

## DRUG RESISTANCE

It refers to unresponsiveness of a microorganism to an antimicrobial agent.

### Types

- Natural
- Acquired.

#### Natural

→ Some microbes show resistance inherently.  
→ this is because they lack the metabolic process or target sites which is affected by that drug.

- eg: ✓ penicillin G - gram negative bacilli  
✓ Metronidazole - aerobic organisms.  
✓ Aminoglycosides - anaerobics.  
✓ Tetracyclines - M. Tuberculosis.

#### Acquired

• It refers to development of resistance by an organism {which was sensitive before} due to the use of an AMA over a period of time.

Resistance can be developed by.

- mutations.
- gene transfer.

{ Table on pg page }

#### Transformation

• resistant bacteria may release genetic material into the medium which is taken up by another bacterium.

eg: pneumococci - penicillin

#### transduction.

plasmid DNA is transferred through bacteriophage

Staphylococci - penicillin.

#### Conjugation.

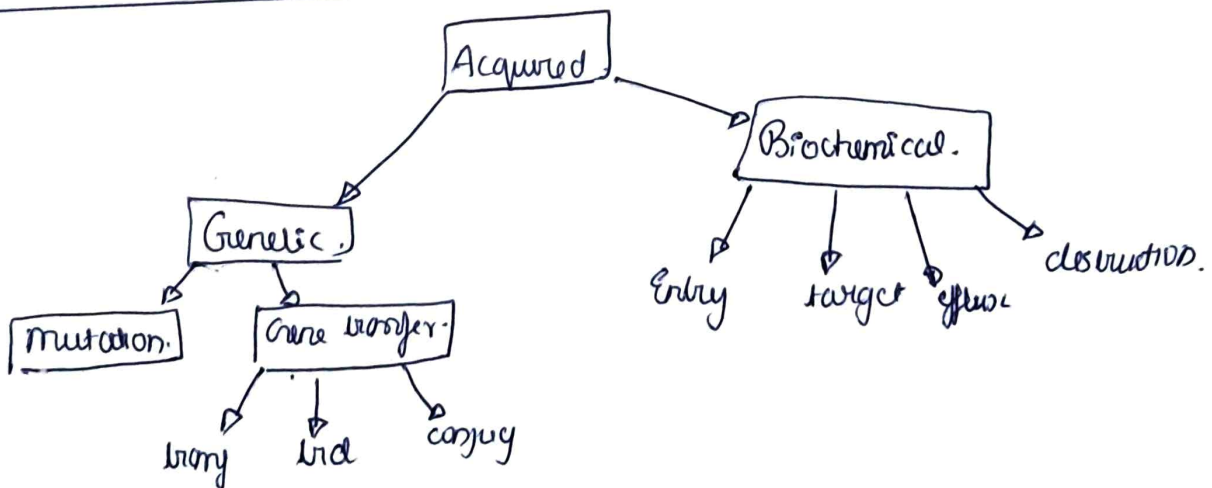
The resistance factor is transferred from cell to cell.

Salmonella  
chloramphenicol - typhi

STC

Q) Superinfection \* MOA of AMR - with diagrams.

	Mutation.	Gene transfer.
definition. :	stable and heritable genetic change that occurs spontaneously and randomly among microbes.	- resistance causing gene is passed from one organism to another.
transfer of resistance	vertical.	Horizontal.
Time	Slow process.	rapid process.
degree of resistance.	low	high.
resistance acquired by.	Single step. multistep	conjugation transduction transformation.



## Biochemical Methods.

### ① ENTRY

- decreased entry → Aminoglycosides.

### ② Efflux

- Increased efflux → Quinolones.

### ③ MODIFIED TARGETS

altered PBP in MRSA.

### ④ DRUG INACTIVATION

- $\beta$  lactamase.
- chloramphenicol acetyl transferase.

Resistant organism can be broadly of the following 3 types:

#### → Drug tolerant

It loses affinity for a PABA.

#### → Drug destroying

• enzyme that inactivates drug.

#### → Drug impermeable

loss of porins.

## CROSS RESISTANCE

• resistance seen among chemically related drugs.

→ development of resistance to one drug is also resistant to other chemically related drugs.

eg: among tetracyclins.

## Prevention of DRUG RESISTANCE

### ① Avoid inadequate use

eg: Non compliance.

### ② Avoid indiscriminate use.

eg: viral URTI

### ③ use narrow spectrum, rapid acting whenever possible

### ④ use Combination regimen.

## POST antibiotic effect

- Bactericidal effect is present even when the serum concentration falls below MIC.
- after a brief exposure to the organism is placed in an antibiotic free medium, the organism will start multiplying again after a lag period.
- this lag period is referred to as post antibiotic effect.

eg: Aminoglycosides

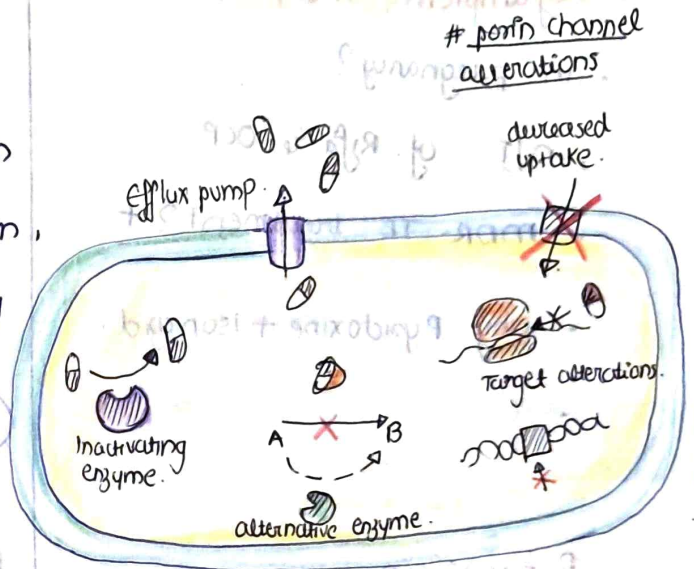
↓  
g<sup>-</sup> bacilli

↓  
2-6 hours PAE

## Significance.

- ① allows less frequent dosing especially for drugs with long PAE.
- ② helps reduce toxicity as there is less frequent dosing.
- ③ Imp't in designing dosing regimens.

## Resistance Mechanisms



- ① efflux pump
- ② decreased uptake
- ③ inactivating enzymes
- ④ alternative enzyme
- ⑤ target alterations