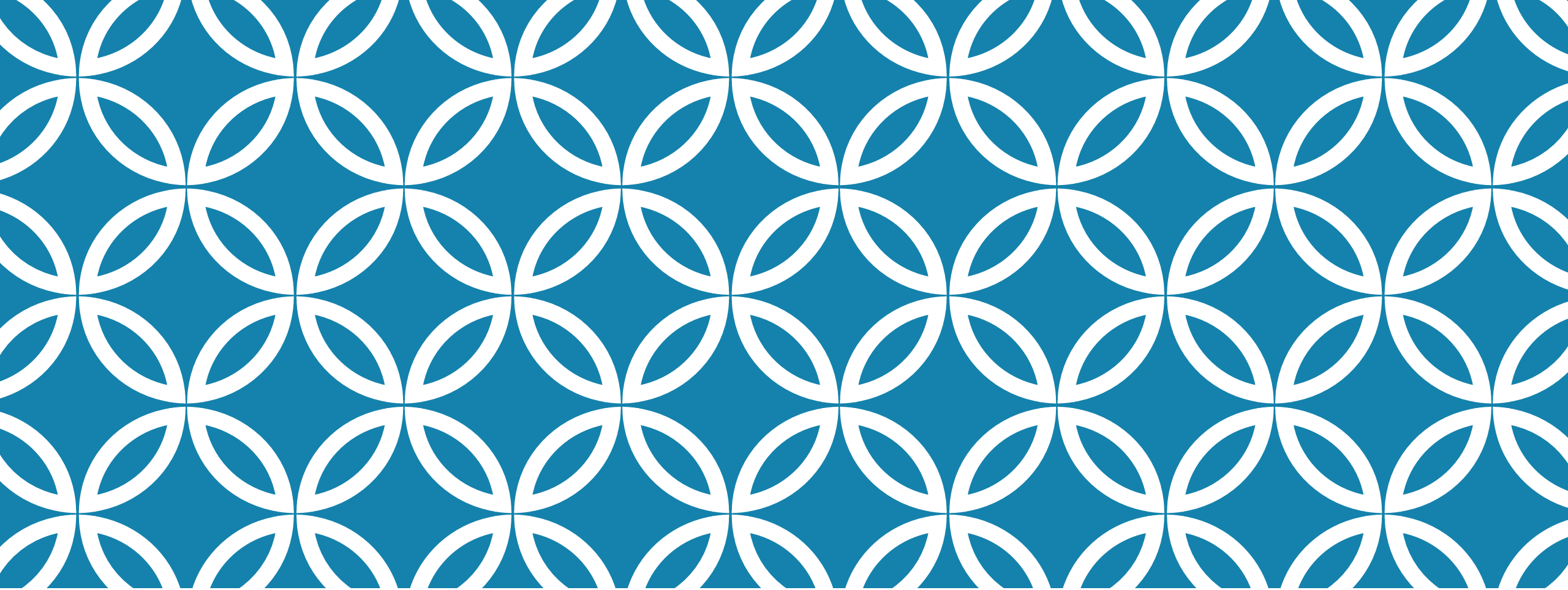

PHARMACOLOGY - II

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PHARMACOLOGY !!

- Welcome back to Pharmacology !!!

EXCITING STUFF WE WILL EXPLORE THIS SEM

Chemotherapy

- 30 hrs

Immuno-modulators

- 9 hrs

Drugs for Endocrine systems

- 11 hrs

Hematological Disorders

- 10 hrs

CHEMOTHERAPY

Chemotherapy

- Drugs to treat general infections
- Anti-fungal
- Anti-viral
- Drugs for TB, Leprosy, Malaria
- Drugs for Amoebiasis
- Anthelmentic Drugs
- Anti-cancer drugs

IMMUNO-MODULATORS

Immuno-modulators

- Understanding immune function
- Drugs use to stimulate or suppress immune function
- Immune modulators used to treat cancer, HIV
-

