Pseudomembranous colitis is of uncertain pathogenesis. It is not identical with staphylococcal enterocolitis. Indeed, no consistent bacteriological findings have yet emerged from studies of lincomycin-clindamycin colitis; all three of Benner & Tellman’s (1970) cases showed a profuse growth of Proteus morganii from the stool, but this is of doubtful significance.

The list of unwanted drug effects lengthens constantly. Other recent additions are the platelet defect induced by carbenicillin (Brown et al., 1974), the fibrosing alveolitis which sulphasalazine may induce after several months of treatment (Jones & Malone, 1972; Davies & McFarlane, 1974; Thomas, Seaton & Edwards, 1974), and the claim that clindamycin may on occasion produce liver damage (Elmore et al., 1974).

The general lessons have long been evident. Early studies of a drug, however painstaking, often fail to identify unwanted effects later revealed by more prolonged and extensive experience; less common side effects may first be reported a very long time after the drug is in established use. Recognition is especially difficult if the effect is much delayed, or of unexpected character. None of us find it easy to report disasters we inflict on our patients, and published reports of unwanted effects are often followed by much confession, in public and private, of comparable experience.

Methods of identifying, recording and informing doctors about unwanted drug effects are attracting increasing and deserved attention, but at the heart of the problem lies a deeper one, a failure in medical and health education. Reports of fatal colitis from a drug given with no good reason for its particular use, or even for the use of any antimicrobial agent, induce a feeling of déjà vu, so reminiscent are they of many tragedies from penicillin anaphylaxis or chloramphenicol aplasia. Prescribing is influenced by a complex interaction of medical, economic and social factors, and the persistence of irrational antibiotic usage is one aspect only of a much larger problem which doctors, sociologists and administrators have scarcely yet begun to tackle.

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For and against carbenicillin—
a matter of resistance?

The mechanisms of drug production are such that often an antibiotic appears on the market before full details of its use have appeared in widely read medical journals. Consequently

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the appearance of a new antibiotic is often followed by a flurry of correspondence in one of the medical journals which dissect the virtues of that preparation. Carfecillin is no exception to this (Bendall, 1974; Ingham, Selkon, 1974; Knudsen, 1974). This drug is the phenyl ester of carbenicillin and is deesterified by the ubiquitous esterases of the body, into carbenicillin and phenol (which appears to be rapidly removed). The resulting blood levels of carbenicillin are too low, even in severe renal failure, to adequately treat a systemic infection caused by anything but the most sensitive organisms. However, the urinary levels of the antibiotic should be high enough to treat sensitive organisms, including *Pseudomonas aeruginosa*, unless the degree of renal failure is severe.

Disagreement has arisen over the recommendations for the clinical usage of this drug. The manufacturers suggest that carfecillin be used for urinary tract infections caused by any sensitive organism. It can be argued that carbenicillin is such a useful drug in treating *Ps. aeruginosa* urinary tract infection that it is logical to reserve its use for such infections. A further argument against carfecillin is that the widespread use of carfecillin will lead to an increase in resistance to carbenicillin amongst *Ps. aeruginosa* and other Gram-negative bacteria in general. *Pseudomonas* urinary tract infection is very uncommon outside hospital practice and the widespread use of carfecillin may well encourage the selection of β-lactamase producing Enterobacteriaceae. Ampicillin may have already increased such resistance, as the mechanism of resistance is the same in both drugs and it is therefore as logical to withhold ampicillin from general practice as it would be to stop using carfecillin. In closed communities, such as hospitals, the position is rather different. With a higher rate of pseudomonas sepsis it is probable that incautious use of this drug will lead to an increased number of resistant strains. In contrast, ampicillin in this situation has selected out more resistant organisms, including *Ps. aeruginosa*, but in hospitals where carbenicillin has not been widely used these tend to be the carbenicillin sensitive strains. Presumably the selection pressure is on the organism rather than the R-factor. There remains the theoretical possibility that carbenicillin as such, or its ester carfecillin, will exert in the gastro-intestinal tract a greater resistance selection pressure than ampicillin. This is because carbenicillin is more resistant to the action of some β-lactamase than ampicillin (Richmond & Sykes, 1971), and so will be able to act longer upon the bacteria. Whether this will be borne out in practice will no doubt emerge. At the present time one good reason for not prescribing carfecillin other than where specifically indicated is cost because carfecillin is about three times the price of an equivalent amount of ampicillin.

A further important point is that scientific reports on a drug often appear long after the drug itself is in use even though extensive pharmacological, microbiological and clinical investigations have to be done before the release of the new agent. Perhaps there is need for better synchronization of a drug's appearance and publication of the scientific reports.

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