

Penicillin*

Class: β -lactam

Overview

Penicillin is the prototypical β -lactam and is still an important antimicrobial tool. The naturally occurring penicillin, penicillin G (benzylpenicillin), and biosynthetic stable penicillins developed for oral use, like penicillin V (phenoxymethyl penicillin) and phenethicillin, are examples of narrow spectrum penicillins used in veterinary medicine. Penicillin is bactericidal against most susceptible bacteria. These narrow spectrum β -lactamase sensitive penicillins are active primarily against Gram positive organisms.

Resistance

Soon after the initial widespread use of penicillin in the early 1940s, penicillinase-producing *Staphylococcus aureus* began to emerge. The penicillinases disrupt the β -lactam ring through enzymatic inhibition and render the organism resistant.

Vertical evolution of resistance refers to the acquisition of resistance by mutation and selection. Through this process pneumococci were able to alter the target protein to which penicillin binds.

Organisms previously susceptible to penicillin can also acquire resistance through transduction. Resistant *S aureus* can transfer β -lactamase production capabilities to susceptible *S aureus* by transferring plasmid DNA enclosed in bacteriophages, viruses with bacterial hosts.

Organisms can also acquire resistance through transformation, the uptake of exposed DNA from dead bacteria and resultant altered genotype (recombination of DNA). This is likely the principle means for the spread of penicillin resistance in *Streptococcus pneumoniae*.

Conjugation is another means of acquisition of resistance against penicillin. Conjugation involves the unilateral transfer of plasmids or other extrachromosomal DNA between bacteria of the same or different genera. This transfer occurs through mediation by fertility factors and is carried out by the extension of sex pili from the donor to recipient. This mechanism is often responsible for the transfer of multi-drug resistance. This phenomenon occurs when a series of closely linked genes carrying resistance transfer factors against multiple antimicrobials are exchanged. These plasmids carry resistance to penicillin by transferring genes possessing information necessary for formation of β -lactamases.

Other methods of acquiring resistance shared by all β -lactams are chromosomal uptake through increased cell permeability or transfer through porin channels (proteins that form water filled conduits through which molecules gain entrance to the cell), and drug efflux, the active transport of compounds out of the cytoplasm or periplasm. Drug efflux limits the accumulation of the compound at its site of action. Horizontal evolution of resistance is the general term applied to the genetic exchange of resistance between organisms (includes conjugation, transduction and transformation).

Effectiveness

Penicillin is bactericidal against most agents, with the exception of *Enterococcus* species. Narrow spectrum β -lactamase sensitive penicillins, penicillin G and penicillin V, are the drugs of choice for pneumococci, streptococci, meningococci, and gonococci. Many spirochetes, such as *Treponema pallidum*, clostridial organisms, and *Bacteroides*, with the exception of *Bacteroides fragilis*, are also sensitive. Non penicillinase-producing *Staphylococcus* organisms also remain sensitive. Penicillin is also usually effective against *Corynebacterium pyogenes*, *Erysipelothrix rhusipathiae*, *Actinomyces ovis*, *Leptospira canicola*, *Bacillus anthracis*, *Fusiformis nodosus* and *Nocardia* species.

Penicillin G and V are no longer the drugs of choice for *Neisseria gonorrhoea*, due to the development of resistance. These drugs are also not effective against enteric Gram-negative organisms.

Penicillin is inhibitory to *Actinomyces israeli*, *Listeria monocytogenes* and *Pasteurella multocida*.

In vitro sensitivities of enterococci to penicillin or cephalosporins, with the exception of the third-generation cephalosporin, cefoperazone, do not indicate in vivo activity. In fact these drugs are generally ineffective in vivo against enterococci.

***References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**