

## Mode of action of vancomycin

SIR,—Vancomycin, an antibiotic produced by *Streptomyces orientalis* (McCormick & others, 1956), has been found to produce osmotically sensitive spheres in *Pseudomonas fluorescens* (Durham, 1963). No reports have appeared on the induction of similar forms in *Escherichia coli*.

Experiments have been made on the effect of 50, 100, 250 500, and 1000  $\mu\text{g}/\text{ml}$  of vancomycin hydrochloride on *E. coli* at 35° in nutrient broth, containing 0.33 M sucrose and 0.25% w/v magnesium sulphate,  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ , of final pH 7.4. Microscopical examination showed that spherical forms were induced within 5 hr with 500 and 1000  $\mu\text{g}/\text{ml}$  of the antibiotic, but not with the lower concentrations. The spheres (spheroplasts) lysed if the osmotic pressure of the surrounding medium was suddenly reduced, indicating cell wall fragility, but not necessarily the complete absence of cell wall constituents (Brenner & others, 1958).

In a further series of experiments, vancomycin was tested against *E. coli* at 35° when  $\text{Mg}^{++}$  was omitted from the medium. Spheroplasts were not induced with any concentration of the antibiotic. Such results are in accord with those obtained with penicillin (Hugo & Russell, 1960) and with glycine (John & Russell, 1963), when it was shown that  $\text{Mg}^{++}$  ions were essential for stabilisation of the cytoplasmic membrane.

It is known that substances which inhibit bacterial cell wall synthesis will induce spheroplast formation (see review by McQuillen, 1960). Vancomycin can thus be added to those substances, which include the penicillins, cycloserine, glycine and certain D-amino acids, which produce spheroplasts in susceptible bacteria. It might thus be expected that the cell wall is the primary site of action of vancomycin, and Jordan (1961) and Jordan & Inniss (1961) have stated this to be so, although the action of this antibiotic was not entirely similar to benzylpenicillin (Jordan & Inniss, 1961; Reynolds, 1961, 1962). From his studies on the effect of some antibiotics on the incorporation of three radioactive amino-acids into the protein, and of ( $^{14}\text{C}$ )-glycerol into the lipid, of the protoplast membrane of *Bacillus megaterium*, Yudkin (1963) concluded that the bacterial cell wall was not the primary site of action of vancomycin.

Spheroplast induction in *Ps. fluorescens* (Durham, 1963) and in *E. coli* could thus be the result of a secondary effect of the drug.

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