⇒ mucosa of URT (entry) → lymphoid organs → skin ⇒ typical eruptions

↳ Infec of cowpox, orf + milker's nodule virus ⇒ RARE + harmless

↳ lesions remain localised on skin (contact site) + local lymphadenitis

↳ occupational infec

↳ Molluscum Contagiosum virus = unusual cos in-vitro culturing = still unsuccessful

↳ Epidermal benign tumours – "Molluscum Contagiosum Warts"

Diagnosis: ① EM of pustule contents (if not yet dried out or superinfec by bac)

↳ orthopox + parapox viruses ⇒ morphologically

② MCV ⇒ histologically

Tx, Prevention etc: Variola – diseased humans only – direct + aerogenic

↳ vaccina – only accidental laboratory infec

↳ zootropic poxviruses – infected animal contact

↳ MCV ⇒ inter-human contact

p53 = tumour suppressor gene

(14) Papillomaviruses - HPV! non-enveloped

↳ ds circular DNA - circular ; icosahedral

↳ infects sq. epi + mucous mem ⇒ warts + fibropapillomata

↳ HPV: diff types - depending where it infects - cutaneous/genital warts

Low malig ↳ Types 1-5: keratinised epi of hands + feet "verruca vulgaris"

Intern Malig ↳ > 30 types: mucosal epi - anogenital tract + (oro)laryngeal cavity; types 6, 16, 18

High malig ↳ Types (2) + (57): skin + genital mucosa "Cervical Intraepithelial Neoplasia (CIN)"

↳ They are grouped acc. to oncogenic potential

Transformation: E7 binds to pRb (→ onco genes of viral DNA bind to tumour suppressor gen products that are required for final diff. of keratinocytes) pRb = Retinoblastoma protein

E6 binds to p53 (→ viral DNA gene E6 binds to the cellular onco gene, p53 which normally allows the cell to repair DNA damage before resuming cell cycle)

Clinical: children + young adults ⇒ (1) verruca plantaris or verruca vulgaris

↳ Mucosal warts (2) ⇒ Condyloma acuminata = sexually active adults;

↳ women = vulva, cervix, within vagina

↳ men = penis shaft + peri-anal skin & anal canal

Histologic - benign lesions w/ hypertrophy of all epidermal layers w/ hyperkeratosis of stratum corneum.

(13) Laryngeal Papillomatosis: benign sq. papillomatosis on resp mucosa in laryn

↳ infec. via vaginal birth

(4) ↳ oral sex ~~asexually latent infec~~ hoarseness of voice; children - weak cry

↳ Sq. cell carcinomen can be due to HPV

↳ Malig. progression of cutaneous warts in renal transplant (allograft) patient

Lab diagnosis: (1) histology to view koilocytes (dysplastic sq. cell found in precancerous cervical lesions)

↳ ↑ nl, hyperchromasia

(2) Serologic detection of antibodies used for post-exposure testing

↳ In situ hybridisation of exfoliated cells ⇒ HPV DNA (3)

(15) Hep B virus – only hepatitis virus which is a DNA VIRUS! (partial) ds circular

↳ blood, sexual transmission ; IV drug abusers ; " Hepadna virus " polymerase

↳ enveloped + icosahedral nucleocapsid core of protein (incl viral DNA + DNA

↳ consists of : HBeAg + HBcAg + HepB virus DNA polymerase + HBx (viral protein)

↳ Hep D needs HBV envelope particles to become virulent

↳ incubation period of upto 6mnths ⇒ follows the dose-related effect ⇒

↑ dose of virus = ↓ incubation time

↳ causes (1) hepatitis (chronic), since it can become precancerous ⇒ (2) hepatocellular carcinoma

↳ hepatitis → (3) cirrhosis → carcinoma ; acute → (4) jaundice

↳ Carriers are usually asymptomatic but in 25% → chronic hep/cirrhosis → hepatocellular cancer

↳ exposure ⇒ infection

HBsAg ⇒ hep B surface antigen

Prevention : Hep B vaccine ⇒ HbsAg use (viral envelope proteins)

↳ also screening is imp + common before operations

Diagnosis : (1) HbsAg is overpsd + empty vacuoles are found in the serum

found in serum ; invade + cause hep D

↳ 3 antigens are imp for diagnosis but only 2 can be found in serum ⇒ HbsAg + HBeAg

↳ if the host can't clear the infec, HbsAg = undetectable + followed by IgG antibodies to he surface Ag + core Ag (Anti Hbs + Anti HBc IgG)

↳ "Window period" = time between removal of HBsAg + appearance of anti Hbs

↳ person –ve for HbsAg but +ve for Anti-HBs < cleared the infec OR vaccinated

Lab Dx:

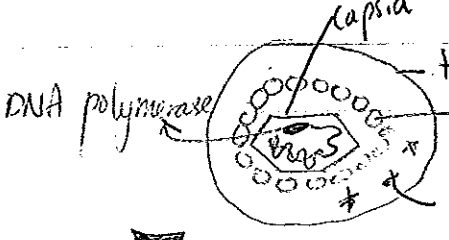
↳ Assess (1) antibodies for anti-HBs, anti HBe + anti-Hbc

↳ PCR – (2) HBV DNA detection – assess the infec, Status + monitor treatment

↳ "VIRAL LOAD"

↳ Hepatal enzyme detection

Symp: malaise, anorexia w/ weakness + muscle pain (myalgia), maculopapular rash



50's

Non A, non B hep viruses → Hep C (mainly, but can mention E, D)

↳ RNA viruses

↳ C, D, (IVdrug use) ⇒ ② sexual; ③ blood + can become chronic + precancerous; ① mother → child transmission

↳ E ⇒ faecal-oral route (hands) + DON'T become chronic

↳ incubation period of upto 6 months

↳ Symp: anorexia, malaise, weakness + myalgia, ① maculopapular rash (like Hep B), ② polyarthritis nodosa + ③ glomerulonephritis (due to immune complexes in blood)

↳ ④ fulminant hepatitis (also in A, B) — jaundice appears when symp. disappear

↳ if virus is allowed to keep on replicating → chronic hep → cirrhosis + ⑤ hepatocellular carcinoma

Diagnosis: HCV ⇒ ELISA - IgM + IgG; PCR

HDV ⇒ delta antigen (HDAg), Ab (anti-HD) or viral RNA; PCR

HEV ⇒ ELISA - IgM + IgG

↳ delta antigen: viroid; may infect humans w/ HBV (co-infec) or after an infec (super-infec) HD "-" infects after HB injection

↳ e.g. hep D only occurs when Hep B is/has been present

↳ results in complications: ↑ likelihood of experiencing liver failure, liver cirrhosis + ↑ chance of hepatocell. carcinoma (∴ worse prognosis)

HCV = +ss RNA enveloped, icosahedral

HDV = (-)ss RNA, closed circular RNA ⇒ smallest "virus" known to infect anime

HEV = +ss RNA, icosahedral virus

HDV = viroid — incomplete particle — can only survive in the envelope of Hep BV

HCV - no vaccine, only infects humans

(17) Parvoviruses ← smallest

↳ linear SS DNA viruses ; smallest viruses found in nature ; icosahedral

↳ Family: Parvoviridae Genus: Parvovirus Parvovirus B19

↳ human parvoviruses are not in genus parvovirus, but in others - e.g. erythrovirus

↳ all parvoviruses need dividing cells for replication coz they depend on cellular factor in cell stages - late S + G2 cell cycle for replication

↳ ∴ infect intestinal mucosa, haematopoietic tissue + fetus ⇒ Reticulocytopenia (↓ reticulocytes → RBC's) (B19)

Clinical: ① Rash "erythematous maculopapular rash" → intense erythema on cheeks ⇒ SLAPPED CHEEK SYNDROME aka 5th disease - childhood ↳ 1 week after exposure symp. appear

② Non-specific resp tract disease

③ Joint disease - not rheumatoid arthritis coz rheumatoid factor (-ve)

④ Aplastic crisis → anaemia (Reticulocytopenia) (erythropoiesis stopped) need b. transfusion

Transmission: infected resp. droplets - via nasal mucosa

↳ Individuals w/ (B19) IgG antibodies = immune to recurrent infec.

