consider whether the treatment is likely to prove more fatal than the disease.

Antidepressants and stimulants may be usefully employed, and occasionally a mixture of amylobarbitone and dextroamphetamine does get the patient through an unhappy flat period. Antidepressants, such as imipramine or amitriptyline are sometimes as useful as, if not more than, other official antirheumatic drugs. Patients may derive benefit from a small dose of a barbiturate or some other form of sedative and recently we have been rather impressed with diazepam (Valium) and to a less extent chlordiazepoxide (Librium).

Let us now consider the corticosteroids. Dr A. G. S. Hill has emphasized how a modest evening dose of 5–6 mg will maintain its effect throughout the night and relieve the patient's feeling of morning stiffness. Unpleasant hormonal overtones do not arise at this dosage level but will become evident if higher doses are administered over many months. However, if you can improve the patient's condition by giving no more than 6 mg of prednisone or prednisolone daily, that is legitimate treatment. In the potentially fatal disorders, such as *disseminated lupus erythematosus* one may increase the dosage as high as is necessary to control the disease.

In the selection of drugs, I have always been greatly aware of the 'choosey' patient, who says "I can take aspirin—but not Disprin", and so on; the same degree of selectivity applies equally to the doctor when he is making his own choice for the patient. There are doctors who are 'codeine-positive' or 'ibufenac-positive' or 'indomethacin-negative' towards various drugs. This favouritism often applies to substances which have different titles but which are the same substance.

As far as the ordinary analgesic, anti-inflammatory agents are concerned, there are no hard and fast rules for selecting the right one. My own choice depends on the particular conditions of each individual case.

Gout

Dr J. T. Scott, M.D., F.R.C.P. (*Consultant physician, Charing Cross and West London Hospitals; and the Kennedy Institute of Rheumatology*)

Gout, as you know, has been described and recognized for over 2,000 years and I cannot in this short space of time cover such a noble lineage completely.

The manifestations of gouty arthritis, chronic and acute, can be related to the presence of excess quantities of uric acid or urate in its solid form in the tissues. Since urate was first isolated from tissues nearly 200 years ago, there has been no question that the manifestations of chronic gouty arthritis are due to its presence. If the solid deposits which are present in gouty arthritis are examined under a microscope or chemically analysed they are seen to consist of urate crystals. Garrod's original view that uric acid was the cause of the acute attack was however questioned for many years, and there were certain reasons for this. Colchicine, which is so effective in relieving the acute attack, does not lower the uric acid level in the blood, and some people, such as the relatives of a gouty patient, may have a high uric acid level for a long time without developing gout. More recently it has been found that urate crystals can always be detected in the joint fluid of acute gouty arthritis. It has also been shown that injecting

crystals of urate, or other microcrystals for that matter, into a joint will produce an attack of acute arthropathy very like acute gout, so we now believe that all the manifestations of gout are related to the presence of urate in one form or another.

We will not discuss the differential diagnosis of acute gout, though it can be a problem sometimes. With an acute gouty toe, there is not much difficulty, but gout also occurs at other sites and we must always keep gout in the back of our minds.

Uric acid is the end product of purine metabolism in man. Purines are formed from the breakdown of nucleic acids and are also derived to some extent from the diet. Certain foods are high in purines; pancreas, heart, liver, anchovy, sardines, and roe contain abundant purine and the uric acid level will go up if you eat a lot of them. Purines are also formed by synthesis from simple precursor substances. They go through a complicated metabolic pathway, and in man the end product is uric acid. In the course of evolution the enzyme uricase, which breaks down uric acid to simpler substances, has been lost by man and other primates, and so we have to dispose of uric acid as such. Some of it is excreted into the gut, where it is broken down by bacteria which possess this enzyme uricase; but most of it we excrete through the kidneys. We can therefore envisage an increase of uric acid in the blood being due either to overproduction from one of several sources, or to impaired excretion.

