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Antimicrobial Agents

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Antibacterial agents

Antimicrobial agents include: antibacterial, antiviral, and anthelmintic agents.

antibacterial is the biggest group

Antibacterial Agents

antibacterial agents **:Substances that**

kill (or stop the growth) of bacteria without harming the host.

► The differences between human and other organism (such as bacteria) are used to design antibacterial agents

History:

it start with **Arsenic: used in the 1800s to treat syphilis.**

Sulfonamides: 1935: The oldest antibiotics they are not used now because of resistance but specific type of sulfonamides are still used nowadays (we will talk about in the next slide). They are synthetic antimicrobial agents

Penicillin(Antibiotics): 1940.

Antimicrobials have revolutionized the treatment of bacterial infections as well as enhanced the advancement of medical and surgical treatment.

treatment does not depend only on antibiotics but also depend on the Patient's natural resistance (plays a major role.)

Antibacterial Agents

when **Choosing an Antibiotic** you should think a lot of things (not just antimicrobial the drug itself) such as :

The infecting organism (determining the kind of bacterial help us choose the correct antibiotic .

you must have an idea about the Site of infection to determine the best Route of administration.

Drug history of the patient (we must know if the patient has allergic for a specific type or if he is currently taking another antibiotic or drug to avoid drug interaction) .

Complicating factors such as pregnancy

Cost

Problems associated with antibacterials you face as a physician include:

Overprescribing (prescribing antibiotics the patient doesn't need)

due to :

- **1) patient demand**
- **2) time pressure on clinicians**
- **3) diagnostic uncertainty**

Sulphonamides

Almost obsolete nowadays because of:

1)Bacterial resistance.

2) Bacteriostatic(don't effective in killing bacterial)

3) Toxicity:

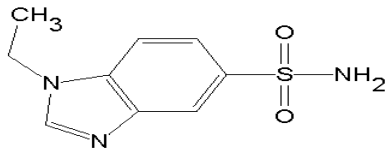
Nausea.(mild)

Rashes(mild)

Blood dyscrasia(severe)

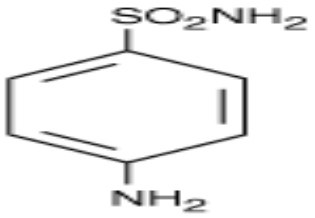
the presence of abnormal material in the **blood**, usually applied to diseases affecting **blood** cells or platelets. Evidence of **dyscrasia** can be present with a WBC count of over 1,000,000.

4) Precipitation (crystallization) in urinary tract and stone formation

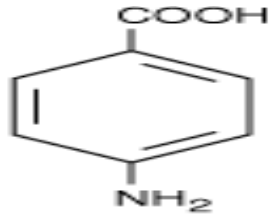


Don’t memorize structure but we need to know the features to structure

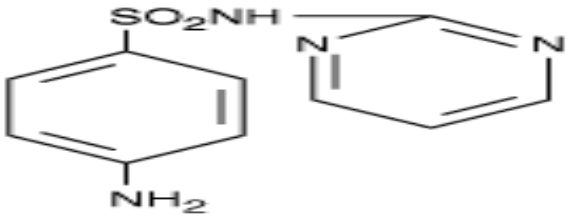
Common to all of these structures is benzene ring binding sulfur group and NH3