↳ 1 week after infec - viraemia in secretion followed by high IgM titre + IgG

↳ virus in blood stream

Lab. Id: Specific antibodies

↳ haematologic changes after 2 weeks of inoculation - reticulocytes are absent + haemoglob. diseases

① Ab's

② ↓ Reticulocytes.

T: No treatment

No prevention

(18) Poliovirus - Genus "Enterovirus" ⇒ +ss RNA + protein capsid

↳ Poliomyelitis ⇒ paralysis + death - affects motor neurons in S.C, B.S or motor cortex

↳ icosahedral, non-enveloped - "simplest significant virus"

↳ faecal oral route ∴ utensils, food ⇒ replicates in the alimentary tract + shed in the faeces ; 3 serotypes

↳ (95%) of the time only 1° viraemia + infec ⇒ asymptomatic (1)

↳ (5%) virus spreads + replicates in other sites ⇒ brown fat, muscle, reticuloendothelial tissue

↳ causes (2° viraemia) - fever, headache, sore throat (2)

↳ (<1%) paralytic polio (3) - virus enters CNS + replicates in motor neurons

① virus attaches to the intestinal wall via specific receptors + replicates in these cells

② Commonly causes asymptomatic immunising response

③ virus' foodstuff - pasteurisation is needed (<60°C)

↳ incubation period 3-21 days

↳ risk factors : • immunodef

• malnutrition

• tonsillectomy - ↓IgA secretion into pharynx

• pregnancy - can cross placenta but fetus unaffected cos passive immunity fm mother for first few months of life

Severe muscular activity ⇒ paralysis of the muscles used

Diagnostics : RTPCR for RNA detection in CSF (1) (Reverse Transcriptase PCR) "rare"

↳ because its RNA.

↳ Stool sample (2) or pharyngeal swab

↳ Specific IgG + IgM assays (3)

Vaccination : oral - live attenuated vaccine (↓ virulence of a pathogen, while still keeping it alive)

PICE – echoviruses
└ coxsackieviruses

(19) Enteroviruses other than polioviruses

↳ Echoviruses + Coxsackie viruses
↳ +SSRNA – can be translated directly by host ribosomes ; non-enveloped

Echoviruses: found in the (GIT)
↳ exposure to it causes other opportunistic infec + diseases
↳ highly infectious ; children – kids/infants – in wards! – high spread
↳ (1) acute febrile illness + (2) aseptic meningitis
↳ 34 serotypes ; epidemic potential
↳ incubation – 5 days w/ fever, URT symptoms ; diarrhea

Pathogenesis: sne: viral replication in nasopharynx after infec then to regional LN
↳ Host: swallowed ⇒ Lower gut – binds to specific receptors here.
↳ Spreads to lower intestinal tract, replicates but no major cellular effects
↳ then spreads to 2° sites: CNS, liver, spleen, b.marrow, heart + lungs
↳ Spread via (1) air 1–3 weeks after infec. + via (2) faeces 8 weeks after infec
↳ all age groups – older = ↑ prod of specific antibodies to echovirus ∴ better prognosis
↳ (No) specific treatment ; just relief of symptoms.

Coxsackieviruses: non-enveloped +ssRNA, injestion of contaminated food or water faecal-oral route
↳ main cause of (aseptic meninigitis)
↳ Group A: skin + mucous mem ⇒ (1) herpangina (mouth blisters), (2) acute haemorrhagic conjunct (AHC) + hand-foot & mouth (3) (HFH) disease.
↳ infect the heart, pleura, pancreas + liver – (4) pericarditis, (5) hepatitis, (6) myocarditis
↳ Group B: epidemic of myalgia or (1) Bornholm disease – fever, sudden pain in muscles of the chest. In infants ⇒ severe + fatal myocarditis
↳ major cause of human (2) myopericarditis w/ initial influenza like symp followed by clinical Heart Disease.
↳ ~~Group~~ B diag: (ELISA)

(No) cure treatment against it. Depends on disease (Group A)
Palliative care (group B)
No vaccine!

(20) Hep A virus - Doesn't become chronic

↳ Picornavirus - +ssRNA, non-enveloped, icosahedral capsid

↳ only 1 serotype

↳ (1) Infectious hepatitis - 60% of acute viral hep.

↳ incubation 14-45 days - (2) malaise, muscle pain + headaches, fever, ab pain, nausea

↳ as symp. improve - (3) jaundice appears

↳ faecal-oral route - contaminated food/water

↳ no carriers; mildest in children - 5% get jaundice; adults 50%.

Pathogenesis: ① HAV enters bloodstream thru epi of oropharynx or intestine

② blood takes it to the liver - multiplies in hepatocytes + kupffer cells

③ virions secreted into the bile + released into stool

④ HAV is excreted in large quantities abt 11days before appearance of symp or anti-HAV antibodies

Diagnosis: (1) ELISA - anti-HAV IgM + IgG or IM + total Ig

IgM → present in blood following an acute hep infec.

IgG → acute stage of illness has passed + person is immune to further infec

↳ During the acute stage (2) ALT ↑↑↑ in blood

↳ viraemia + faeces of infected ppl 2 weeks before clinical symp.

Vaccination - for ppl travelling to countries w/ hepA.

No treatment available.

(21) Orthomyxoviruses

↳ Includes Influenzae A, B + C, Isavirus + Thogotovirus (- salmons; Tick, mosquito, mammals)
↳ -ssRNA, envelopes w/ viral spikes inclusions — haemagglutinin (H) — Neuraminidase (N)
↳ influ A, B, C - depending on antigenic diff in their nucleoprotein + matrix protein
↳ influ B - only humans; A + C ⇒ multiple species
↳ most prominent features of the influ. virus ⇒ antigenic drift + shift

Clinical: • Influ. A: short incubation - 4 days, most virulent. H1N1 - pandemic
↳ sudden onset - chills, fever (38-41°C for abt 3 days), headache, myalgia, anorexia
↳ resp. symp. (U+LRT infect dry & cough)
↳ Some age specific symp: febrile convulsions + otitis in kids; elderly - dyspnoea
• Influ B: similar to A but more GIT symp.
• Influ C: afebrile URT inf - young children

Complications: 1° influenza pneumonia, bac. pneumonia may develop fm S. aureus or Strep. pneumoniae

Diagnostics: resp. specimen - Gram stain - immunofluorescence - detection of influ antig
↳ PCR (1): viral RNA detection
↳ ELISA (2): IgM + IgA
↳ best ones: nasal washes/aspirates (sample); nasopharynx washing
throat swabs if taken early
(3) Serologic: confirmation when ×4 ↑ in antibody titre against specific virus
(4) Complement fixation tests (CFT) using nucleocapsid antigens type specific distinguishes A - B - C infections.
• Pandemics ⇒ these viruses have (1) elevated virulence (2) person-person transmission

Prevention: dead vaccine for high risk persons, e.g. w/ circulatory disease
- Aerogenic transmission
↳ only protects against subtypes present in the population
↳ Dangerous for immunocomp, pregnant + elderly.
↳ some subtypes = dangerous for young ppl w/ good immunity ⇒ due to "cytokine storms" ⇒ immunity over-reaction → +ve feedback loop between cytokines + immune cells
↳ antigenic drift ⇒ common ⇒ tiny changes of antigenic structures
↳ " shift ⇒ new subtype is formed from atleast 2 diff strains of a virus, w/ a mixture of both surface antigens (H+N) ⇒ NEW HYBRID FORMED

URT infect + pneumonitis = RSV

(22) Respiratory Syncytial virus + parainfluenza viruses (RSV) ⇒ "human pneumovirus"

G + F (F fusion causes syncytia)

↳ resp tract infec - LRT! (No VACCINE); mainly first 1/2 of yr!

↳ Treatment: OXYGEN! ; Group = Paramyxoviridae

↳ -ssRNA

↳ No H or N (like influ) but (G) (glycoprotein) ⇒ receptor for cell surface attachment

↳ Also F ⇒ fusion protein causing syncytia (large cell like structure, filled w/ cyto + many nl

↳ F + G ⇒ needed for entry into the cells + determine the antibody response

Clinical: (1) Bronchiolitis - babies (≤1yr) ⇒ bronchiolar inflam acts as one way valve ⇒ hyperinflation of the lungs ⇒ hospitilisation

↳ characteristic X-ray

⇒ ↳ (2) URT infected w/ bronchiolitis = RSV!

