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Dear Joe:

Just a passing thought gleaned on reading an article by ~~Richard~~ Cooper on mechanism of penicillin action in current Bact Rev. He quotes a finding that penicillinamide is considerably more resistant to penicillinase than penicillin itself. Why not screen for other resistant modifications of penicillin; E.G.: add a good slug of penicillin to your fermentation broths (I know many actinos are susceptible to it); after the fermentation, add penicillinase and assay product on penicillinsensitive and resistant indicators. The point is that penicillinase is the main basis of resistance in natural populations, and the other advantages of penicillin might well be retained in a penicillinase-resistant conjugate of penicillin; the actinos would simply be screened for their ability to modify penicillin. Most lab-resistant mutants have another mechanism of resistance besides penicillinase, and I would expect cross-resistance here with the hypothetical conjugates.

Yrs

Joshua Lederberg

Has there been
any clinical trial
of penicillinamide?