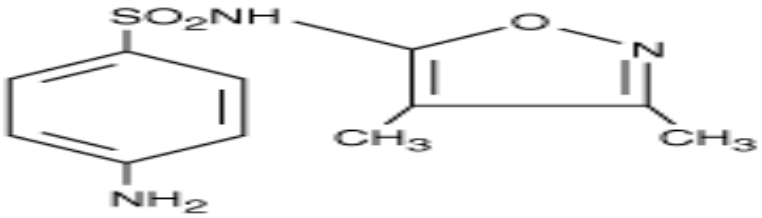
Sulfanilamide



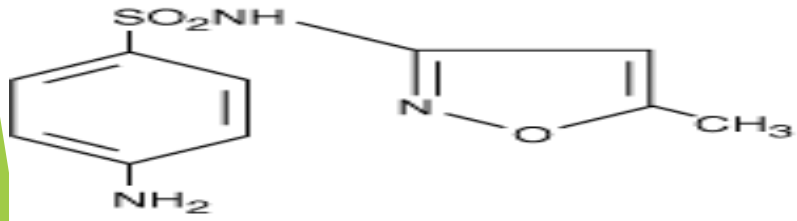
***p*-Aminobenzoic acid (PABA)**



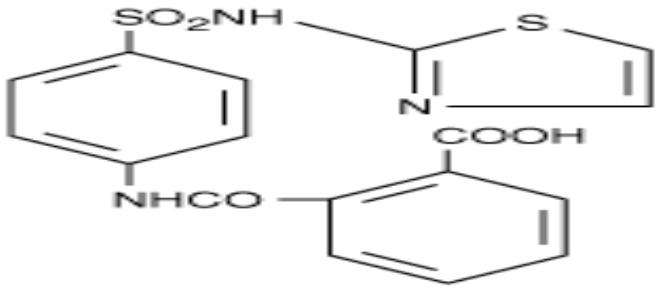
Sulfadiazine



Sulfisoxazole



Sulfamethoxazole

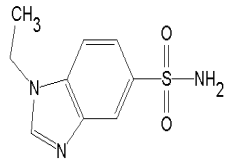


Sulfathalidine (phthalylsulfathiazole)

Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

Chemical features

The presence of the benzene ring and its attachment to the sulfur is an essential feature of the chromophore which is present in all Sulfonamides group



- **SO2NH2 group is not essential as such** **(not necessarily found in all Sulfonamides)**
- **the important feature is that the sulfur is linked directly to the benzene Ring**

The NH2 group is essential
(it is necessarily found in all Sulfonamides)

Sulphonamides

Cotrimoxazole-Trimethoprim Combination (Bactrim, Septrin, Balakatrin)

One of the few, still used, sulfa drugs.

Very effective fixed combination.

No resistance. Why? Because when killing pathogens it uses multiple mechanisms

(we will have an idea about the reason later on)

