The ideal patient for chenodeoxycholic acid treatment is over 45 years old with a functioning gallbladder containing radiolucent gallstones. Even so, not all radiolucent stones respond, for the fact that they are radiolucent does not guarantee that they are rich in cholesterol and therefore likely to dissolve in bile that has been rendered unsaturated with cholesterol. The *x*-ray interpretation is likely to be most misleading when there are multiple small irregular stones, for in about one-fifth of patients these stones are composed of bile pigment.[3] For this reason, an analysis of bile composition may help. Pigment stones occur in bile that is unsaturated with cholesterol, whereas for cholesterol stones the reverse is true. The association of radiolucent stones and saturated bile obtained by duodenal drainage is a reliable way of predicting that the gallstones are rich in cholesterol.[4]

With increasing experience we now know that the size of the gallstone is also an important determinant of outcome. Most small stones dissolve in between three and 12 months, whereas gallstones over 10 mm in diameter may need up to three years' treatment.[2 5] Dissolution probably depends on the secretion of unsaturated hepatic bile, and most investigators have monitored biliary lipid composition in patients being treated with chenodeoxycholic acid. Patients likely to have their stones dissolved generally have bile that is unsaturated when judged by analysis of a random, fasting sample of bile-rich duodenal fluid. Conversion of saturation to unsaturation may be taken as an index of potential success, while failure to achieve unsaturation indicates that dissolution is unlikely and that the dose of chenodeoxycholic acid should be increased.[5] Nevertheless, there are exceptions: stone dissolution has occurred in some patients in whom random bile samples have been found to be saturated.[6 7] Obese patients appear to be resistant to chenodeoxycholic acid, and their bile remains saturated despite relatively large doses of the bile acid.[2]

Overall far fewer patients seem suitable for treatment with chenodeoxycholic acid than was thought at first; indeed, possibly only one in five of all patients with gallstones will prove to be candidates for medical treatment. So inevitably selection for suitability and prediction of success need a complex series of decisions and plan of surveillance.[2]

[1] Bouchier, I A D, *British Medical Journal*, 1976, **2**, 870.
[2] Dowling, R H, *Clinics in Gastroenterology*, 1977, **6**, 141.
[3] Bell, G D, *et al*, *Gut*, 1975, **16**, 359.
[4] Bruusgaard, A, *et al*, *Scandinavian Journal of Gastroenterology*, 1977, **12**, 97.
[5] Iser, J H, *et al*, *New England Journal of Medicine*, 1975, **293**, 378.
[6] James, O, Cullen, J, and Bouchier, I A D, *Quarterly Journal of Medicine*, 1975, **44**, 349.
[7] Barbara, L, *et al*, *Digestion*, 1976, **14**, 209.

Planning treatment for rheumatoid arthritis

There is no treatment for severe rheumatoid arthritis that is both safe and really effective. Analgesic and anti-inflammatory drugs such as aspirin produce partial symptomatic relief at a high cost in toxicity. Corticosteroids and corticotrophin are the only agents which predictably suppress the inflammatory process, but harmful side effects preclude their use in all but extreme cases. The slow-acting drugs such as gold produce a modest but measurable effect in the longer term but expose the patient to hazards such as bone marrow aplasia.

Against this background the pharmaceutical industry has sought to produce new nonsteroidal anti-inflammatory drugs without the toxicity of aspirin, particularly gastric irritation. Numerous preparations have appeared for which these claims are made, usually heralded by sales promotion on a scale that leaves no doubt about the profits to be made from a product which enjoys even temporary popularity. Many of these drugs are propionic-acid derivatives, which tend to be both somewhat less potent and less toxic than aspirin in full doses. Opinions differ whether these preparations have replaced or should replace aspirin as the first line of treatment in rheumatoid arthritis; but there does seem to have been a steady shift in prescribing habit away from aspirin and towards the newer drugs. This may be more obvious in countries such as Britain, where the consumer is cushioned against the high cost of these preparations.

What, then, should be the policy in prescribing for patients with rheumatoid arthritis? The apparent confusion of choices may be simplified by a classification such as that put forward by Huskisson,[1] who grouped the drugs into five categories. Firstly, the simple analgesics: paracetamol, codeine, Distalgesic (paracetamol and dextropropoxyphene), and aspirin in small doses (2 g daily or less). Group two includes the analgesics with minor anti-inflammatory properties: ibuprofen, naproxen, ketoprofen, mefenamic acid; group three those with major anti-inflammatory properties: indomethacin, phenylbutazone and aspirin in full doses (at least 3·6 g daily). Fourth are the pure anti-inflammatory drugs, corticosteroids and corticotrophin, and fifth the "slow acting" drugs: gold, penicillamine, the antimalarials, and immunosuppressives.

Those who believe that aspirin is no longer the sheet anchor of treatment should start the new patient on a drug from group two. If pain is not relieved, this may be supplemented with single doses of a group one drug. Patients with morning stiffness benefit from indomethacin, up to 100 mg on retiring (capsules or suppository). If symptoms are still not relieved then group three drugs should be given, starting with full doses of aspirin and supplementing with a group one drug. If the disease remains active and progressive joint destruction occurs, use of a slow-acting drug should be considered. Corticosteroids should be reserved for patients with serious systemic disease (vasculitis) or for those in whom unacceptable pain and disability due to inflammation cannot be controlled by other means.

This scheme relies on non-steroid anti-inflammatory analgesics. Which of these newer preparations should be chosen? Huskisson *et al*[2] compared ibuprofen, fenoprofen, naproxen, and ketoproten in a short double-blind crossover trial. Naproxen combined greater effectiveness with a lower incidence of side effects and emerged as first choice; but the differences between the drugs were not great, and there was considerable individual variation, some patients doing well on one preparation, others on another. These drugs should, therefore, be seen as alternatives. In a more extended trial Mowat *et al*[3] showed that naproxen (250 mg twice daily) continued to give satisfactory results over 10 months of treatment.

In conclusion it is sadly necessary to point out how seldom the individual patient benefits from drug treatment to the extent implied in many drug advertisements—or indeed in many of the enthusiastic drug trial reports. And all these drugs are potentially toxic; even naproxen, the current front runner, may occasionally cause severe gastrointestinal haemorrhage.[4]

[1] Huskisson, E C, *Reports on Rheumatic Diseases, no 54*. London, Arthritis and Rheumatism Council, 1974.
[2] Huskisson, E C, *et al*, *British Medical Journal*, 1976, **1**, 1048.
[3] Mowat, A G, *et al*, *Annals of the Rheumatic Diseases*, 1976, **35**, 498.
[4] Hart, F D, and Matts, S G F, *British Medical Journal*, 1974, **2**, 51.