* (1) ELISA + (direct) (2) tissue culture *

↳ most ppl only mild symp. - cnt separate fm common cold.

Complications: (3) middle ear infc ("otitis media") + dev of asthma later

Parainfluenza: human parainfluenzae viruses (HPIVs) - only last a few hrs in the environment - soap/water kills them

↳ 4 serotypes, -ssRNA

↳ detected via (1) cell culture, (2) immunofluorescence micro + (3) PCR, (4) EIA/ELISA (explained (FT)

↳ there are some cross-reactions

↳ NO VACCINE!

Clinical: 2nd most common cause of (1) LRT infec in young children

↳ repeated infec throughout life ∴ later infec ⇒ (2) URT illness (cold, sore throat, NO FEVER!)

↳ flu like cough

↳ incubation period: 1-7 days

↳ immunocomp. (eg. transplant patients) = (3) severe pneumonia ⇒ FATAL!

Serotypes

HPIV-1: Croup (group of resp. diseases that affect children <6yrs; barking cough); URT + LRT illnesses

(4) types HPIV-2: croup + some U + LRT illnesses

HPIV-3: associated w/ bronchiolitis + pneumonia

HPIV-4: subtypes 4a + 4b

↳ has (H) (N) + (F) surface proteins

↳ causes cell membranes to fuse leading to syncytia formation ⇒ ⇒ resulting in release of viral machinery into the cell

on one 1 spike (in influenza - 2 separate spikes)

(23) Mumps virus — MUMPS!

all are enveloped - viral proteins fnd in this ↳ seen as spikes

↳ -ssRNA ; part of Paramyxoviridae ; enveloped

↳ aerogenic spread ; person-person ; highly contagious

↳ grossly (1) enlarged + tender parotids ; infec. of other glandular organs

↳ virus first replicates in the resp tract, then causes viraemia → parotid (mainly)

↳ usually a benign disease but sometimes complications e.g. meningoencephalitis (2), pancreatitis (3), deafness ; post-pubertal boys - orchitis (4) (inflam. of testes + swelling + infec)

↳ incubation period - 15 days followed by flu-like symp.

↳ has 2 types of spikes - HN => HN protein - haemagglutination activity
F protein => responsible for fusion w/ cell membrane

Diagnosis : direct - immunofluorescence or enzyme immunoassay (2) ELISA + (3) cell culture

↳ replicate well in cell cultures fm human tissues

Prevention : MMR vaccine - measles, mumps + rubella "

↳ live attenuated vaccine

↳ 2 doses : 1st ~ 1yr then 2nd ~ 4/5 yrs. (not a booster)

(dose to produce immunity in 2-5% of ppl who fail to develop measles immunity after the 1st dose.

↳ recommended in some adults w/ HIV

→ No AVD available

RSV - G + F protein
HPIV - H+N, F
Mumps - H+N, F

(27) Arboviruses: Bunyaviruses – eg: Hantaan Virus

↳ only Arbovirus that is (-) sense

(-) sense ssRNA

↳ -ssRNA, enveloped, icosahedral; genome = 3x -ssRNA - Large, Medium, Small; nucleocapsid has 3 helical

↳ mosquito, tick or sandfly apart from HANTAVIRUSES ⇒ contact w/ deer mice faeces

↳ Haemorrhagic fever w/ renal syndrome (1) (HFRS) → high fever, lung oedema + pulmonary failure

↳ usually benign forms (2) of encephalitis, eg. California encephalitis + La Crosse virus infec – USA

Diagnosis: Serology – IgM detection ELISA + PCR + cell culture

↳ cell culture + PCR from blood + liver

↳ Animal test (as required)

↳ Active vaccination avail for Rift Valley fever protection

↳ fever, headache, myalgia + liver abnormalities

Prevention: avoid bites

(3)V: Hantaan Virus
California Encephalytis Virus
La Crosse Encephalitis Virus

(4) Diseases: (1) Encephalitis
(2) Haemorrhagic fever (Hantaan Virus)
(3) Arthralgia
(4) Pulmonary Failure (Hantaan Virus)

↳ little red spots

(28) Rubella virus => Rubella / "German Measles"

↳ also if infec. during first weeks of preg => (1) "Congenital Rubella Syndrome"
↳ myocardial damage

↳ ssRNA, icosahedral capsid, enveloped

↳ normally harmless childhood disease can cause severe embryopathies during first trimester of pregnancy ↳ exanthem (2)

↳ direct contact transmission; airborne droplets

Pathogenesis: First replicates in lymphoid organs at the portal of entry + nasopharyngeal space → viraemia → exanthem.

↳ Pregnancy: mum → placenta → embryo → congenital deformaties or embryonic death
↳ myocard. damage

↳ organs in dev. stages at this time - affected

↳ deafness (3), cataracts (4), cardiac defects (CRS), spina bifida (5)

Diagnosis: Serology: IgM detection (ELISA) or ↑ antibody count
↳ Indication fr 1st trimester abortion

Prevention: MMR (see Q23)
live attenuated vaccine

↳ incubation 2-3 weeks; no carriers

(29) Arenaviruses - LASSA VIRUS (sand (ribosomes from host in viral virus)) (−/+) ss RNA helical, enveloped

↳ "ambisense" viruses - possess genomic elements w/ (−) & (+) (Antisense) (sense) polarity

↳ ss RNA, enveloped

↳ incl. (1) Lymphocytic choriomeningitis (LCM), (2) haemorrhagic fever viruses ⇒ Lassa, Junin + Machupo viruses

↳ they cause persistant infections in rodents + passed onto humans as zoonoses

Pathogenesis: incubation period 10-14 days

↳ enter by per os (mouth) aerogenically or by skin contact

↳ viraemia develops then organ manifestations

↳ LCM: normally harmless + flu-like (also → (3) meningitis or (4) encephalitis)

↳ Lassa virus: Pantropic! haemorrhagic fever (Lassa fever) affecting nearly all internal organs + ↑ lethality rate! Death from shock + anoxia.

↳ Junin + Machupo: similar to Lassa but CNS involvement is more freq. + lower lethality

L LCM

Diagnosis: Serologic + genomic findings - RT-PCR (ELISA + PCR)

- Lassa virus: swine; blood = highly infectious - proper handling care! (aerosol formation ↑)
- Acute stage: patient's blood

Treatment: LCM: - supportive treatment

↳ Lassa: Ribavirin - limited activity against arenaviruses (inh. of nucleic acid synthesis) ↳ if given early on in the infec (within 6 days)

↳ Maintaining fluid, electrolyte + osmotic balance

Junin + Machupo - LCM → Encephalitis, Meningitis or ICI

Lassa - Lassa fever (haemorrhagic fever) - ↑ mortality

LCM Virus - LCM

(30) ~~Rhabdoviruses~~ Filoviruses ← thread like viruses in E.M.

↳ -ssRNA, enveloped, helical nucleocapsid

↳ incl. 2 (African) viruses - related to each other ① Marburg (haemorrhagic fever)
② Ebola (haemorrhagic fever + GI bleeding)

↳ they cause (1) haemorrhagic fevers w/ high lethality rates

↳ fever, headache + neck pain, conjunctivitis + diarrhea followed by (2) hepatic, renal + CNS involvement

↳ then due to coagulation → extensive haemorrhageing + shock

↳ haemorrhages + fibrin deposits in almost all organs!

Diagnosis: either in blood w/ an (EM) OR

immunofluorescence on tissue specimens (3)

cell cultures (4)

Serological - ELISA (IgM) + PCR (2)

↳ viral antigen

Treatment: only supportive; (no) anti-virals avail.

Spread: via contamination w/ blood-stained body fluids or tissues

Nosocomial spread (docs + nurses)

↳ Name from Latin - filum ⇒ thread like appearance of virus particles in EM

↳ Sub-saharan Africa; Zaire, Sudan

REO - Respiratory + Enteric; Orphan (not associated w/ any disease)

(31) Reoviruses + Rotaviruses

- group of respiratory + enteric viruses not associated w/ any known disease (Resp, Enteric, Orph
- dsRNA double layered protein capsid, non enveloped, icosahedral
- stable over a wide pH + temp ranges + in airborne aerosols.
- Reoviridae ① Orthoreoviruses (↔ aka "mammalian" reoviruses) → asymp. infec. in humans
  - ② Rotaviruses ↔ human infantile gastroenteritis, very common disease
  - ③ Orbiviruses + coltiviruses

Reoviruses: ubiquitous, very stable virions; 3 serotypes: 1, 2, 3 ⇒ based on neutralisation + haemagglutination-inhibition tests

- worldwide, any age; most infections are asymptomatic or very mild ∴ undetected
- Diagnosis: Isolation - done in cell cultures + not a routine method

Rotaviruses: infantile diarrhoea (serious diarrhoea) worldwide + in elderly as well + immunosupp. (b. marrow trans.)