Primary and secondary gout

Gout can be divided into primary gout, where the cause or causes remain as yet undetermined, and secondary gout where the mechanism of hyperuricaemia is known. In both, metabolic and renal factors may be involved. Too much uric acid may be produced; and a proportion of gouty patients (but not all of them) can be clearly shown to make too much uric acid. Impaired excretion of uric acid also plays a part, gouty subjects have a rather lower mean renal clearance of uric acid than that of a normal population. In primary gout there is often a combination of these two factors, which themselves represent many other causes; there is incomplete knowledge as to the relative importance of each.

Sometimes we have a better idea of the cause. For instance, if there is overproduction of uric acid due to increased turnover of nucleoproteins, as in the proliferative haemopoietic diseases such as polycythaemia rubra vera or leukaemia, especially when being treated by radiotherapy or by cytotoxic drugs, there will be excessive production of uric acid; this may precipitate gout, especially if there is a baseline of hyperuricaemia to begin with. Various renal factors may operate. These include advanced renal failure itself; impairment by drugs of tubular secretion of uric acid (most commonly chlorothiazide which tends to raise the uric acid level in the blood, or the antituberculous drug pyrazinamide); excess lactic acid in the blood, which is found in toxaemia of pregnancy and in some forms of glycogen storage disease; ketosis, as in starvation or in diabetic coma; and perhaps hypercalcaemia as in hyperparathyroidism. Lactic acid and ketone bodies compete with uric acid at the renal tubule, so that the excretion of uric acid falls and the uric acid level in the blood rises. It is clear that we cannot think of gout as a single entity; there are often various factors operating even in an individual patient.

Treatment

You are familiar with the concept of dealing with the acute attack in the first place and later with the management of chronic gout. Do not try to lower the uric acid level in acute gout; do not give probenecid or similar drugs because, if anything, they may make the attack worse. What is necessary is to get the acute attack over as quickly as possible and then assess the situation with proper biochemical control. For acute gout in a toe, knee or finger, the patient should rest the joint and protect it from damage, and take one of three very effective anti-inflammatory drugs: (1) colchicine, 1 mg stat

and 0.5 mg every two hours until the attack subsides or until diarrhoea or nausea supervenes; (2) phenylbutazone 200 mg four times a day (too high a dose for maintenance treatment as in rheumatoid arthritis but quite all right for a few days in acute gout) or; (3) indomethacin 25 mg four times a day (some people give rather more than this).

These drugs can be used alone or in combination, but with the exception of phenylbutazone they will have no effect on the uric acid level. Phenylbutazone is weakly uricosuric, and salicylates also affect the blood level of uric acid (though salicylates have little place in the treatment of gout). If there is any diagnostic doubt, it is as well to draw some blood for a uric acid estimation before the patient takes any drugs.

In the management of chronic gout, diet is not important because we can control uric acid levels by other means, but I think it is as well to warn the patient which foods have a high purine content and to advise him that they should be eaten sparingly. He should also avoid excessive alcoholic bouts which tend to precipitate acute gout. The uric acid level can be lowered either by suppressing its formation by the use of allopurinol or by enhancing its elimination with uricosuric drugs, such as probenecid, sulphinpyrazone, or ethebenecid. The anti-inflammatory drugs have a part to play at this stage, either in patients in whom we do not wish to lower the uric acid level or during the early stages of uricosuric treatment, when paradoxically the patient is particularly liable to get acute gout. It is therefore as well to use small doses of these drugs in addition to allopurinol or the uricosuric agent until there has been freedom from gout for two or three months.

But we do not always want to lower the serum uric acid level. It is as well to think in terms of certain definite indications; (1) the presence of tophi or chronic joint damage; (2) frequent acute attacks; (3) impairment of renal function (because there is some evidence that a prolonged high uric acid level is deleterious to the kidneys); (4) a uric acid level persistently about 8 mg per 100 ml associated with gout, because experience shows that the patient is probably in for progressive trouble. But if he has had only one or two attacks and the uric acid level is not very high, or if there is any diagnostic doubt, it is a mistake to begin prolonged uricosuric treatment, because once it has been started it should be maintained for life. Both you and the patient must be satisfied that this is the proper, necessary treatment.

