

Towards an accurate PZA susceptibility test

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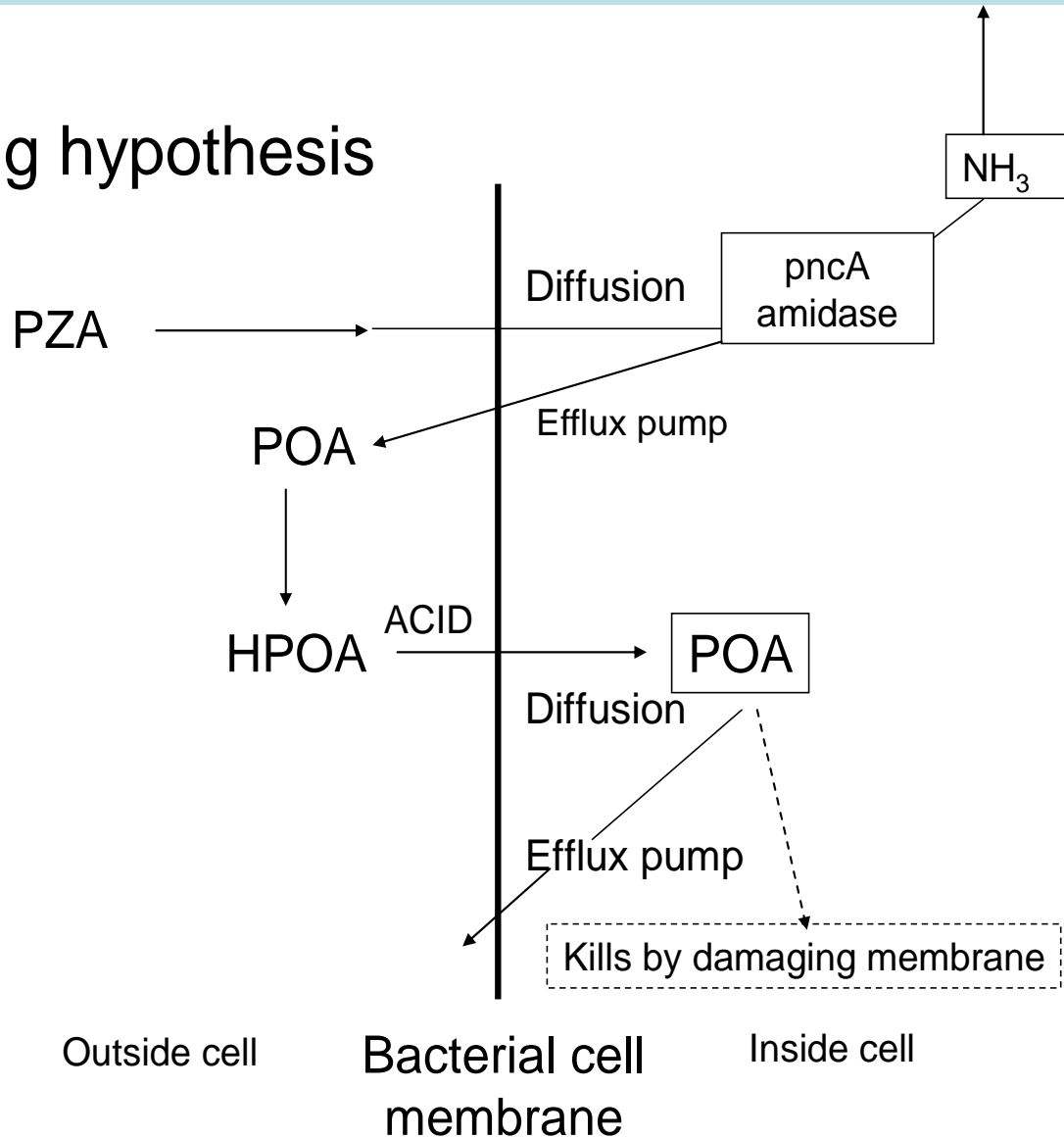
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Problems in PZA DSTs

- At only slightly acid pHs (eg pH 6.0), PZA is insufficiently bactericidal
- At more acid pHs (eg pH 5.6), PZA is more bactericidal but some TB strains are inhibited by acid
- Aim: To increase bactericidal activity without inhibition of growth