- groups A-F - subdivided into subgroups, serotypes etc.
- enter by mouth, droplet infection & replicate in the villi of the s. intestine
- Diagnosis: don't grow easily in cell culture ∴ EM or in antigen assays - ELISA, latex agglu.
- faecal-oral route spread
- No specific antiviral therapy; supportive therapy
- infects cells lining the s. intestine → produces an enterotoxin → gastroenteritis → severe diarrhoea → death (possible)!

Coltiviruses → Colorado tick fever - fever, headache, severe myalgia

Orbiviruses → animals

REverse TRanscriptase – RNA → DNA → translation into proteins

(32) HIV + other retroviruses ↓ T_h cells Non-Oncogenic Virus

HIV: lentivirus (long incubation period) → causes AIDS (immune sys begins to fail)
→ opportunistic infec (TB, Pneumocystis carinii pneumonia, CMV) & lymphomas.

↳ Transmission: ① blood (transfusion, open wound, IV drug users), ② mother → child (in utero, at childbirth or via breast milk), ③ sexual transmission

↳ within body fluids (blood, semen, vag. fluids, pre-ejaculate or breast milk) ⇒ virus found as free virus particle + virus within infected immune cells

↳ spherical, +ssRNA, enveloped, contain enzyme REVERSE TRANSCRIPTASE (reverse transcriptase, from virus particle) → dsDNA

Pathogenesis: ① enters the target cell, ssRNA → dsDNA

② This dsDNA then gets integrated into cellular DNA by virally encoded integrase; genome is transcribed

② virus infe cell, 2 pathways poss: ① becomes latent + infec. cell continues to func

② virus becomes active + replicates + large no. of virus particles liberated - infect other cells

↳ 2 species of HIV – HIV-1: more virulent + infective + global
HIV-2: less " + " + West Africa (poor transmission capacity)

AIDS: manifests as ↓ of T helper cells – after avg incubation period of 10yrs ⇒ collapse of cellular immunity ⇒ opportunistic infec; weight loss, fever, lymphadenopathy, pharyngitis, rash, myalgia

Diagnosis: Serology (HIV) ① ELISA antibodies or viral antigens; antibodies against glycoproteins (gp41 & gp120) using ELISA
↳ circulating virus count (load) ⇒ quantitative ② RT-PCR
↳ if +ve = Western blotting confirmation
↳ AIDS = assume HIV +

Therapy: inhibitors of RT + protease; many anti-HIV drugs bt limited effectivity → HAART (Highly Active Anti-Retroviral Therapy)

Prevention: Exposure prevention – esp when blood is involved (drug addicts, healthcare staff)
↳ sexual intercourse

3 main enzymes: RT: ssRNA → dsDNA in host cell, soon after entry
integrase: integrates viral DNA into the host cell's genome
protease: ① during assembly of new HIV1 virion: polyprotein (gp160) goes thru ER → Golgi; cleaved by protease → gp41 / gp120 ⇒ HIV envelope glycoproteins
② During maturation, HIV proteases cleave polyproteins into individual functional HIV proteins + enzymes. Inhibited by protease inhibitors

- Some retroviruses have oncogenic cell transformation capabilities ⇒ aka oncovirinae:
Human T cell leukemia virus: T cell leukemia / T cell lymphoma.

(33) Caliciviruses, astroviruses & "small round structured" viruses

↳ strains look like rabbies.

Caliciviruses: +ssRNA, unenveloped, icosahedral symmetry; form of a star of David ★ (calyx like concavities)

↳ ① faecal-oral or ② respiratory route

↳ classified depending on genomic similarities: ① Human caliciviruses (HuCV) ② "small round structured viruses" (SRSV) < SRSV I / SRSV II

↳ cause enteritis - most freq in children - minor epidemics during winter months

Diagnosis: EM or antigen assays (ELISA) in stool

↳ incubation period 12-72hrs (½-3 days)

① HuCV - hep E

② SRSV - Norwalk virus

Astroviruses: +ssRNA, icosahedral, non-enveloped; 5/6 pointed star-like surface

↳ low level of pathogenicity; GASTROENTERITIS - diarrhoea, vomiting, fever

↳ worldwide; young children + older ppl weakened by some other diseases

Diagnosis: EM, ELISA, PCR, immunofluorescence

↳ they detect virus particle, antigens or viral nucleic acid in stools of infected ppl

↳ No vaccine or anti-viral treatment but personal hygiene ↓ incidence

SRSV I ⇒ incl Norwalk virus + no. of small viruses

Caliciviruses also incl. Hep E! - traveller's disease

↳ benign + resembles hepA; no chronicity

↳ ELISA to detect antibodies

↳ contaminated drinking water

No therapy needed, only rehydration in case of diarrhea.

→ virus is crowned by bulbous structures

(34) Coronaviruses

↳ *ssRNA, enveloped, helical symmetry

 → viral spikes(s) - proteins on virus surface + determine host tropism (determines if cell is gona be infected.)

↳ Incl. causative agents of rhinitis like infec + SARS (China 2002) (severe ~~disease~~ acute respiratory syndrome)

↳ Human Coronavirus (HuCV) - 2 serotypes

↳ URT infec (nose + trachea) ⇒ "common cold" (1) - 30% of - Short lived Immunity (by IgA) ∴ reinfec are freq (also due to antigenic variability); infect via the gut or resp tract (inhalation of droplets/aerosols generated by infected individuals coughing/sneezing)

↳ old, very young ~~immunocomp ppl~~ ⇒ severe LRT infec.

↳ immunocomp ppl ⇒ pneumonia (2)

↳ incubation period 2-4 days

SARS: China 2002

↳ fm wild (captive) animal → human; aerogenically

↳ person-person needs close contact; 20% of patients → ARDS

↳ incubation period ~1 week; mortality - 5%

↳ severe; sometimes fatal; (1st) non-spec. signs = fever, malaise, myalgia; URT symp. rarely seen

↳ symp ↓ then (2) severe atypical pneumonia; (3) diarrhoea poss.

Diagnosis: Common cold - grown in organ cultures (4) of human tracheal tissue OR in human diploid cells.

↳ Serodiagnosis - Complement binding reaction, IMF, ELISA & EM

SARS: PCR or isolated in the vero cell line

Prevent exposure; therapy w/ RIBAVIRIN + intensive care - SARS mortality = 10%

↳ inhibition of nucleic ac. production

(35) Rhabdoviruses ← rod shaped virus — Rabies or Lyssavirus

Rhabdos = rod = shape of viral particle

↳ -ssRNA, enveloped, bullet shaped ⇨ (helical, nucleocapsid)

↳ 7 genotypes: Type 1: classic worldwide type = "virus fixe" - Pasteur - "street virus" - humans + animals - wild animals, bats! dogs

All others = (Bats!)

