DISEASE CONTROL & DRUG DELIVERY SYSTEM

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- Inhibition of cell wall synthesis-
- Bacteria possess cell wall, this structure is critical for the life and survival bacterial species.
- A drug that target cell walls can therefore selectively kill or inhibit bacterial organisms.
- Example: penicilins, cephalosporins, bacitracin and vancomycin.

- Mode of action-
- Peptidoglycan continues with transpeptidation and the binding of soluble uncrossslinked, nascent peptidoglycan to the preexisting, cross linked, insoluble cell wall peptidoglycan matrix.

- Inhibition of protein synthesis-
- Several types of antibacterial agents target bacterial protein synthesis by binding to either the 30s or 50s of intracellular ribosome.
- This results in disruption of the normal cellular metabolism of the bacteria, and consequently leads to the death of the organism or the inhibition of its growth and multiplication.
- Example: chloramphenicol, lincosamides, streptogramins, tetracyclines.

- Mode of action-
- chloramphenicol binds to the ribosome subunits thus inhibiting peptide bond formation.

- Inhibitors of nucleic acid synthesis-
- DNA and RNA are keys to the replication of all living forms, including bacteria.
- Some antibiotics work by binding to components involved in the process of DNA or RNA synthesis, which causes interference of the normal cellular process which will ultimately compromises bacterial multiplication and survival.
- Example: quinolones, metronidazole, rifampin.

- Mode of action-
- Quinolones and their derivatives, inhibit enzymes that are required for bacterial DNA synthesis.

- Inhibitors of other metabolic processes-
- Other antibiotics act on selected cellular processes essential for the survival of the bacterial pathogens.

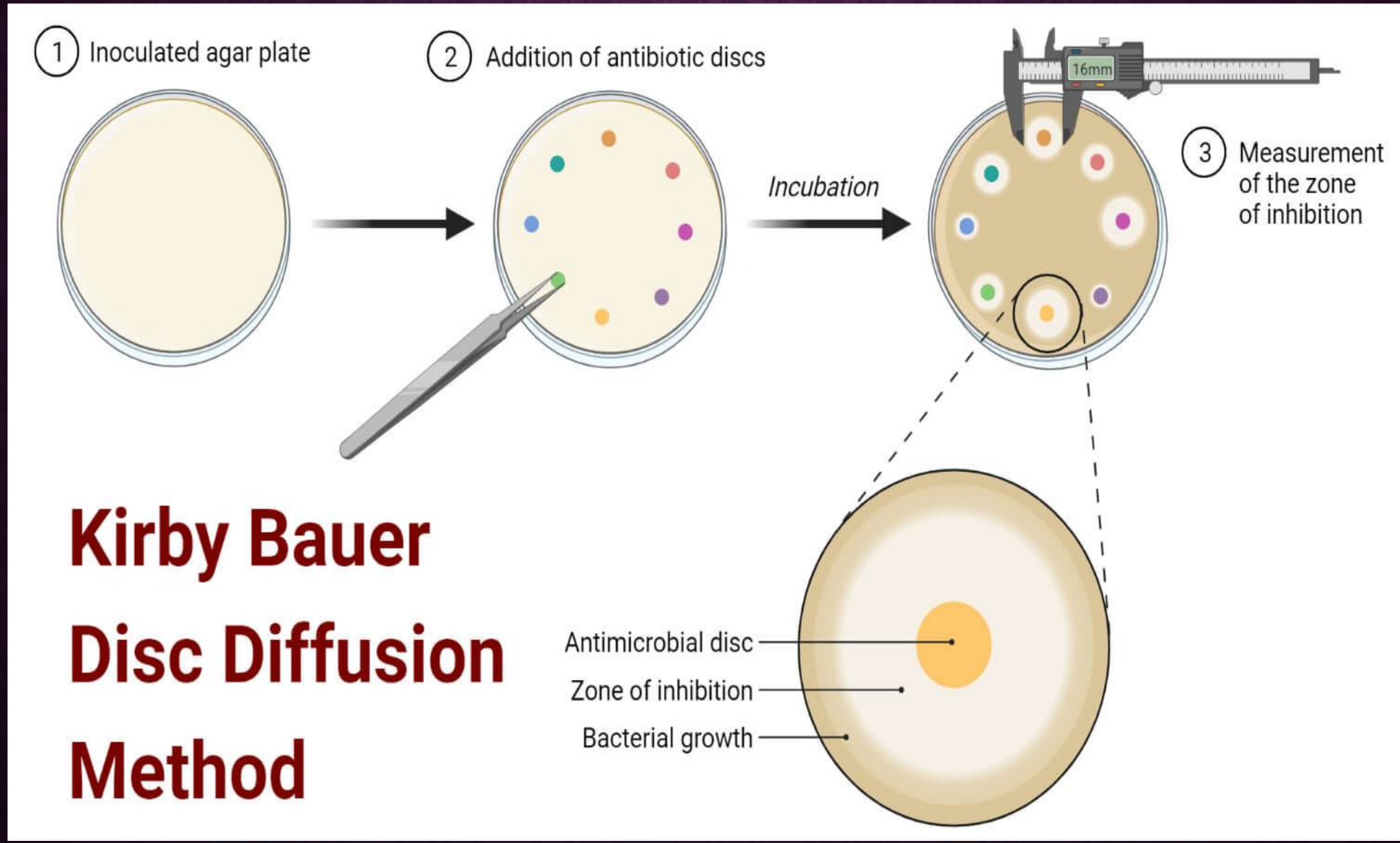
- Mechanism of action-
- Enzyme bind into its active site-acid is no longer synthesized-Cell wall stop dividing