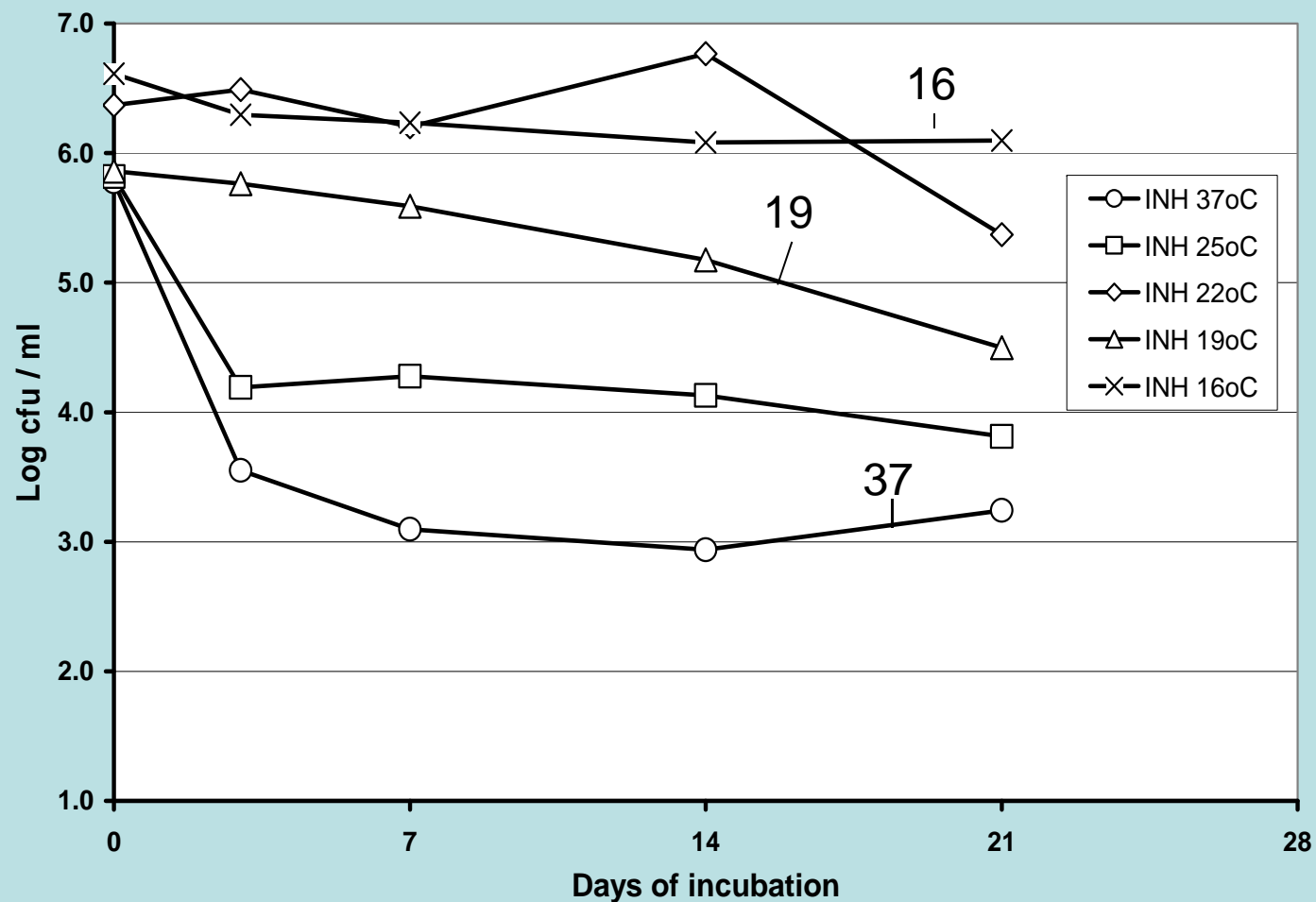
Mode of action of PZA

Zhang hypothesis

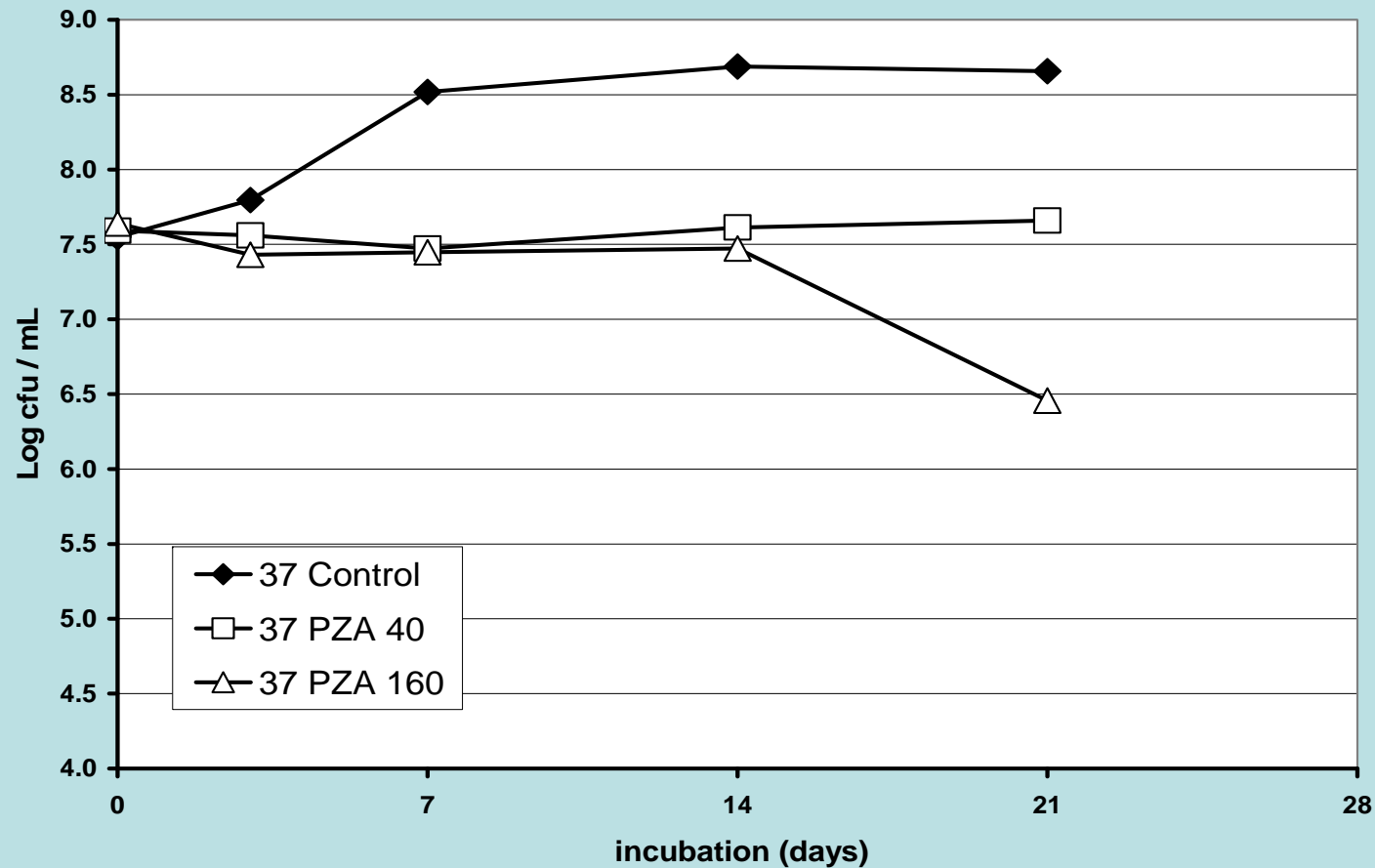