↳ transmitted by (infected animal bite (saliva)) → once infections fully manifest, always lethal! (Rabies)

↳ Rabies virus: human is bitten → virus replicates locally at the wound site for a few days & then migrates slowly (weeks → yr) up nerve axons → CNS → encephalitis (+) → contamination of saliva

→ salivary glands, cornea + kidneys

"Dumb Rabies" ↳ 3 stages of rabies: ① Initial: itching/burning at wound site, nausea, vomiting

"Furious Rabies" ② Excitative: cramps + spasms of the larynx + pharynx, (Sight of water = induces spasms) "hydrophobia"

↳ other mild visual/acoustic stimuli → violent anger, hitting, biting, screaming, (Death in 3-4 days)

③ Paralytic: instead of death; ascending paralysis + (asphyxia) → exitus (death)

Treatment: Post-exposure prophylaxis: wash wound properly w/ soap + water → Iodine sol or alcohol

↳ then passive immunisation w/ 20IU/kg (human rabies Ig) (RIG) = 1/2 Intramus. + 1/2 wound site

Prevention: Rabies vaccine (attenuated vaccine) - dogs, cats - domestic animals

↳ Human Diploid cell Vaccine (HDCV) → nowadays used ones; prod. there

Diagnosis: During life: examining an impression preparation from the (cornea) or (skin biopsies) w/ IHF

↳ Post-mortem: rabies virus - found in the (brain tissue)

↳ Antibody prod begins so late ∴ serologic diagnostics = no good

(36) Agents of spongiform (holes appear in cerebral cortex) encephalopathies (prions) (also product of normal cellular gene, so (NO) immune response is form) - Prion disease

↳ Transmissible spongiform encephalopathies (TSEs) => group of progressive conditions that affect the brain + NS of many animals

↳ by prions + myriad tiny holes appear in the cortex → looks like a sponge (- autopsy + micro)

↳ mental + physical abilities deteriorate; impairment of brain func: memory, personality changes

↳ e.g. (1) Creutzfeldt-Jakob disease (CJD), (2) fatal familial insomnia, (3) kuru

PRION => infectious protein agent; mistakes in protein ("proteinaceous, infectious particle")

↳ misfolded forms of a cellular protein - NOT VIRUSES cause adverse reactions in the body

↳ long incubation period (months → years)

↳ transmitted by inoculation / ingestion; intracerebral route = shortest incubation period; NOT AIR

↳ non-inflam. processes in the brain

↳ 3 main groups of diseases of TSE: ① Idiopathic ② Familial ③ Acquired

↳ NO form of screening for human prion diseases + NO specific treatment avail.

↳ brain exam. at autopsy => definitive diagnosis

↳ no immune response to the prion protein (PrP): serodiagnostic methods are useless

↳ PrP detected in lymphoid tissue biopsies using monoclonal antibodies

↳ CJD occurs sporadically - 1 in 1000,000 / pa yr

Retinal Transplant

Mycology

Stain G+

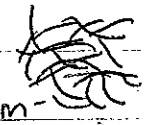
① Fungi + fungal diseases of man

Fungi: eukaryotics (mem. bound organelles - mito, ER, 80S ribosomes); chitin cell wall; mostly aerobes, heterotrophs - need exogenous nutrient source

① Yeasts, ② Moulds, ③ Mushrooms, ④ Dimorphic fungi

↳ 2 morphological forms of fungi: ① Yeasts - budding; unicellular fungi

② Hyphae - in filamentous fungi; Mycelium - web structure of hyphae



↳ Dimorphic fungi: depending on the environment conditions can grow as yeasts or mycelium

↳ 3 subdivisions: ① Moulds (filamentous fungi) - branching filaments

↳ Reproduce by (a)sexual spores - many kinds - blastospores, sporangiospo

② Yeasts: mainly unicellular

↳ oval/round shape

↳ asexual reprod. by budding

③ Dimorphic fungi: (above)

D:

① Mycoses - fungal inflammations

② Mycotoxicoses - toxical action

③ Mykoalergoses - alergy to fungi

④ Mycetism: fungus only present tissue

↳ Generally, slow cell cycle ∴ low infection speed.

Diseases: Pathogens: called mycosis; 1% of fungi = pathogenic

↳ Systemic or opportunist

↳ Severity: ① Type of fungi ② Degree of exposure ③ Site of exposure ④ Method of entry ⑤ Host immunity - compromised or not

↳ Worldwide - soil, vegetation etc.

Types of infec: ① Superf. mycoses (skin, hair, nails) < Ringworm, Yeast infec (Candida + Malassezia fur

② Subcutaneous (skin, subcut. tissue, fascia + bone) - mycetoma, chromomycosis + sporotrichosis

↳ fm traumatic inoculation fm soil → subcut. tissue

③ Systemic: deep infec - fm inhalation of spores e.g. Coccidioides, histoplasma, blastomyces

↳ Incidence depends on hobbies, occupation, living conditions

↳ Ringworm of foot (athelet's foot) → pools + sports ppl.; Animal ringworm → farmers, vets.

↳ Systemic mycoses → construction workers

DIAGNOSIS: depends on infec. - Culture, Serology (ELISA, latex agg (test fr antigen)), test fr antibodi

PCR (DNA of fungal material)

T: ↳ Antimycotics!

MOLDS! Feed on Keratin!

② Dermatophytes + Ringworm infec → Tinea Corporis

↳ fungi that infect tissues w/ lots of Keratin = (skin) (hair) + (nails)

↳ 3 genera: ① Trichophyton (T. mentagrophytes (→ ringworm), T. rubrum, T. tonsurans)
② Microsporum (M. canis, M. gypseum (soil)) - skin of dogs and cats → ∴ gardeners
③ Epidermophyton (E. floccosum)

↳ Transmission: ① human contact, ② animal-human or ③ objects (swimming pools, gyms, clothes)

↳ 1° foci = contact site

↳ feet, uncovered skin (hair, head, facial skin) mostly affected

↳ Freq. dermatophytes mycoses:

① Tinea Corporis - Ringworm - T. mentagrophytes + M. canis. Affect hairless skin
② Tinea Pedis - Athelet's foot - T. rubrum + T. mentagrophytes + E. floccosum. Lower legs! Toes!
③ Tinea Capitis - T. tonsurans + M. canis - Affects scalp hair
④ " Unguinum - T. rubrum + T. mentagrophytes + E. floccosum → usually Toenails
⑤ Onychomycosis (nail mycosis) - various dermatophytes + Candida

DIAGNOSIS: skin (hair), nail scrapping, infected hair

↳ Micro.: under KOH preparation; visually

TREATMENT: locally-applied antimycotic agents

Orally allylamine terbinafine or Azoles (eg. fluconazde)
Griseofulvin (↓ usage now)

CLOTRIMAZOLE

③ Superf. mycoses other than ringworm + Candidosis

① Pityriasis (or tinea) versicolour → surface infec of skin by Malassezia furfur ; part of norm skin flora (yeast) cells ⇒ oval / thick walled ; Gr+
↳ mainly in tropics ; young adults
↳ causes hypopigmentations small, sharply demarcated, non-inflam - upper trunk + neck
↳ M. furfur depends on long chain FA fr energy

→ solitary, irreg, pigmented macule

② Tinea Nigra : mainly in tropics ; traumatic inoculation of the fungus → superf layer epidermis
↳ Exophiala werneckii (new name Hortaea werneckii)
↳ causes dark brown / black painless patches on the soles of the feet + hands / palms
↳ children + young adults

③ White + black piedras ∴ infec. of the hair
White = axilla + groin
black = scalp hair
↳ Trichosporon beigelii OR Piedraia hortae ; tropic / subtropic
↳ hair shaft has firm, irregular nodules (black or white) ↳ poor hygiene!

DIAGNOSIS + TREATMENT of ① : micro of skin scales w/ 10% KOH
topical therapy w/ 1% selenium sulphide OR azoles
Head and shoulders.

② micro of skin scraping in 10% / 20% KOH
topical therapy - azole creams Whitfield ointment

③ micro ⇒ hyphal elements / budding yeast cells found, then mycologic media without cycloheximide :
topical therapy - azole creams ; improve hygiene

④ Subcutaneous Mycoses

↳ fungi that cause these grow in the ① soil + ② dying plants
↳ penetrate through skin injuries → subcut. c.t. = local, chronic, granulomatous inf
↳ tropics + subtropics ; all 3 are chronic

① Sporotrichosis : by Sporothrix schenckii (dimorphic fungus - grows as yeasts in host cells,
↳ initial site of infec : ① ulcerous 1° lesion - extremity & then multiple nodules + abcesses along the lymphatic vessels ②
DIAGNOSIS : pus (infected) or tissue ① → culture ②
↳ confirmation : by converting mycelial growth → yeast form by subculture at 37°C
Treatment : oral potassium iodide (KI) in saturated sol.
Itraconazole
Fluconazole (if can't stand anything else)

② Chromomycosis (Chromoblastomycosis) : by a no. of species of black moulds
↳ Fonsecaea pedrosoi, Fonsecaea Compacta, Cladophialophora carrionii
↳ ① verrucous lesions → flat plaques
↳ established infec = multiple, large, warty, "cauliflower like", within same region
DIAGNOSIS : skin scraping / biopsy - micro - 20% KOH
Treatment : early, solitary lesions ⇒ Removed
Itraconazol