REASONS FOR DEVELOPMENT OF RESISTANCE

- Acquisition of antibiotic resistance genes
- Enzymes that degrades the antibiotic
- Pumps which rapidly expel the antibiotic
- Barriers which resist penetration of antibiotic
- Molecular changes which prevent binding of the antibiotic to the target site.

KIRBY BAUER DISC DIFFUSION METHOD FOR ANTIBIOTIC SUSCEPTIBILITY TESTING

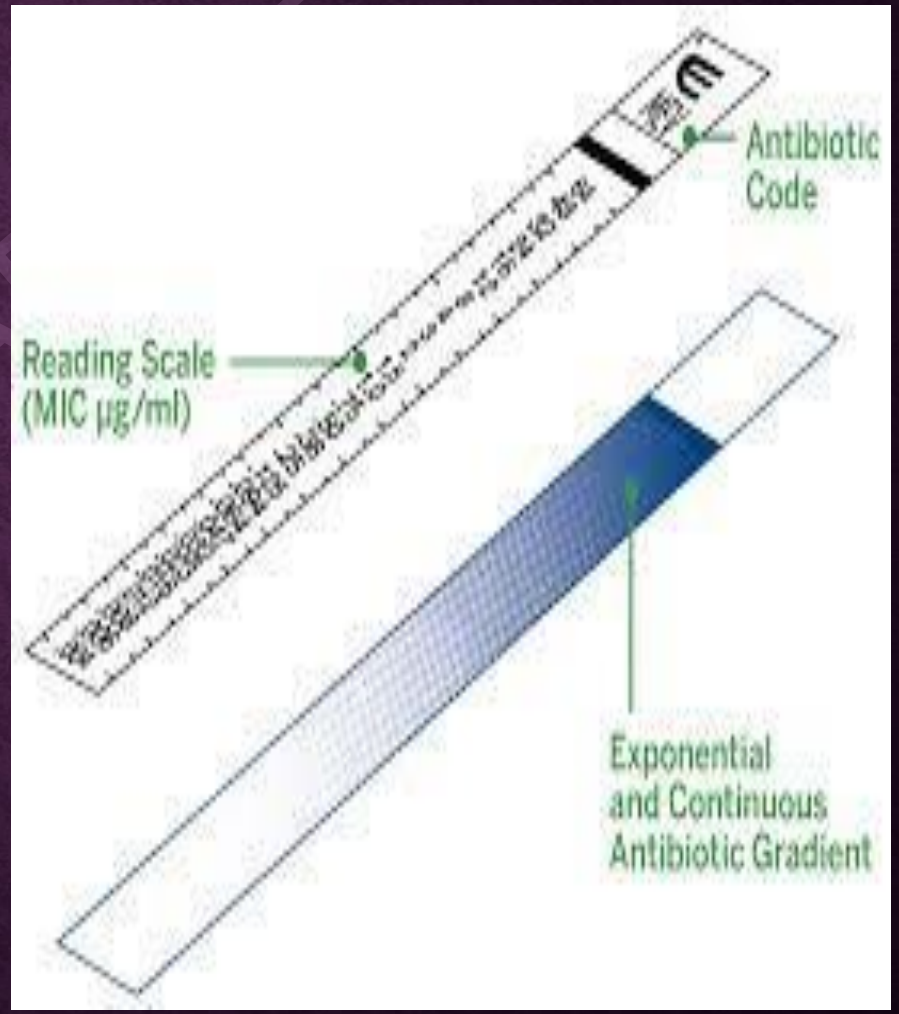
- M .M. Kirby and A.W. Bauer proposed a single disc diffusion method for antimicrobial susceptibility testing
- Purpose- to determine the sensitivity or resistance of pathogenic bacteria to antimicrobial compound.


1 Inoculated agar plate
2 Addition of antibiotic discs
Incubation
16mm
3 Measurement of the zone of inhibition
Kirby Bauer Disc Diffusion Method
Antimicrobial disc
Zone of inhibition
Bacterial growth

E TEST FOR DETERMINING MIC

- E test is a quantitative technique for determining the antimicrobial susceptibility of gram positive and gram negative bacteria.
- The system comprise a antibiotic gradient which is used to determine the minimum inhibitory concentration (MIC) of different antimicrobial agents against microorganisms as tested om agar media using overnight incubation
- MIC is defined as the lowest concentration of antimicrobial agent required to inhibit growth of the organism.