Uricosurics or allopurinol

The serum urate level is lowered with 1–2 gm probenecid daily or equivalent doses of the other uricosuric agents. It is a prolonged effect, and lasts indefinitely while the drug is taken. Uric acid excretion persists at a rather higher level than is normal. The alternative is to inhibit the enzyme xanthine oxidase (which is responsible for the formation of uric acid) by giving allopurinol. Both serum and urinary levels of uric acid fall. 300 mg per day is the usual effective dose, but sometimes 400 or 600 mg is necessary. In both types of treatment the dosage should be regulated according to the serum urate level.

In early, uncomplicated gout, there is probably little to chose between allopurinol and uricosuric treatment. Both are perfectly satisfactory, and the more conservative of us may still probably prefer to use uricosuric treatment because the other drug is newer, though so far no serious toxic effect has been ascribed to allopurinol. There are, however, certain situations where allopurinol is definitely indicated, either alone or in combination with uricosuric treatment. In severe tophaceous gout it is rather more effective than uricosuric therapy; some cases of gout cannot be controlled by uricosuric treatment (although the usual reason for this is that the patient is not taking his tablets) or there may be intolerance to uricosuric drugs; and where there is known to be gross overproduction of uric acid it is as well not to have this all going out through the kidneys. Uric acid stone formation is now an absolute indication for allopurinol, which has

revolutionized the treatment of this condition. In gout with advanced renal failure uricosuric drugs become ineffective, but allopurinol will continue to lower the uric acid level. The drug is also valuable in the rather specialized conditions seen by those treating malignant disease, when excessive breakdown of tissue nuclei in patients who are being treated with cytotoxic drugs and radiotherapy may lead to blockage of the ureter by crystals of uric acid.

Surgical aspects of treatment

A. Kates, F.R.C.S. (*Consultant orthopaedic and traumatic surgeon, Chelsea and Kensington Hospital Group*)

"The good that men do lives after them, the evil is oft interred within the bones and joints". Shakespeare *almost* said that and I think that we ought to bear this in mind when we are speaking about the exciting new phase in surgical treatment of rheumatoid arthritis. I would like to start by quoting from an extract in *World Medicine* for February, 1967:

"In 1962 a young man suffered his first symptoms of rheumatoid arthritis, for four years he was treated by his general practitioner chiefly with aspirin and he was told that he had rheumatoid arthritis, nothing more could be done and that he would have to learn to live with it. Now he has a gross deformity of his feet, knees, hands and hips, and physicians and surgeons of the unit of rheumatology to which he has been referred cannot be optimistic about his future".

In treating rheumatoid arthritis by operation, the surgeon must be aware of all the problems of the rheumatoid arthritis sufferer if he is to treat him intelligently. These patients are often depressed. We do not know why, but we do know that they have suffered from their disease for many years and when they learn that something can be done surgically for them, there seems in many cases to be a complete change in their personality. They almost become euphoric about what might be done. One must be careful though never to sell an operation to any rheumatoid patient. The patient must always be told precisely what the operation involves and the possible limitations of success. An enthusiastic patient is extremely loyal to his surgeon and is therefore biased in his assessment of the operation result.

Surgery in various phases

In the rheumatoid normal joint, the villain of the piece is the synovium. In early synovitis there is swelling which goes on to erosion of the bone, stretching of capsules, destruction of bone and subluxation, until finally the joint is completely dislocated. Surgery can be divided into three phases: (1) Prophylaxis in the early stages before the bone is affected. These changes are reversible, and my plea is to get practitioners to send cases early so that prophylactic surgery can be carried out, with the hope of lasting cure in the joint; (2) Once a joint is subluxated, simple procedures such as synovectomy are no longer of use, a more complex operation—such as joint reconstruction—may be necessary; (3) Finally, patients with rheumatoid arthritis of many years' standing have such gross joint deformities that surgery at that stage is undertaken to make the life of the patient a little more tolerable.

Surgery can help by relief of pain. In my experience it is this that gives both the