Pyrazinamide

PLAY PICMONIC

INDICATIONS

Mycobacterium tuberculosis

Mic-bacteria and TB-TV

Pyrazinamide is used in the treatment of tuberculosis in the initial 4-drug regimen (which also includes ethambutol, rifampin, and isoniazid).

MECHANISM

Pyrazinoic Acid

Pirate-zit Acidic-lemon

Pyrazinamide is a prodrug converted to pyrazinoic acid by the bacterial enzyme pyrazinamidase.

Most Efficient at Acidic pH

#1 Foam-finger and Acidic-lemon pH-scale

Pyrazinamide works best in an acidic environment, such as the inside of macrophages and caseous granuloma. This effectiveness makes it especially relevant in the context of slowly-multiplying intracellular bacilli.

Unknown Mechanism

Question-mark Mechanism

Pyrazinamide's mechanism of action is poorly understood.

It is known that pyrazinoic acid exits the mycobacteria and, if it encounters an acidic environment, like the one in a granuloma or a macrophage, it becomes protonated. It then reenters the bacteria through diffusion and turns the internal environment acidic.

Some authors have indicated that this causes changes in membrane permeability, while others propose the theory that this inhibits fatty acid synthase I, an enzyme that participates in mycolic acid synthesis.

SIDE EFFECTS

Gout (Hyperuricemia)

Gout-goat

Hyperuricemia and the potential for the development of gout are concerns with the use of pyrazinamide. If gout develops, the medication needs to be suspended.

Liver Toxicity

Liver with Toxic-green-glow

Liver toxicity and the potential for the development of hepatitis are other main concerns with the use of pyrazinamide. If liver enzymes rise and there are clinical signs of hepatitis, the medication must be stopped.