Bactericidal action of INH 1 $\mu\text{g/ml}$ at various temperatures

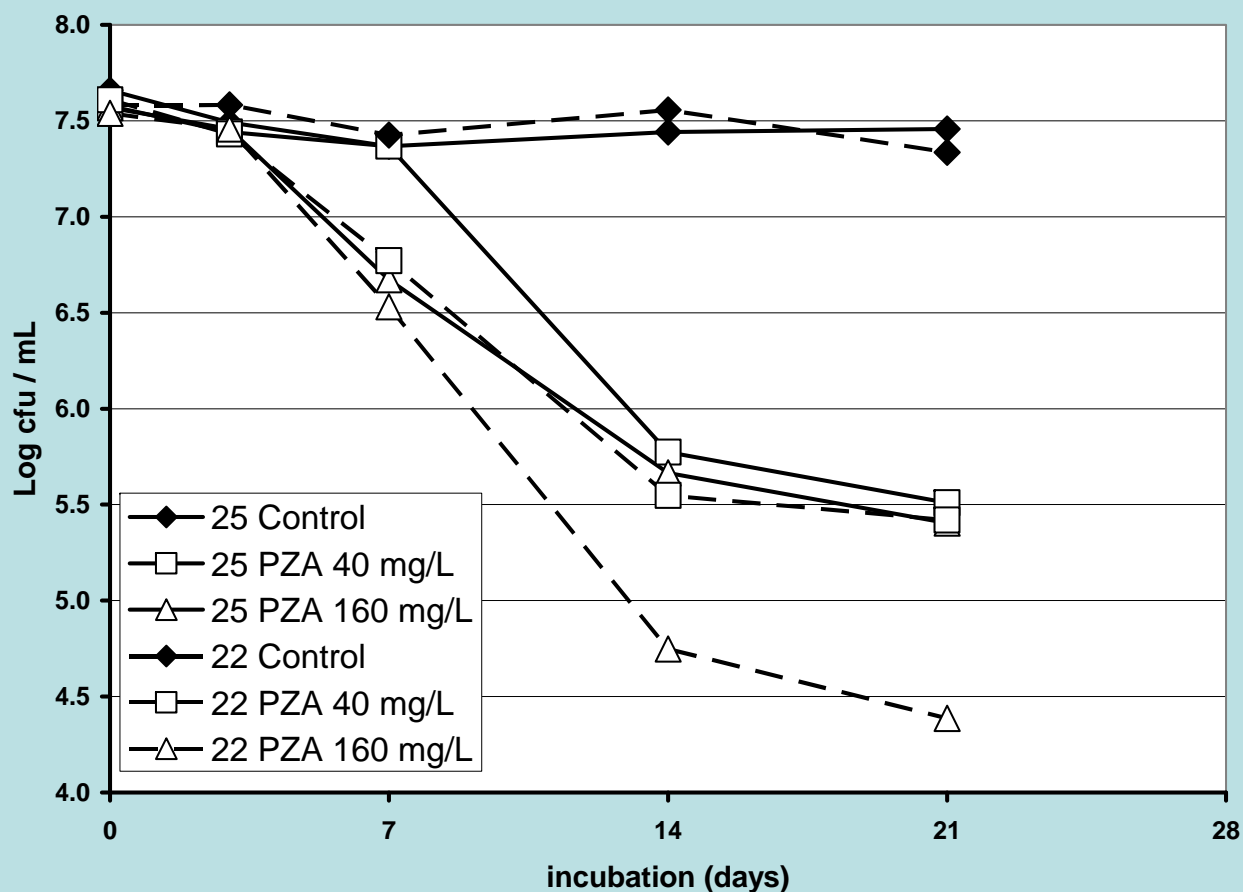
Coleman, Waddell, Mitchison J Antimicrob Chemotherap 2010; 66,146-50



