ensure that the treatment is justifiable. At present the routine screening of blood pressure in normal children or teenagers has no prophylactic value.

[1] Buck, C. W., *Journal of Chronic Diseases*, 1973, 26, 101.
[2] *British Medical Journal*, 1973, 1, 690

Antibiotic-induced Meningitis

Among the many and varied side effects of antibiotic treatment a predisposition to superinfection with bacteria resistant to the antibiotic plays a considerable part. It is a novel idea that a fresh infection arising during treatment should be caused by a sensitive organism and should involve the meninges. Apparently cephalothin is the only antibiotic against which this accusation can be levelled.

A series of five cases in which meningitis developed during treatment with cephalothin for infection elsewhere is reported by R. J. Mangi and colleagues,[1] of the Yale University School of Medicine, and they cite three earlier single case reports of the same condition, the meningitis having been pneumococcal in one and meningococcal in the others. Their own patients were a man of 72 with multiple myeloma, a man of 62 suspected of cholecystitis (this diagnosis was not confirmed, and no other is mentioned), a 56-year-old male diabetic and alcoholic, a woman of 20 with Hodgkin's disease receiving multiple chemotherapy, and a 49-year-old female diabetic and alcoholic with hepatic cirrhosis. The diagnosis in each except the second was pneumonia, and not only sputum but blood cultures were positive in all four, the organism found being a pneumococcus in two, a *Klebsiella*, and in the patient with Hodgkin's disease *Listeria monocytogenes*. These were the organisms subsequently found in the cerebrospinal fluid; that from the patient suspected of cholecystitis was a meningococcus. All were treated with intravenous cephalothin, usually in a dose totalling 6 g daily, one patient receiving kanamycin and one gentamicin in addition. There were no signs of disease of the central nervous system when treatment began, and in three patients lumbar puncture had yielded a normal fluid. The intervals between the start of treatment and the first signs of meningitis were 24, 40, and 42 hours and four and five days. All the patients except the last-named recovered after treatment with ampicillin (given to three, in one combined with gentamicin) or chloramphenicol.

The organisms isolated in all five cases are said to have been sensitive to cephalothin, but these tests were performed only by the Kirby-Bauer method, which employs high-content discs. It would be more helpful to know what were the minimum inhibitory concentrations determined by an accurate dilution method. Likewise, there is no information about the concentrations attained by cephalothin in the cerebrospinal fluid during treatment. According to the authors "there seems to be wide variation in the degree of penetration of cephalothin across the blood-brain barrier," but a fair idea of what is to be expected can be got from studies of experimental meningitis. S. Oppenheimer and colleagues[2] found that in dogs with pneumococcal meningitis the levels attained by cephaloridine, cephalothin, and methicillin were respectively 10·9, 5·6, and 2·9% of those in the blood. Thus cephalothin as an agent for treating meningitis appears to be inferior to its near relative cephaloridine. The levels attained by any penicillin or cephalosporin in the absence of meningitis are well known to be much lower. Thus when the meninges were initially invaded the concentration present may well have been subinhibitory. A believer in the applicability of the Arndt-Schultz law to antibiotics, kleine Dosen reizen grosse Dosen lähmen ("small doses stimulate, large doses damage"), at least in some situations, might reasonably suspect that this low concentration had an actually stimulating effect on the bacteria.[3] Something seems to be missing in the argument about the causation of this condition. Could this be it?

The paper concludes with a discussion of the place of cephalothin in the treatment of meningitis, which is admitted to be limited. Some might say that it has none. But what is in question here is not the treatment of meningitis but that of infections located elsewhere which may apparently be followed by meningitis if cephalothin is used in their treatment. It seems to have become fashionable to treat a variety of acute infections with cephalothin, often together with an aminoglycoside, as in two of these cases. Admittedly this is a combination with a very wide spectrum, but is it good routine practice? By a strange coincidence two reports from France, coming from Paris[4] and Rouen[5] have appeared simultaneously in British journals, each describing three patients in whom treatment with cephalothin and gentamicin caused acute renal failure. The diagnoses in these six cases were staphylococcal septicaemia in two, pneumonia, peritonitis, enteritis, and ulcerative colitis. It seems thus that in France this combination is highly regarded for a variety of indications. Admittedly it is a good one for a life-endangering infection which could be, for instance, either staphylococcal or coliform, until the aetiology is known, and might then still be indicated for its synergic effect on a staphylococcus. Many other bacteriological diagnoses would call for a change of treatment as soon as they are made. If, for instance, the cause proves to be a pneumococcus, where is the need for anything but penicillin? For some coliform infections, and particularly *Pseudomonas*, gentamicin could be continued, but with carbenicillin replacing cephalothin. There would be few cases in which treatment with cephalothin and gentamicin should be continued without confirmatory evidence of the necessity for it.

[1] Mangi, R. J., Kundargi, R. S., Quintiliani, R., and Andriole, V. T., *Annals of Internal Medicine*, 1973, 78, 347.
[2] Oppenheimer, S., Beaty, H. N., and Petersdorf, R. G., *Journal of Laboratory and Clinical Medicine*, 1969, 73, 535.
[3] Garrod, L. P., *British Medical Journal*, 1951, 1, 205.
[4] Kleinknecht, D., Ganeval, D., and Droz, D., *Lancet*, 1973, 1, 1129.
[5] Fillastre, J. P., *et al.*, *British Medical Journal*, 1973, 2, 396.

Links Overseas

Just 110 years ago the B.M.A. founded its first overseas Branch, in Bengal. Though this failed to survive a local quarrel over a paper on homoeopathy a few years later, other branches followed throughout the British Empire and subsequent Commonwealth. The next to be founded, the Jamaica Branch in 1877, continues today as the Medical Association of Jamaica, affiliated to the B.M.A. To such good effect did the