THE EFFECT OF NUTRIENT DEPLETION ON THE DRUG RESISTANCE OF A POLYMYXIN-SENSITIVE PROTEUS MIRABILIS

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Proteus species are characteristically highly resistant to polymyxin while Pseudomonas aeruginosa is sensitive. The wall probably confers resistance for Proteus (Teuber, 1969; Brown & Wood, 1972) and is involved in the sensitivity of P. aeruginosa (Brown, 1975). Changes in the envelope caused by specific nutrient depletion resulted in P. aeruginosa changing its sensitivity to drugs (Finch & Brown, 1975; Dean & others, 1977).

A polymyxin-sensitive clinical isolate of Proteus mirabilis (designated RBH) was studied for sensitivity to phenol, chlorhexidine, cetrimide or polymyxin B. The effects on sensitivity of nutrient depletion in batch culture by glucose (C-) Mg^{2+} (Mg-) or PO_4^{3-} (P-) were followed using a colony counting procedure. To achieve this the quantitative nutritional requirements in simple salts media were determined. The requirements were the same as for a typical Pr. mirabilis NCTC 5887. In the salts medium, stable, small colony variants with a different drug sensitivity pattern tended to emerge when subcultured on nutrient agar. This occurred with RBH, NCTC 5887 and 5 other strains of Pr. mirabilis. Growth in nutrient broth or in salts media with relatively high concentrations of K^+ greatly reduced this phenomenon.

With Pr. mirabilis RBH, both Mg- and P- cultures showed an increased resistance to polymyxin and phenol compared to C- cultures. With chlorhexidine P- gave reduced resistance compared with both C- and Mg-. With cetrimide the Mg- culture gave reduced resistance and the P- culture gave increased resistance compared with the C-.

These results are different from those obtained with the typical polymyxin-resistant Pr. mirabilis NCTC 5887 where P- gave an increase in resistance to chlorhexidine compared with C- and Mg- gave an increase in resistance to cetrimide compared with C-. The use of MIC data do not reveal these differences. Apart from polymyxin, the MIC's to cetrimide, chlorhexidine and phenol were similar for RBH and NCTC 5887.

These results suggest that nutrient depletion brings about different envelope changes for the two strains. The in vivo implications of such changes are not clear (Brown, 1977). In vitro it is possible that the use of specific nutrient depleted cultures may help in the design of challenge tests for disinfectants or preserved pharmaceuticals (Brown, 1975).

Brown, M. R. W. (1975). Pharmaceutical Journal, 215, 239-242.
Brown, M. R. W. (1975). In: Resistance of Pseudomonas aeruginosa pg.71, Ed. M. R. W. Brown, John Wiley, London.
Brown, M. R. W. (1977). Journal of Antimicrobial Chemotherapy, 3, 198-201.
Brown, M. R. W. & Wood, S. M. (1972). Journal of Pharmacy and Pharmacology, 24, 215-218.
Dean, A. C. R., Ellwood, D. C. & others (1977). In: Continuous culture: applications and new fields pg.270. Ed. A. C. R. Dean & others. Ellis Horwood, Chichester.
Finch, J.E. & Brown, M. R. W. (1975). Journal of Antimicrobial Chemotherapy, 1, 379-386.
Teuber, M. (1969). Journal of Bacteriology, 98, 347-350.