Bactericidal action of PZA 40 & 160 $\mu\text{g/ml}$ at 37°C



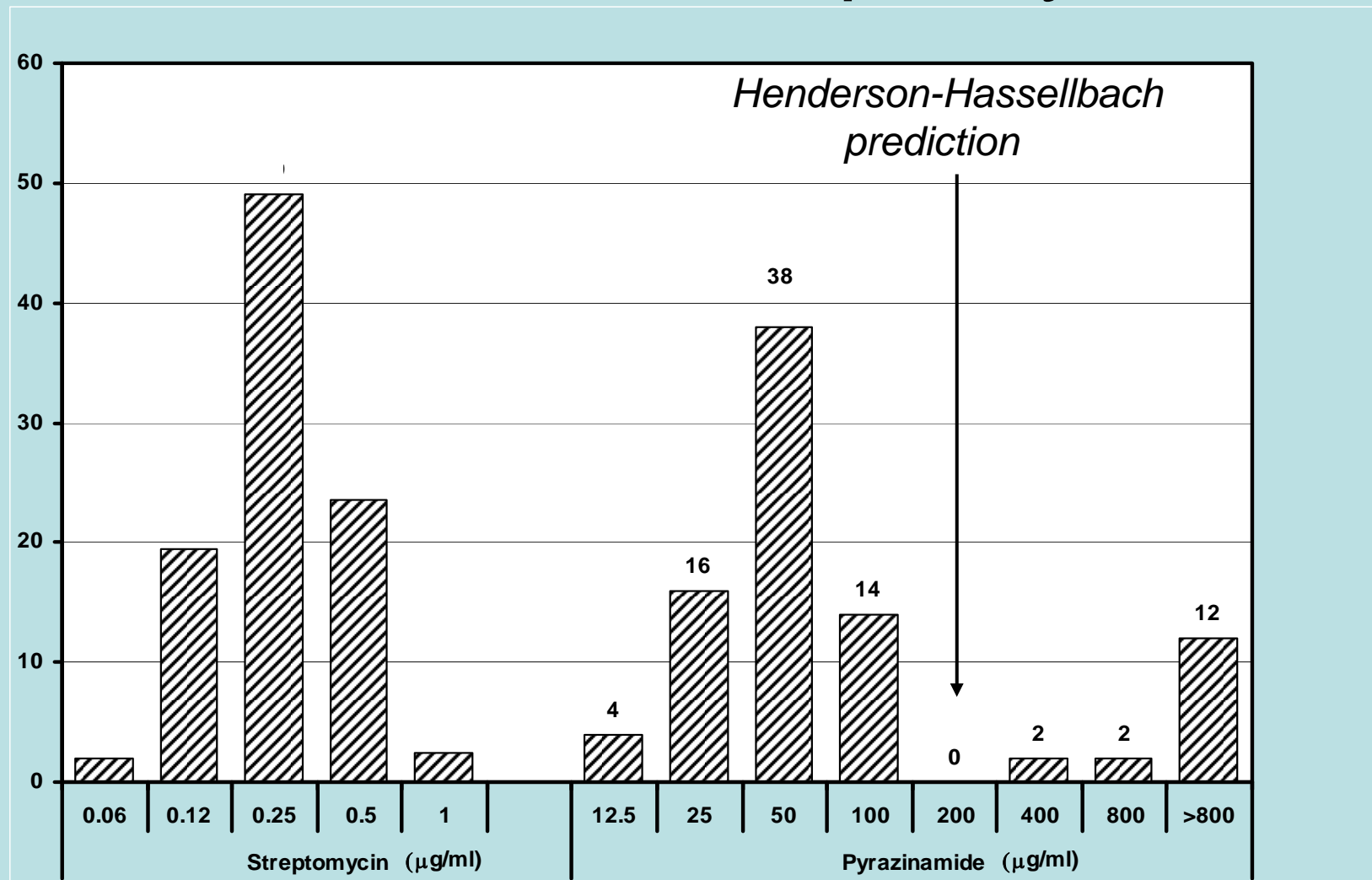
Bactericidal action of PZA 40 & 160 $\mu\text{g/ml}$ at 22°C & 25°C



The PZA DST

- Slopes of buffered LJ at pH 5.95 with 12.5-800 $\mu\text{g/ml}$ PZA in 2-fold steps
- Inoculate with standard BMRC inoculum
- Incubate for 14 days at Room Temp (18-19°C) covered with black cloth
- Incubate for 28 days at 37°C

Distribution of PZA DST results with those for streptomycin



Genetic analysis of pncA

• MIC	All	No. analysed	No. with mutations
• >800	12	11	10 (1)
• 800	2	2	2
• 400	2	1	1
• 100	14	2	0
• 50	28	8	1 (1)

Collaborators at St George's

- David Coleman
- Marcus Pond
- Simon Waddell