PHARMACEUTICAL SIGNIFICANCE OF PLASMID-MEDIATED MERCURY RESISTANCE

R.J. Pinney, Microbiology Section, Department of Pharmaceutics, The School of Pharmacy, University of London, Brunswick Square, London, WC1N 1AX

Antibiotic resistance due to transmissible plasmids is well documented but many plasmids also confer resistance to heavy metals including mercury (Novick, 1969). The effects of such plasmids on survival of Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus in solution of phenylmercuric nitrate (PMN) and thiomersal (TML) have therefore been investigated.

Resistance levels were determined by streaking plasmid-containing (P^+) strains and isogenic P^- derivatives on nutrient agar (NA) + PMN, by spectrophotometric measurements of cultures growing in nutrient broth (NB) + PMN, and by following viability in aqueous PMN solutions and in Davis minimal medium (DM) + PMN or TML. Viable counts were determined by diluting in NB and plating on NA + 0.1% thioglycollic acid. S.aureus strain PS81, which harbours a plasmid conferring mercury and penicillin resistance, grew on NA + 1 µg/ml PMN and in NB + 1 µg/ml PMN. Under the same conditions, E.coli strain J5-3 carrying the transmissible R plasmid R471a grew in 10 µg/ml PMN, and P.aeruginosa strain PAO2 harbouring sex plasmid FP2 grew in 100µg/ml PMN. No growth of the respective isogenic P^- strains occurred under these conditions. R471a and FP2 were conjugally transferred at frequencies of 2.5×10^{-3} and 9.1×10^{-4} per input doner respectively in 5 hr matings, and the S.aureus plasmid was transduced by phage 80 at a frequency of 1.2×10^{-5} per phage particle.

The survival of P^+ S.aureus and P.aeruginosa strains was significantly greater than their respective P^- derivatives in 10 µg/ml PMN in water at 25°. Decimal reduction times (D values) in systems inoculated with S.aureus at 10^7/ml or P.aeruginosa at 5×10^7/ml were increased from 140 min to 300 min and from 70 min to 115 min respectively by the presence of the plasmids. Both the P^+ and P^- S.aureus strains showed greater then 50% survival after 5 hr in DM + 10 µg/ml PMN. After 24 hr the viable count of the P^+ strain was reduced to 2×10^5/ml and that of the P^- strain to 5×10^3/ml. After 48 hr there were still 3×10^3/ml P^+ cells present, but no viable P^- bacteria were demonstrated. The P^- P.aeruginosa strain had a D value of approximately 60 min in DM + 10 µg/ml PMN and no viable organisms were recoverable after 24 hr. The viability of the P^+ P.aeruginosa decreased to 1×10^5/ml after 5 hr. However, after 24 hr incubation there was no further fall in viability. The count remained constant for 2 weeks, when viability increased to reach 2×10^8/ml and 4×10^8/ml after 3 and 5 week respectively. A similar pattern of death followed by growth was observed with the P^+ P.aeruginosa in DM + 10 µg/ml TML but in this case the viable count recovered to 2×10^8/ml after only 72 hr. No viable cells of the isogenic P^- strain were recoverable under the same conditions.

Plasmids conferring mercury resistance therefore increase the survival of E.coli P.aeruginosa and S.aureus in PMN and THM. Minimum inhibitory concentrations are increased in complex media, death rates are decreased in aqueous systems, and perhaps most alarmingly, death may be followed by growth in minimally nutrient media. Since mercury resistance is often linked to antibiotic resistance determinants on the same plasmid, pathogenic organisms that survive in systems preserved with mercury may also be resistant to chemotherapy.

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Novick, R.P. (1969). Bact. Rev., 33, 210-263.