③ Mycetoma : actinomycetes (filamentous bac) or moulds (Aspergillus, Madurella)
① ↳ subcutaneous abcesses ⇒ hands or feet
↳ abcesses spread into musculature + bones ; ② fistulae are formed with grains.
DIAGNOSIS : biopsy (pus) = need grains → micro - 20% KOH
Grains - used to differentiate between actinomycetoma + eumycetoma (has grains)
Treatment : not effective - ∴ need amputation (eumycetoma type)

(5) Coccidiodomycosis, Histoplasmosis, Blastomycosis & Paracoccidioidmycosis

(1) Coccidiodomycosis: (2) indistinguishable species < Coccidioides Immitis - California
" posadasii - outside California

↳ most virulent of all human mycotic pathogens

↳ inhalation - of only a few = (1) asymptomatic pulmonary disease or (2) fever, cough, chest pain + weight loss

⇒ ↳ if disseminates fm lungs = poor prognosis

↳ grows as moulds in soil

Diagnostics: CSF, (1) skin scraping → 10% KOH + micro, urine, (2) tissue biopsy ⇒ MICRO

(10-20% KOH w/ Calcofluor white mounts; tissues ⇒ Groscott's methenamine silver (GMS))

Serologic: (1) Immunodiffusion / (3) CFT for antibody detection

Treatment: Amphotericin B followed by an azole (fluconazole)

(2) Histoplasmosis: Histoplasma Capsulatum (Capsulatum duboisii (African type)) inhalation - Worldwide

↳ intracellular mycotic infec.

↳ asymptomatic; only detected by a +ve skin test reaction

↳ dissemination common in elderly ppl or infants (immdef. ppl)

Diagnostics: CSF, (1) skin scraping, urine, (2) tissue biopsy: (3) 10-20% KOH w/ calcofluor white mount

Serologic: Immunodiffusion / CFT - antibody detection Tissue = GMS

Treatment: Amphotericin B followed by oral itraconazole

(3) Blastomycosis: Blastomyces dermatitidis - inhalation of spores

↳ slow progression; untreated = poor prognosis

(1) ↳ pulmonary stage freq. followed by dissemination (2) (abscesses + granulomatous disease in most organs)

↳ Chest x-ray - resembles TB / carcinoma

Diagnosis: same as above; Treatment: Same

(4) Paracoccidioidomycosis: dimorphic pathogen - Paracoccidioides brasiliensis inhalation

↳ chronic granulomatous infection (presents as ulcerative granulomatous inflam of (oral + nasal) mucosa)

↳ involves liver + lymphatic systems

Diagnosis + Treatment: Same

OPPORTUNE!

⑥ Cryptococcosis, aspergillosis, systemic candidosis + Zygomycosis

① Cryptococcosis : by cryptococcus neoformans (encapsulated yeast)
↳ CNS disease - via inhalation though (1° pulmonary cryptococcosis) → haemotogenous spread
↳ bird shit ; opportune pathogen ↳ asymp. carriers
↳ AIDS patients get it (immunocomp. ppl) - skin lesions/manifestations = 2nd most common site of dissemination
↳ Dangerous (1) Meningoencephalitis (symp. develop over months - headache, stiff neck, confusion)
↳ Fungal meningitis

Diagnostics : CSF, blood, urine, biopsy tissue → GMS => Exudates + fluids = India Ink
↳ any +ve micro from anywhere => investigated for disseminated disease
Serology : esp fr meningitis = ELISA / latex agg.
Treatment : healthy ppl : Amphotericin B + oral fluconazole / itraconazole (Azoles)
Immunocomp : amphotericin B w/ flucytosine

② Aspergillosis - genus Aspergillus (flavus, niger, terreus, nidulans, fumigates) everywhere! => Large numbers Rotting plants
↳ Allergic aspergillosis : ppl w/ ↑IgE ; 10-20% of asthmatics react to A. fumigates
↳ fewer hrs later = fever, breathlessness + malaise
↳ ~~Aspergilloma~~ Aspergillosis : Invasive poor prognosis (diagnosed after death)
↳ immunocomp. ppl / after transplant
↳ A. fumigates

Aspergilloma : fungus-ball ; asymp. or cough
↳ haemoptysis during fungus growth - if fungi enter bloodstream = FATAL
(cough up)
Diagnosis : Sputum, tissue biopsy (if disseminated) => 10% KOH w/ Calcofluor white mount ; Tissue = GMS
Serology : agg. reactions = Aspergillus specific antigen
↳ Antibodies in system " => Immunodiffusion (ELISA), PCR → Aspergillus DNA
Treatment : Amphotericin B ; surgical removal of the aspergilloma

③ Systemic Candidosis : Immunosupp ppl / after transplant / ppl w/ neutropenia
↳ DM, preg, vit B12 deficiency - ↑ risk for this
↳ When candida spreads thru body ; life-threatening ; can incl. brain, heart, kidneys, eyes, liver, joints, genital tract
↳ usually C. albicans! (broad spec. ath)

↳ Difficult to diagnose : Micro: wet mount - 10% KOH + Calcofluor

↳ Tissue = GMS, H&E

Serology: ELISA (antibody detec) PCR

Treatment: Amphotericin B, oral fluconazole

④ Zygomycosis - Rare ; by Rhizopus, Mucor + Absidia

↳ rapid tissue destruction

↳ in a debilitated person - most acute + severe

↳ Rhinocerebral zygomycosis ⇒ most common ⇒ nasal cavity, paranasal sinuses + orbit

↳ lungs, GIT, skin

↳ associated w/ starvation, severe burns, IV drug abuse, acute DM, leukaemia/lymphoma

Diagnosis : Micro: 10% KOH w/ Calcofluor white mounts ; H&E or GMS stain.

Treatment: High does of amphotericin B + surgical intervention

(1) Prevent synthesis of ERGOSTEROL
(2) bind to sterols in membrane - Disrupt - Polyenes (Amp B,

(7) Anti-fungal drugs

↳ anti-mycotics kill fungi without dangerous effects on human cells. May have side effects (cos they are toxic fr human cells).

↳ Target their cell membrane - by preventing synthesis of ergosterol OR bind to sterols (in mem) & destroy the mem. structure

(1) Polyenes : Bind to mem. sterols
↳ Amphotericin B - systemic mycoses

(2) Azoles : disrupt ergosterol biosynthesis
↳ Fluconazole - oral or IV ; surface + systemic mycoses + cryptococcal meningitis AIDS
↳ Itraconazole - oral or IV ; systemic or cutaneous " + aspergillosis
↳ Voriconazole - " " " ; Candida + Aspergillus

(3) Anti-metabolites : Infers w/ DNA synthesis
↳ oral in Candidiasis, Aspergillosis + cryptococcosis

(4) Allylamines : Inhibits ergosterol biosynthesis : Terbinafine
↳ Oral + topical to treat dermatomycoses

(5) Echinocandins, Caspofungin : Oropharyngeal + oesophageal Candidiasis
↳ Inhibits synthesis of glucan (fm cell wall)

(6) Griseofulvin : oral fr dermatomycoses
↳ old
↳ must be taken fr months

⑧ Candida - mainly candida albicans - most imp. medical (yeast)

↳ opportunistic oral + genital infec ; Aerogenic transmission

↳ part of gut flora (>80% ppl, no harmful effects); overgrowth = (Candidiasis)

① ↳ Oropharyngeal Candidiasis: incl. thrush, glossitis, stomatitis — DM, babies, AIDS, smokers

↳ rarely seen in healthy adults - Immunocomp. ppl -

↳ symp (if present) ⇒ dryness of the mouth, loss of taste, pain in swallowing

→ is thick, white/cream coloured deposits on mucosal mem.