DRUGS TO TREAT ENDOCRINE DISORDERS

Endocrine disorders

- Thyroid & Ant-thyroid drugs
- Drugs to treat diabetes
- Bone mineral homeostasis
- Oxytocics
- Oral contraceptives

DRUGS TO TREAT HEMATOLOGICAL DISORDERS

Hematological disorders

- Drugs used in Anemia
- Coagulants, Anti-coagulants
- Thrombolytic and Anti-platelet agents

WHAT EXCITING STUFF WE WILL EXPLORE

Chemotherapy

Immuno-modulators

Drugs for Endocrine systems

Hematological Disorders

CHEMOTHERAPY

- *What is Chemotherapy ?*

- Use of CHEMICAL compounds in treatment of INFECTIOUS diseases, so as to destroy offending ORGANISM and PARASITES without damaging the HOST tissue

BRIEF HISTORY OF CHEMOTHERAPY

Pre-Ehlrich Era before 1891

Period of Paul Ehlrich

Period after 1935, Antibiotic Era

BRIEF HISTORY OF CHEMOTHERAPY

- Paul Ehlrich (Organic Chemist)
- Certain Dyes specifically killed/stained certain bacterial cells
- Generated a thought/Idea "Synthesize chemicals that can Kill organism" – Magic Bullet
- *Methylene Blue to treat Malaria*
- *Arsenic compounds to treat other infections*

BRIEF HISTORY OF CHEMOTHERAPY

- Paul Ehlrich proposed the concept of “RECEPTORS’
- Specific chemical group on cell cell surface
- Both Organisms/Human would have RECEPTORS
- Drug + Human Receptor = BAD effect (Organotropic Compound)
- Drug + organism Receptor = Killing Effect on Organism (Parasitotropic Compound)
- Drug “ARSEPHENAMINE” designed to treat Syphillus
- Awarded NOBLE PRIZE for his work in 1908

BRIEF HISTORY OF CHEMOTHERAPY

- Domag & His group continued ahead with Ehlrich's work
- Protonsil: Azo Dyes + Suphonamide side chain = treated Streptococci infection
- Later, discovered that Sulphonamide get's released in body, affects *Streptococci*
- *Domagg awarded Nobel Prize in 1939*

BRIEF HISTORY OF CHEMOTHERAPY

- Early in last century an Interesting idea was floated
- *"Use one microorganism to cure infection by other organism"*
- Pasteur (1885) demonstrated the Proof of this concept
- Common bacteria prevented growth of Anthrax bacilli
- Another group: Emmerich found extracts of *Pseudomonas Aeruginosa* could destroy variety pathogens

BRIEF HISTORY OF CHEMOTHERAPY

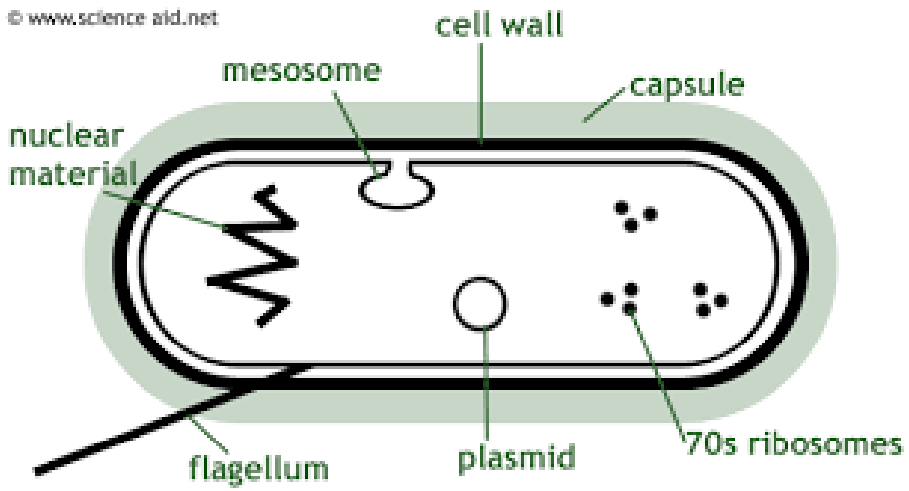
- In 1928, Sir Fleming while working on Staphylococcal variants saw a fungal growth around
- This fungus appeared to stop the growth of Staphylococcal
- He cultivated the fungus, named it penicillin
- Subsequent work by Florey, Chain & Abraham's work: In 1941- Penicillin was established as potent drug during WW-II to treat infections
- Florey, Chain & Abraham awarded Nobel prize in 1945

