Letters to the Editor

EFFECTS OF PRE-MEDICATION ON BACTERIAEMIA FOLLOWING DENTAL EXTRACTION

Sir,

May I be permitted to express disagreement with the conclusion reached by O. Khairat (Nov. 1966, p. 561) from his study of the effects of pre-medication on the bacteriaemia following dental extraction? His principal finding is that an intravenous injection of 275 mg. pyrrolidinomethyl tetracycline immediately before extraction 'sterilized' all but three of 100 blood cultures made after it. As he says, such an injection produces a very high concentration in the blood: assuming this to have been 24 $\mu\text{g./ml.}$ there must have been 8 $\mu\text{g./ml.}$ in his broth cultures and 1.6 $\mu\text{g./ml.}$ in his pour plates, concentrations quite adequate to prevent the growth of most bacteria likely to be present. In other words the 'sterility' of these cultures may have been only apparent, and due to inhibition of growth by the antibiotic in the inoculum.

It is not surprising that other authors, seven of whose papers are quoted, have obtained equivocal results in experiments of this kind. Pre-medication shortly before extraction does not prevent the entry of bacteria into the blood stream: it can only affect them once they are there. What anti-bacterial drug is there that can exert a substantial bactericidal effect within a few minutes? Even a bactericidal antibiotic such as penicillin needs longer than this; the authors who found a 42% reduction in positive blood cultures (Schirger *et al.*, *J. Lab. clin. Med.* 1960, 55, 376) gave 4,000,000 units of penicillin in four doses during 24 hours before extraction, and the effect of this must have been mainly on the bacterial population of the mouth. Still less can be expected of an antibiotic which is only bacteristatic.

It is true that according to Knothe and Mahler (*Dtsch. med. Woch.*, 1959, 84, 1687) tetracycline is bactericidal in high concentration, but they were able to demonstrate this only by adding further antibiotic to their preparation after two, four, six, and eight hours in order to maintain the original high level of 25 $\mu\text{g./ml.}$, and in 'stationary' preparations the effect was slight. In no such experiment was actual sterility ever attained, even in 24 hours. I submit that in view of such results it would be dangerous to rely on a single dose of a tetracycline to clear the circulation of living bacteria. It is generally agreed by others who have studied this subject that what is needed for this purpose is an antibiotic capable of exerting a total bactericidal effect. Penicillin is the first choice. If the patient is already under treatment with penicillin for the prevention of rheumatic fever, streptococci in the mouth will be more resistant to it, and possible alternatives are a large dose of penicillin together with streptomycin, a combination usually bactericidal even for resistant strains, or vancomycin (Garrod and Waterworth, *Brit. Heart J.*, 1962, 24, 39). This is inconvenient to administer, and cephaloridine is now preferable: Tozer, Boutflower, and Gillespie (*Lancet*,

1966, 1, 686), have shown that this antibiotic is bactericidal for penicillin-resistant strains of streptococci.

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OPTIMAL CONCENTRATION OF NICOTINAMIDE ADENINE DIPHOSPHATE IN PYRUVATE ASSAYS

Sir,

During the course of investigating pyruvate levels in neurosurgical patients, we noticed that the concentration of the reduced nicotinamide adenine diphosphate (N.A.D.H.), supplied in the 'pyruvate kit'¹ had been changed without notification from 0.003 M to 0.012 M around February 1964. As we had performed a number of assays using the former concentration and found the levels to be much lower than expected, we decided to check the recoveries of pyruvate using a range of N.A.D.H. concentrations. We found that 0.012 M N.A.D.H. was the optimum concentration.

Using 0.012 M N.A.D.H., the recovery was 100% for all standards; however, the percentage recovery using 0.003 M N.A.D.H. was limited above a concentration of 0.06 mM/litre. Accounting for a dilution factor of 1.23 in the estimation of pyruvate levels in blood, concentrations above 0.074 mM/litre blood could not be detected using 0.003 M N.A.D.H. Pyruvate levels in blood

estimated with the 'pyruvate kit' before the new concentration was introduced should be regarded with caution.

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