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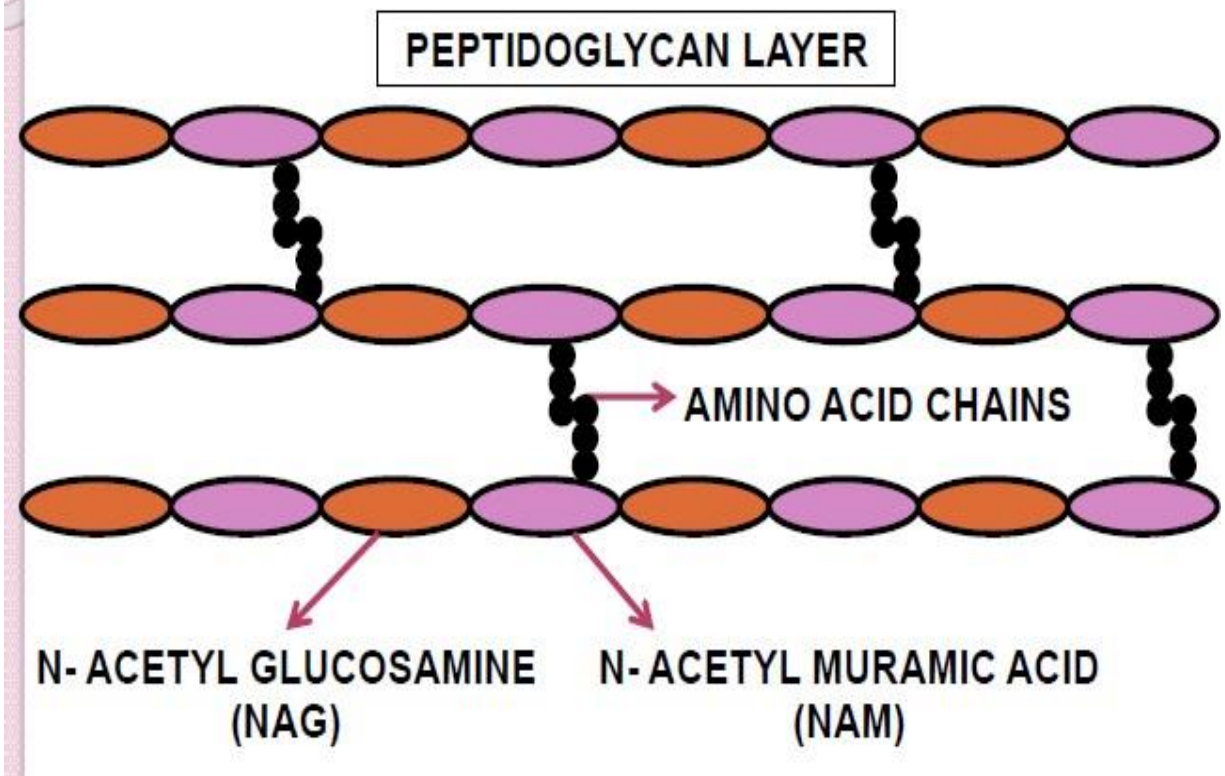
PENICILLIN

Scottish biologist and pharmacologist

After World War I elected **Professor of Bacteriology** at the University of London in 1928

Mechanism of Action

- Interferes with bacterial cell wall synthesis



Fleming received the **Nobel Prize in 1945** Accidentally discovered Penicillin while studying properties of Staphylococci

Described the mould as being from the **genus Penicillium**

Named the substance released as Penicillin

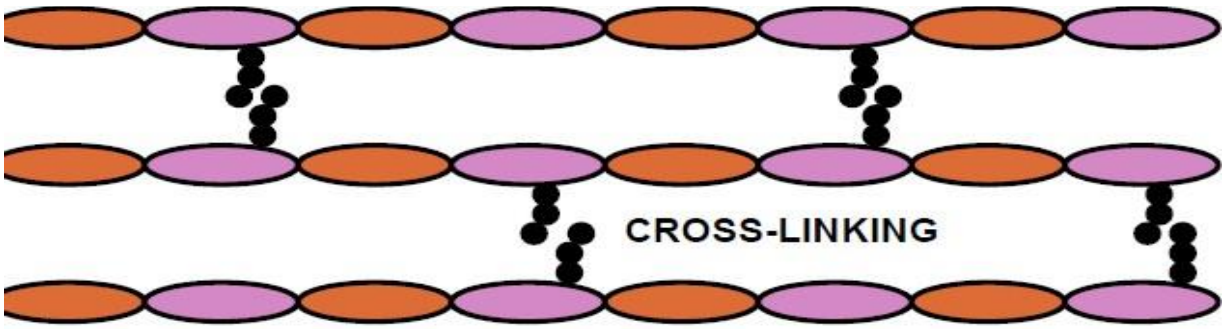
PENICILLIN WAS BORN 7TH MARCH, 1929

History

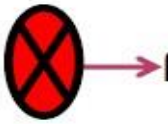
Mass production of the new drug for use in World War II

Penicillin saved many lives during the war that may have been lost due to infected wounds Penicillin was also said to treat **diphtheria, gangrene, pneumonia, syphilis and tuberculosis** Penicillin- **first antibiotic** to be used clinically