BRIEF HISTORY OF CHEMOTHERAPY

- Penicillin work led to screening of thousands of microrganism
- Schatz et.al reported isolation of Streptomycin from *S. griseus*
- Major advancement since Streptomycin was effective against G-ve
- This group also coined word “Antibiotic”
- Most of Antibiotics derived from Fungi but some from bacteria as well

HOW TO TARGET THESE MICRO-ORGANISM ??

- The IDEA is to find what is different between these organism & our cells !
- Strategy or Plan then would be to target that difference

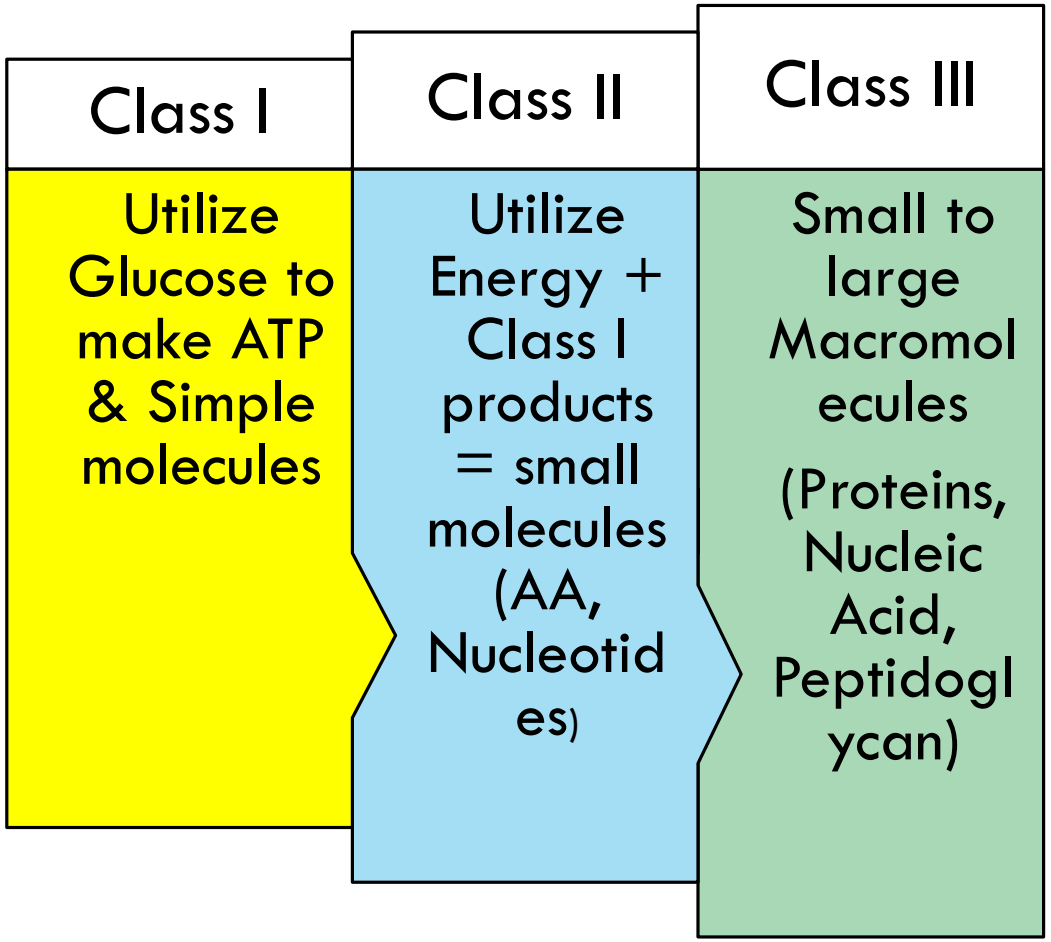


You can target

1. Biochemical Reactions specific to bacteria
2. Specific Bacterial Structure

HOW TO TARGET THESE MICRO-ORGANISM ??

Biochemical Reactions that are specific to Bacteria can be Potential Targets



HOW TO TARGET THESE MICRO-ORGANISM ??

Biochemical Reactions that are specific to Bacteria can be Potential Targets

Class I

Utilize Glucose to make ATP & Simple molecules

Class I Reactions:

- Not very Promising
- Both Host & bacteria use similar pathways (TCA, Embden-Meyerhof)
- Even if glucose oxd is blocked, Bacteria are smart/adapt to use other pathways

HOW TO TARGET THESE MICRO-ORGANISM ??

Class II

Utilize Energy & Class I products = small molecules (AA, Nucleotides)

- Folate Biosynthesis
- Humans get it from outside
- Bacteria has to synthesize !
- We can target this pathway, That's what SULPHONAMIDES do !!

HOW TO TARGET THESE MICRO-ORGANISM ??

Class II

Utilize Energy + Class I products = small molecules (AA, Nucleotides)

- **Nucleotide Biosynthesis:**
- Purines & Pyrimidines Analogs
- Strategy: To disrupt, block Nucleotide biosynthesis