② ↳ Vaginal Candidiasis: (vaginitis) affects vagina & /or vulva

↳ odorous, (white-creamy discharge) w/ burning, swelling + itching

↳ multifactoral: diet, hormones, preg, diabetes

↳ intestine (= reservoir) ∴ need local + systemic treatment

③ ↳ Skin Candidiasis: common in babies "diaper dermatitis" (Nappy Rash)

Diagnosis ⇒ skin + mucosal form = (swabs) → transport medium (Fungi Quick or CAT)

culture ⇒ Chromogenous media (colourless → colour) (greenish colour (CAT)) ↳ albicans; tropicalis - blue

↳ usual culture mediums ⇒ Round, whitish colonies

↳ Sabouraud Agar ⇒ w/ antibiotics = SELECTIVE MEDIA

↳ prevents growth of bacteria

Biochemical ⇒ Auxacolour

Micro ⇒ wet mount (CAT)

↳ Gram + Giemsa staining ⇒ oval, budding cells ⇒ "Pseudomyelia"

→ CAT ⇒ only TRANSPORT MEDIUM FOR CANDIDA

Treatment: Azoles - topical ; deep candidiasis - amphotericinB

Serologic: (ELISA) or (RIA) - usually -ve in immunocompromised ppl, esp at beginning of Infec

Carinii

anlage

⑨ Pneumocytis Carinii ⇒ Atypical interstial Pneumonia

↳ atypical fungus, yeast

↳ atypical pneumonia in malnourished infants + AIDS (fatal)

↳ weight loss, cyanosis, rapid labaured breathing, non-prod. cough (no sputum)

↳ worldwide ; "bubbly" sound when auscultate

↳ aerogenic transmission

↳ treatment only needed in immunocomp. ppl ⇒ Co-trimoxazole or Pentamidine or Both

Micro: direct IHF or PCR

↳ pulmonary biopsy → GMS → to see cysts

Giemsa - shows trophozoites + sporozoites

Atypical because:

↳ no response to atb like β-lactams

↳ normal leukocyte count (not ↑)

↳ moderate amount of sputum

↳ longer course

Bite → sporozoites enter blood → hepatocytes multiply into MERAZOITES and rupture; TROPHOZOITES enter RBC's → RBC's adhere to endothelium → clot → ANOXIA (6)
TROPHOZOITES → MEROZOITES + GAMETOCYTES.

(10) Malaria Parasites ⇒ Plasmodium

↳ most freq. tropical parasitosis (worldwide - travellers)
↳ bite of Anopheles mosquito
↳ initial symp: non-specific (headache, fatigue, nausea, fever) (1) ICI mistaken as influenza!
→ ↳ untreated malaria (P. falciparum) → lethal - (2) ANOXIA
↳ 4 plasmodium species: fever on 1st day then 48hrs later = 3rd day
- ↳ P. vivax - tertian malaria; Rings + enlarged RBC
- ↳ P. ovale - " " ; " + slightly " "
- ↳ P. malariae - quartan " ; " + " Shrunken"
- ↳ P. falciparum - (malignant) tertian malaria; ring form + normal RBC

Pathogenesis: (1) Infected mosquito bites
(2) Sporozoites fm mosquito's gland → bloodstream → liver parenchyma
(3) Multiply in the liver until they mature - hepatocyte ruptures & thousands of individuals → bloodstream (merozoites)
(4) Then enter RBCs + multiply + rupture cell
P. vivax + P. ovale - some parasites remain in the liver - new infection 2yrs later

Clinical symp - caused in the erythrocytic stage of parasite
↳ first symp = release of parasite
→ ↳ P. falciparum ⇒ RBCs adhere to endothelium of capi → obstruc → anoxia
↳ in the BRAIN = cerebral malaria (1)
↳ " " KIDNEYS = renal failure (2)

Treatment: Daily dose of chloroquine or mefloquie - until 4 weeks after leaving risk area
Prevention: Other protective measures
~~Diagnosis~~ Treatment: quinine, quinidine, tetracyclines + clindamycin

Diagnosis: Smear using thin smear + thick ~~drop~~ smear
↳ FRESH, NON-CLOTTED BLOOD
↳ Giemsa stained

Thick ⇒ drop mixed w/ corner of another slide
Not fixated

Thin ⇒ Spread on the slide by special movement + fixated

(11) Toxoplasma gondii & Cryptosporidium parvum

↳ tissue parasite

↳ T. gondii => coccidian parasite, protozoan

↳ protozoa, unicellular, spore forming

↳ intracellular; birds, humans, cats etc; Reservoir host = (CATS!)

↳ only reproduces in cats

↳ humans eat undercooked meat or handling cat faeces

↳ ppl w/ dogs at risk coz dogs run abt etc - get covered in stuff.

↳ usually asymptomatic but affects immunocomp ppl => fever, maculopapulous exanthema, generalized lymphadenitis, hepatosplenomegaly, toxoplasma chorioretinitis, meningoencephalitis

Diagnosis: Acid fast -> Ziehl-Neelsen

Serologic -> antibodies against T. gondii, (ELISA), (PCR)

Treatment: • Clindamycin (cerebral toxoplasmosis)

✓ • Spiramycin (during pregnancy)

Can cause C. difficile related diarrhoea

Cysts in pigs transform into tachyzoites and then cyst bradyzoites in tissue.

Cryptosporidium parvum => in animals or water

↳ immunocomp => severe (diarrhoea) (1) (acute, watery + non bloody)

↳ Cryptosporidiosis => parasitic disease of the (intestinal tract)

↳ anorexia, nausea/vomiting/ab pain (2)

↳ faecal-oral

↳ in healthy ppl => self-limiting, usually mild

Diagnosis: stool for oocytes - Ziehl-Neelsen or IHF, using monoclonal ab

coproantigens detected by (ELISA), (CFT)

↳ IgA + IgG antibodies

IgA - recent infec

IgG - after an infec

Treatment: Nitazoxanide

Fluid replacement

* Preg. women who IgG+ are more protected than those who are IgG-

(12) Entamoeba Histolytica → Entamebosis

↳ anaerobic parasitic protozoan

↳ most imp human parasite

↳ invade colonic mucosa → produces ulcerative lesions → bloody diarrhoea

↳ seen in liver abcesses - live in the walls of abcesses, so even last drop of pus contain the amoeba!

↳ Humans are reservoirs!

↳ infec. due to transmission of mature cysts w/ contaminated food, water or faecally contaminated hands. (usually Cl^- in H_2O kills them)

① ↳ Asymp: intestinal forms.

② ↳ Invasive " " " - invasion of intestinal wall + large intestine disease

↳ acute disease: ab. discomfort + diarrhoea

↳ Extraintestinal forms - develop because of haematogenous dissemination

↳ liver abcesses

Diagnosis: blood stained mucosa - examine within 2hrs - Light M.

detection of coproantigen - ELISA

Treatment: Nitromidazole

- Intestinal
- Protozoan
- colon ulcers → diarrhea
- liver abcesses
- food, water, faeces
- Asymptomatic and Invasive form in Intestine
- Extra intestine forms → Liver abcesses.
- ELISA
- Nitromidazole

(13) Giardia lamblia/intestinalis → Giardiasis

- water borne ; worldwide
- upper s. intestine → mal-absorption of fat, (4) chronic diarrhoea
- dangerous for children
- Trophozite form in humans ; cyst outside humans (excreted in stool
- s. intestine = (2) inflam + (3) malabsorption
- usually asymptomatic ; humans = reservoir
- if symp => chronic + recurrent diarrhoea (4) steatorrhea, fever, upper ab. pain, weight loss

Diagnosis : stool examination using SAFC technique to detect cysts
ELISA for giardia specific antigens

Therapy : Nitroimidazole compounds - metronidazole

(14) Trichomonas Vaginalis ⇒ Trichomonosis

↳ anaerobic, parasitic flagellated protozoan
↳ women – symp. show – cervicitis, vaginitis, itching/burning, vaginal discharge (yellow-green)
↳ men – asymp. (urethritis)
↳ STD – oral/anal sex
↳ usually infx of urogenital tract

Diagnosis: trichomonads in micro
↳ Giemsa alone or Giemsa + Gram staining
↳ CAT – transport + culture medium for Trichomonas
↳ ELISA & for antigen detection
↳ PCR for DNA

Called Culture – Microscopy
① CAT swab + wet mount –
② Giemsa stain

Treatment: for both sexual partners
↳ Nitromidazole – metronidazole (orally)

Urogenital parasite, ♂ asymptomatic

MA VM
Microscopical appearance of Vaginal Microflora:
• immersion 100 x

(15) Trypanosoma

↳ unicellular parasitic flagellate protozoa

↳ T. brucei gambiense + T. b. rhodesiense ⇒ African trypanosomosis (Sleeping sickness)

↳ complex life cycle - involves vector (Tse Tse fly)

↳ Insect bite → chancre → invasion of blood (multiplication) → invasion of NS → Sleeping Disease → Death

↳ Initially ⇒ fever, ↓ lymphadenopathy, later ⇒ (1) meningoencephalitic symp.

