haemorrhages and shock, treatment with antihistamine and anti-5-HT drugs may prove to be an important advance in the clinical management of the snake poisoning.

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The Activity of Ampicillin against *Escherichia coli*

SIR,—The isolation of the penicillin "nucleus," 6-aminopenicillanic acid, has resulted in the development of new penicillins with advantages over the older existing ones. It has become clear from recent work that the penicillins show much variation in their antibacterial activity (Garrod, 1960).

Until recently, the penicillins were regarded as having only a slight inhibitory action on the growth of Gram-negative bacteria in general. Infections caused by such organisms were normally treated with either chloramphenicol or the tetracyclines; a new penicillin, ampicillin, 6[D(−)α-aminophenylacetamido]penicillanic acid, known commercially as Penbritin, has now been formulated which is more effective than either of these antibiotics in infections caused by *Escherichia coli*, *Proteus sp.*, *Shigella sp.* and *Salmonella sp.* (Rolinson and Stevens, 1961; Brown and Acred, 1961).

One of the principal mechanisms involved in the antibacterial action of benzylpenicillin is its interference with, and inhibition of, bacterial cell wall synthesis, with the resultant formation of bacterial spheroplasts. These may be regarded as bacteria which are deficient in a portion of the cell wall responsible for rigidity. At least five other penicillins are known to have a similar antibacterial action (Russell, 1962), and experiments were made to investigate whether ampicillin also possessed this property. Accordingly, 0·1 ml. of a 17-hr. broth culture of *Escherichia coli* grown at 37° was added to 10 ml. tubes of broth containing 0·33 M sucrose, 0·25 per cent w/v $MgSO_4 \cdot 7H_2O$ and varying concentrations of ampicillin. After incubation of all tubes for 5 hr. at 37°, samples were examined by phase-contrast microscopy. It was found that the minimum dose of the drug needed to induce spheroplast formation was 10 μg./ml. The minimum inhibitory concentration of ampicillin against the same organism in nutrient broth was also 10 μg./ml., this reading being taken after 24 hr. incubation at 37°. Further, by means of the method described by Rolinson and Stevens (1961) it was possible, in the space of a few days, to "train" the organism to grow in the presence of 100 μg./ml. ampicillin. Whether or not bacterial resistance to this antibiotic will present a clinical problem remains to be seen. We wish to thank Dr. G. N. Rolinson for a gift of ampicillin.

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New Oral Hypoglycaemic Agents

SIR,—The clinical and experimental aspects of oral hypoglycaemic agents have recently been reviewed by Creutzfeldt and Söling (1961). It would appear that two classes of compounds, the sulphonyl-ureas (tolbutamide and related substances) and the guanidines (biguanide derivatives, such as Phenformin) have supplemented insulin therapy in diabetes mellitus to some extent. However, these compounds have their own limitations and generally insulin has to be administered with them. Consequently, efforts are continuing either to suitably modify these compounds or to arrive at newer compounds, which may replace insulin. Lightbody and Reid (1960) have reported the hypoglycaemic effect of ortho-cresotinic acid.

We have prepared six cogeners of salicylic acid and tested their hypoglycaemic effect on albino rabbits. The compounds were fed to normal healthy rabbits, not less than 1·5 kg., by a stomach tube, in a dose of 15 mg./kg., the solution being made in water with the aid of an equivalent amount of sodium bicarbonate. The effect of each drug on the blood-sugar level of the animals was observed for 5 hr., blood sugar being estimated by the method of Folin and Wu (King, 1951). Preliminary results obtained on these compounds are given in the Table.

TABLE

HYPOGLYCAEMIC EFFECT OF NEW SALICYLIC ACID DERIVATIVES IN NORMAL RABBITS

Compound	Maximum fall in blood sugar per cent. Mean of 3 animals	Mean time of maximum fall (hr.)
2-Hydroxy-4-methylbenzoic acid ..	24·4	2·6
2-Hydroxy-3-ethylbenzoic acid ..	27·8	1·66
2-Hydroxy-5-propylbenzoic acid ..	24·0	3·3
2-Hydroxy-3-propylbenzoic acid ..	33·24	1·33
β-Resorcylic acid	9·6	3·3
2,4-Diacetylresorcylic acid	18.9	4·5

The maximum hypoglycaemic percentage fall is more pronounced with 2-hydroxy-3-propylbenzoic acid, while diacetylresorcylic acid gives a more prolonged action. The series appears to be promising.

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