- This would prevent Bacterial DNA Replication
- Bacteriostatic Effect !

Bacterial enzymes are more sensitive to inhibition compared to humans

HOW TO TARGET THESE MICRO-ORGANISM ??

Class III
Small to large Macromolecules (Proteins, Nucleic Acid, Peptidoglycan)

Pathogens cannot take up macromolecules from environment
Potential targets for drugs

1. Peptidoglycan Synthesis (Bacterial Capsule)
   1. Synthesis vulnerable, can be blocked at various steps
   2. Wide range of antibiotics attack this step
   3. Cycloserine, Vancomycin, Bacitracin, Penicillin's etc

HOW TO TARGET THESE MICRO-ORGANISM ??

Class III
Small to large Macromolecules (Proteins, Nucleic Acid, Peptidoglycan)

1. <u>Nucleic Acid Synthesis</u>
   1. Inhibit synthesis of Nucleotides
   2. Alter base pairing
   3. Inhibit DNA or RNA polymerase enzyme
   4. Inhibit DNA Gyrase
   5. Direct effect on DNA Itself

HOW TO TARGET THESE MICRO-ORGANISM ??

- Targeting "Formed Structures"
- *Plasma Membrane (PM):*
- Bacterial/Fungal PM similar to Humans but can be Easily disrupted
- Polymixins (Cationic peptide antibiotics)
- Act as detergents, disrupting PM
- *Fungal PM has large amounts of Ergosterol*
- Polyene Antibiotics (Nystatin, Amphotericin) leakage of ions (Act as ionophores)
- Azoles block Ergosterol synthesis

HOW TO TARGET THESE MICRO-ORGANISM ??

- Target: INTRACELLULAR ORGANELLES
- **Microtubules or Microfilaments:**
- Drugs target parasitic tubulin (Albendazole)
- **Food vacuole:**
- Drug target malarial parasite polymerase reaction
- Target: MUSCLE FIBRES:
- Anthelmintic drugs have selective action on Helminth muscle cell