Diagnosis ⇒ direct detection of trypanosomes in blood, CSF, lymph node aspirates

↳ Giemsa stained thick / thin smears

Treatment ⇒ • early stage = suramin, pentamidine

Sleeping disease = melarsoprol or tryparsamide (TOXIC!)

T. cruzi - S. America ⇒ Chagas disease

↳ vector = Reduviid bugs (Kissing bugs)

↳ Insect bite → shits → bug feces containing parasite goes into bite wound → invade blood stream → invade RES & muscle tissue (multiply) → loose mem + flagellum → round shape → CHAGAS DISEASE (cardiomyopathy, megacolon) → Death by HF!

↳ Initial - fever, oedema, lymphnode swelling, hepatosplenomegaly

Diagnosis ⇒ • thick blood smears (trypanosomes detectable)

(PCR) DNA

Treatment ⇒ early stage = 80% success = Nifurtimox + Benznidazole

↳ side effects!

(16) Leishmania => leishmaniasis

↳ parasite ; transmitted by sand flies ; warmer countries

↳ (1) visceral leishmaniasis (VL), (2) cutaneous (CL), (3) mucocutaneous (MCL)

↳ Central Europe => leishmaniasis = imported disease + HIV associated

↳ Symp: skin sores (→ weeks → months after bite), fever, damage to spleen + liver + anaem

↳ they occur months → yrs after bite (Splenomegaly!)

↳ VL => most serious + fatal if untreated

↳ CL => most common => sore at bite site. Can progress to any other form

↳ Diffuse CL => widespread skin lesions => diff. to treat

↳ MCL => skin ulcers which spread & causing tissue damage esp nose + mouth

Diagnosis : Tissue Sample from margin of lesion - Giemsa stain (thin smear)

VL => direct parasite detection in aspirate material fm LN or b. marrow in

• Giemsa stained smears, in cultures or using PCR

CL => clinical evidence . Verification by direct parasite detection

Treatment : VL => Pentavalent antimonials (= meglumine antimonate), amphotericin

Antifungal azoles

Parasitic worms = Helminths

(17) Ascaris Lumbricoides & other intestinal nematodes (roundworms)

↳ Ascariosis ↳ LARGE ROUNDWORM ↳ thread like.

↳ contaminated food ; tropical regions + areas of poor hygiene

↳ usually asymp. but maybe accomp by inflam, fever + diarrhoea + hepatosplenomegaly

↳ their eggs - extremely resistant to strong chemicals, dessication + low temp

↳ usually not pathogenic but can invade bile ducts + pancreatic ducts → obstruction (1)

• Life cycle: Ingestion of eggs → hatch in duodenum → penetrate gut wall → enter bloodstream (to heart) → enter pul. circ → 2 moults → migrate via trachea to GIT (coughing + swallowing) → mature in gut lumen for years

Diagnosis: eggs in the stool < fertile egg - round
infertile - longer + irreg.

Treatment: Pyrantel, Nitazoxanicle

• Toxocara canis: dog ascarid ; accidentally affects humans. Can cause Retinal lesions

• Trichuris trichuria → common whipworm → Trichuriasis ; soil

↳ infec of large intestine - usually asymp. (symp → bloody diarrhoea, anaemia, rectal prolapse (rare)

! Intestine infection.

Diag: stool ova → eggs in shit Treat: oral by mebendazole

• Hookworm (Ancylostoma duodenale + Necator Americanus) - Tropics + subtropics

↳ S. intestine ⇒ enteritis + anaemia

↳ bloodsuckers Treat: local cryotherapy (if still in the skin); Albendazole

Diag: eggs in stool (late infec) + not bile stained

• Pinworm (Enterobius vermicularis) ⇒ children worldwide

↳ l. intestine + appendix ↳ Enterobiasis

↳ contaminated food + water + hands ; itchy anal area (eggs are laid over there)

Diag: transparent tape on the anal area - picks up the eggs + micro of the tape

↳ "GRAHAM METHOD" - children ; adults = hairy : harder (stool)

Treat: Albendazole, mebendazole

! Faust + Kato methods for diagnostics ! (end of this section)

↳ counterstain w/ malachite green

(18) Tissue Nematodes

↳ incl. all ① filarial worms, ② Guinea worm + ③ Pork worm

Guinea worm => Dracunculus medinensis → Dracunculiasis

↳ contaminated stagnant water drinking

↳ oedema, blister then ulcer; skin perforation w/ pain, fever + nausea; (2° bac. infec) occ

↳ No vaccine or treatment medication!

↳ Diag: based on clinical manifestations

Wuchereria bancrafti → Elephantiasis. => thickening of the skin + undelying tissues, esp leg (gross oedema)

↳ (mosquitoes); tropics; go to lymphatics + mature there → (lymphatic filariasis)

- Loa Loa → loa loa Filariasis (Disease); deer flies / yellow biting flies; Rainforest + swap forest areas

↳ subcut. tissue → wanders → occ. front of eye

↳ (Fed itchy swellings) below the skin - "Calabar swellings"

Diag: blood sample - thick smear - Giemsa or H&E stain

Treat: Diethylcarbamazine (DEC); Surgical removal of the worm

- Pork Worm Trichinella Spiralis → Trichinosis - asymp or minor ones => nausea, heartburn, diarrhoea, headache, fever, joint pain, muscle pain

↳ worldwide; wide host range

↳ undercooked pork or rat meds.

↳ Death by (myocarditis), (encephalitis or (pneumonia)

Diag: rarely found in stool or duodenal fluid; muscle biopsies (micro, PCR - DNA or histo

Treat: mebendazole or (albendazole) in combination w/ (prednisolone)

(19) Trematodes "The flukes"

↳ blood, liver, lung, intestinal (symp - chronic diarrhoea, ch pain)

↳ Treat: Praziquantel, Niclosamide or tetrachloroethylene

↳ infected water, eating infected aquatic vegetation

- Chinese liver fluke "Clonorchis sinensis"

↳ liver + feeds on bile

↳ lives in the bile ducts + causes inflam. reaction (→ hyperplasia + cholangiocarcinoma)

- Fasciola hepatica "Common / sheep liver fluke"

↳ obstructive jaundice

Diag: eggs in shit Treat: Triclabendazole

- Lung fluke "Paraginimus Westermani"

↳ pul. infec.

Diag: eggs in shit / sputum Treat: Praziquantel

- Blood flukes "Schistosoma species" → Schistosomiasis (snail fever)

↳ chronic illness - damages internal organs

↳ penetrate skin → swimmers itch (dermatitis) → enter blood → liver + mature there → migrate to rectum or bladder veins → miracidium is passed thru rectal mucosa or bladder wall → can see them in faeces + urine

↳ Dysentry, Haematuria

↳ worms themselves not dangerous - granulomas, fibrotic lesions of liver, bladder + organ due to egg deposition

↳ Diag: look for eggs (urine) Treat: Praziquantel

(20) Cestodes – Tapeworms!

↳ digestive tract

- Taenia Saginata - Beef tapeworm 3-5m length (can be upto 20m)
  ↳ raw/undercooked food

life cycle: raw/undercooked food w/ encysted larvae → ingestion → larvae hatch in s. intestine → attach to mucosa + mature → grow

↳ usually asymp. (dizziness, ab pain, headaches, diarrhoea, nausea + loss of apetite)

Diag: segments in faeces (no eggs are laid)

Treat: Praziquantel + Niclosamide (causes eggs to release + infec occurs)

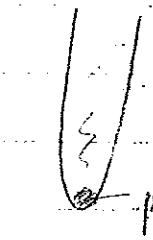
- Pork tapeworm "T. solium" - undercooked pork
  ↳ eggs hatch + form cysticerci in brain → Cerebral cysticercosis

Diag: biopsy of infec tissue + exam. of faeces

Treat: Praziquantel

FAUST + KATO Methods!

Faust : - stool is mixed w/ $ZnSO_4$ sol
- centrifugated
- Supernatant taken for the next step
- Sd. filled upto the top of the test tube + covered by a coverslip
- remove coverslip + place onto half of a slide



Kato : wet mount + Counterstain w/ malachite green ⇒ helminth eggs visible!
parasite eggs!