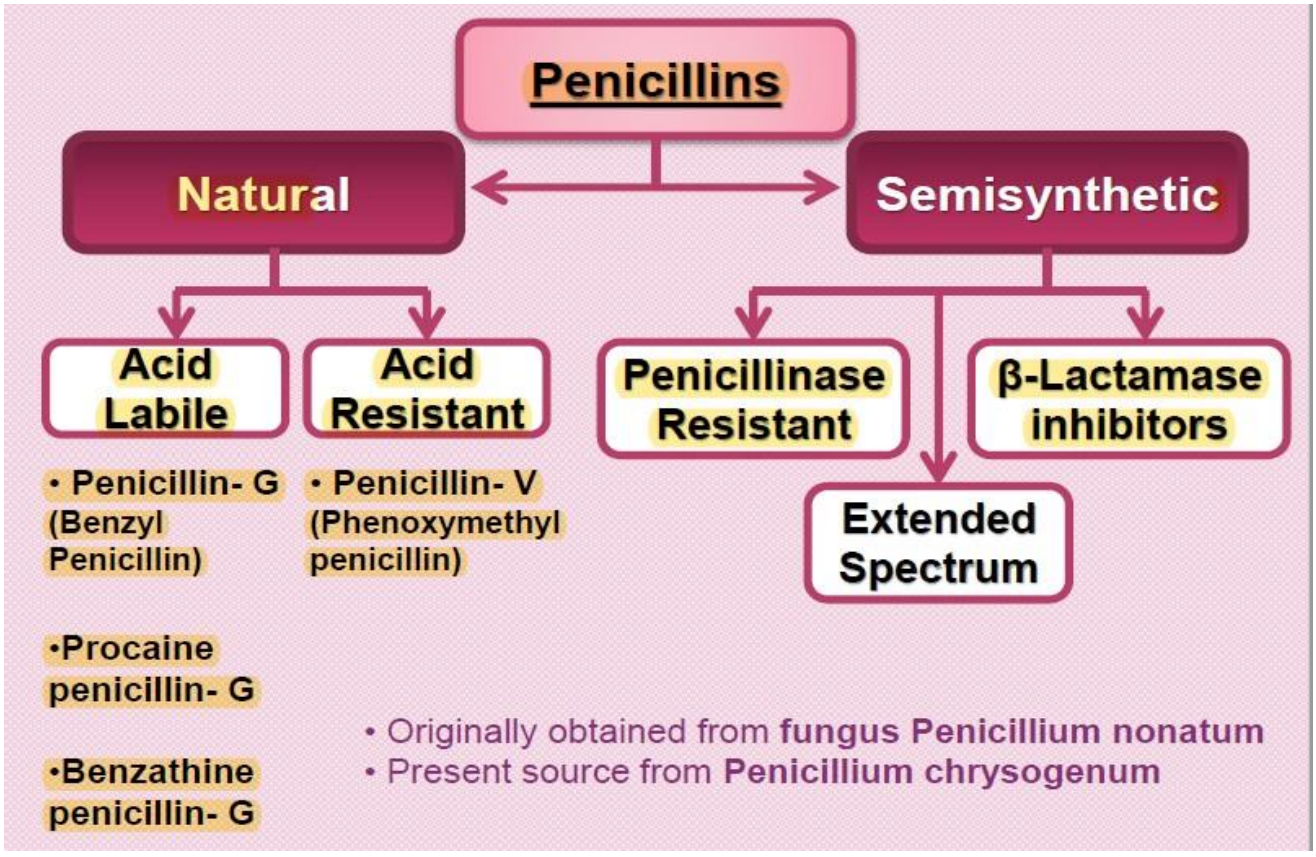
Penicillin was the first antibiotic to be used clinically in 1941 . It is a miracle that the least toxic drug of its kind was the first to be discovered.It was originally obtained from the fungus Penicillium notatum, but the present source is a high yielding mutant of P. chrysogenum. C hemistry and properties The penicillin nucleus consists of fused thiazolidine and β-lactam rings to which side chains are attached through an amide linkage. Penicillin G (PnG), having a benzyl side chain atR (benzyl penicillin:is the original penicillin used clinically.



TRANSPEPTIDASE
PENICILLIN BINDING PROTEINS
(PBPs)



β- Lactam Antibiotic
(Penicillin)



SEMISYNTHETIC PENICILLINS

Semisynthetic penicillins are produced by chemically combining specific side chains (in place of benzyl side chain of PnG) or by incorporating specific precursors in the mould cultures. Thus, procaine penicillin and benzathine penicillin are salts of PnG and not semisynthetic penicillins. The aim of producing semisynthetic penicillins has been to overcome the shortcomings of PnG, which are:

1 . Poor oral efficacy.

2. Susceptibility to penicillinase.
3. Narrow spectrum of activity.
4. Hypersensitivity reactions (this has not been overcome in any

preparation).CLASSIFICATION

1 . Acid-resistant alternative to penicillin G Phenoxymethyl penicillin (Penicillin V).

2. Penicillinase-resistant penicillins Methicillin, Cloxacillin.
3. Extended spectrum penicillins
(a) Aminopenicillins: Ampicillin, Bacampicillin, Amoxicillin.
(b) Carboxypenicillins: Carbenicillin, Ticarcillin.
(c) Ureidopenicillins: Piperacillin, Mezlocillin.

-/actamase inhibitors Clavulanic acid Sulbactam, Tazobactam

BETA-LACTAMASE INHIBITORS

beta-lactamases are a family of enzymes produced by many gram-positive and gram-negative bacteria that inactivate β -lactam antibiotics by opening the β -lactam ring. Different β -lactamases differ in their substrate affinities. Three inhibitors of this enzyme clavulanic acid,sulbactam and tazobactam are available for clinical use.

Clavulanic acid Obtained from Streptomyces clavuligerus, it has a β -lactam ring but no antibacterial activity of its own. It inhibits a wide variety (class II to class V) of β -lactamases (but not class I cephalosporinase) produced by both gram-positive and gram-negative bacteria.

Clavulanic acid is a 'progressive' inhibitor : binding with -lactamase is reversible initially, but becomes covalent later-inhibition increasing with time. Called a 'suicide' inhibitor, it gets inactivated after binding to the enzyme.