Very useful in UTI, RTI, Salmonella, and

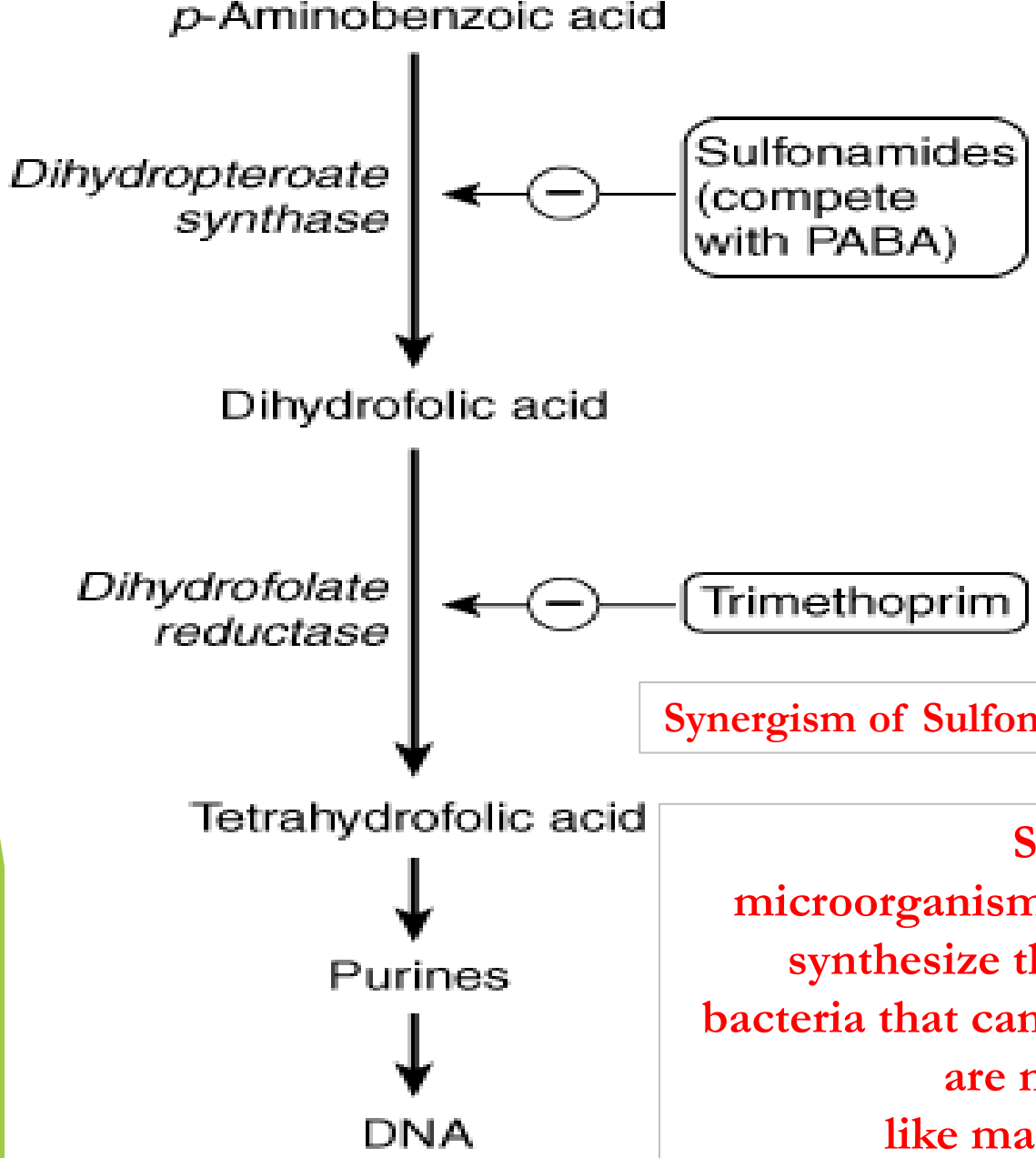
Pneumocystis pneumonia, an opportunistic infection in AIDS patients.

Mechanism of Action

Sulfonamides: structural analogs (similar structural to para aminobenzoic) **and competitive antagonists**(sulfonamides compete para for receptor on bacteria)**of para-aminobenzoic acid (PABA)**

The different between human cell and bacterial cell it the human cell doesn't synthesis folic acid and doesn't use the para aminobenzoic acid

Prevent normal bacterial utilization of PABA for the synthesis of folic acid



Synergism of Sulfonamides

Sensitive microorganisms are those that must synthesize their own folic acid; bacteria that can use preformed folate are not affected like mammalian cells

Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

The diagram in the last lecture explain the mechanism of sulfonamide.

This process start with sulfonamide inhibiting the enzyme (dihydropteroate synthase) by competing with PABA which results in the inhibition of dihydrofolic acid (the enzyme becomes in an inactive state)
 whereas trimethoprim inhibits dihydrofolate reductase.
Both drugs block folic acid synthesis
The reason for using still now is that if the sulfonamide doesn't work the folic acid synthesis is still inhibited by trimethoprim

Quinolones

Interfere with cell division of bacteria

(they stop bacteria from completing division)

1) Nalidixic Acid

Very old urinary antiseptic.

2) Norfloxacin:

Used only for UTI.

3-day course.

3) fluorinated 4-quinolones

such as ciprofloxacin (CIPRO), moxifloxacin (AVELOX), and gatifloxacin (TEQUIN)

Ciprofloxacin: (Effective with toxin producing bacteria

Wide range of activity, even Botulinum.

Expensive.

Prophylaxis for meningitis.

side effect for ciprofloxacin **Can cause g.i upset, and epilepsy**

Botulinum toxin is produced by Clostridium **botulinum** bacteria