E
DOR
32
24
16
12
8
6
4
3
2
1.5
1
0.75
0.5
0.38
0.25
0.19
MIC 0.25 µg/ml


Antibiotic Code
Reading Scale (MIC µg/ml)
Exponential and Continuous Antibiotic Gradient

BASIC PRINCIPAL OF DRUG DESIGNING

- **Novel drug delivery system**
- 1. drug formulation
- 2. medical device or dosage form/ technology
- 3. mechanism for the release

- **Conventional drug delivery system**
- Increased specificity of drug
- Better patient compliance
- Lower healthcare cost
- Shorter hospitalization, etc.

NEW DRUG DELIVERY SYSTEM (DDM)

- New DDS are based on interdisciplinary approaches that combine polymer science, pharmaceutics, biconjugate chemistry, and molecular biology.
- Among drug delivery system one can name soluble polymers, nanoparticles such as microspheres made of insoluble or biodegradable natural and synthetic polymers, microcapsules, and lipoproteins, liposomes, and micelles.
- These new strategies often called new DDS that have been deduced include the following:

a) Transdermal delivery system

b) Carrier based delivery system

c) Variable release delivery system

d) Implantable delivery system

e) Nasal delivery system

TRANSDERMAL DELIVERY SYSTEM

- Transdermal DDS are laminated patches which adhere to the skin and permit absorption of drugs from the skin surface through its layers into the general blood circulation.
- Products which have been commercialized- Transderm- nitro for delivering nitroglycerin as also catarpress

- 1. Ionotophoresis:
- Electrochemical method- transport solute molecule-through skin- with applied electrical current or voltage.
- Migration of ionic drugs into skin

- 2. Phonophoresis :
- Transport of drug through skin using ultra sound.
- Combination of ultrasound therapy with topical drug therapy
- Product is applied to the skin and some times is allowed for drug to begin absorption into the skin then ultrasound unit is applied.

CARRIER BASED DELIVERY SYSTEM

- 1. Liposomes:
- Artificial bilayer made of phospholipid.
- Drugs incorporated in liposomes and administered to the body can be delivered at the desired site, in the needed concentration.
- Therapeutic application of liposomes:
- Leishmaniasis, tuberculosis, malaria, yellow fever, cancer chemotherapy, arthritis, diabetes, use as adjuvants in vaccine.

- 2. Monoclonal antibodies
- Artificially produced proteins- specificity for one single antigen.
- Purpose- destroy diseased tissue without harming healthy one and reduced side effects.

- Therapeutic application of Monoclonal antibodies
- Cancer, melanoma, ovarian disease

- 3. Nanoparticles
- Submicron size act as a carrier of drug molecule which is amorphous.
- Drug is dissolved, entrapped to material
- Distribution of nanoparticle in the body either by coating them with serum or by antibodies.
- Therapeutic application of Nanoparticles
- Therapy in liver, cancer, vaccination

- 4. Microspheres
- Small solid particulate carriers in crystalline form or in solution
- Microspheres made from natural and synthetic polymers.
- Reach target site- by suitable mechanism- into relevant body compartment

- Therapeutic application of Microspheres
- Albuim, fibrinogen, collagen, etc systems

VARIABLE RELEASE DELIVERY SYSTEM

- 1. osmotic pumps
- The technology for osmotic pumps exploits the tendency of a fluid equalize the concentration of substances on both sides of a semipermeable membrane.
- Design to deliver different drugs at different rates. Several benefits- controlled system, minimized side effects, tamper resistant device.
- Acuteim and Acusystem C to release drugs

2. Microencapsulation

- Process of applying relatively thin reproducible coatings to small particles of solids or droplets of liquid and dispersion to produce microcapsules.
- Route of administration of microcapsules primarily determines the procedure used for microencapsulation.
- It may not be possible to encapsulated solids by the same process as liquids.

- 3. Ion exchange Resin system:
- Ion exchange Resin system involves preparation of drug charged resin and its drying to form beads.
- Gastro- intestinal tract the drug molecule is exchanged for an appropriate charged ions and so the drug is released at controlled rate.
- Pennikinetic system used to deliver a variety of antitussives.

- Pellets in capsule system:
- Relatively simpler technology and has been developed to deliver controlled amounts of the drug.
- Naproxen and verpanil, erythromycin

IMPLANTABLE DELIVERY SYSTEM

- Implants are sterile polymeric devices of varied shapes containing one or more medicines for introduction into the body tissues for release in a controlled manner.
- Advantage: provide uninterrupted treatment for prolonged time
- Dual advantages of location and rate control.
- Application- diabetes, cancer, contraception, cardiovascular and brain disease.
- System commercialsed- lacrisert for artificial tear therapy, ocusert for glaucoma management.

NASAL DELIVERY SYSTEM

- Conventional nasal formations in the form of spray and drops have used delivery systems like the single dose pipettes, metered dose spray, aerosol valve devices.
- Commercialised products include calcitonin for metabolic bone disease, desmopressin acetate for primary mocturnal vienuresis.