Yes! I think something's happening! Certainly no side effects. But steady now, quiet, considered opinions please, you know how this brute behaves. Suddenly things are better, and the tiger has slunk off. I'm moving again—I am, I am. Just don't get so excited, that's all part of the game. Here we are back again at square one, you've got to admit it, flurbiprofen hasn't really helped you—actually you're as bad as ever. Where do I go from here? The one wonderful thing for me—and I used to loathe and fear injections to the point of syncope—is cortisone into a joint. It hurts quite a bit, but just hold on for 24 hours, and down goes the swelling. If you happen to have had a couple of joints done, then two or three days later you feel a wonderful euphoria; and the cramping, stranglehold of this rusting, barbed thing suddenly goes. Yes, upstairs two at a time, you're back to your old self. But a few more days and it's slowing up, and soon the battle is rejoined.

So far I'm lucky really, my troubles are periarticular and synovial, and joint damage is minimal. Nevertheless, I could not have even started to understand what this disease meant without

experience, and I doubt whether most medical colleagues have the remotest idea of the subtlety of this torturing prince, and the way you must learn to guard yourself all the time: to hide yourself from its effects; to hope; to try not to fill with self-pity, remembering that others cannot understand; and to persevere in your passage through this gloomy tunnel praying for the sunburst liberation of the day of freedom.

I love the violin, and have played since the age of 6, with a fairly high degree of competence, though I say it myself. I must have been pretty good as a youth, for I found myself competing with a girl for a viola scholarship to the Royal Academy of Music. I played first, and after she had played there was a pause and I was asked to return and play it again. My heart leapt—you've got it, you must have—it's so close they want to hear you again. Then another pause, and the girl was asked in and justly awarded the prize. She became one of our top players. I often wonder, had I won, where would I be now?

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Personal Therapeutics

Rheumatoid arthritis

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Rheumatoid arthritis is a remarkably variable disease in terms of severity and frequency of systemic features. Unfortunately, it is still a major cause of disability in Britain. No cure is yet in sight; there have been no major innovations in therapeutic approach nor is there evidence towards milder disease. Despite this, the past decade has seen major improvements in managing rheumatoid arthritis. Three main factors may be easily identified: a far greater range of effective non-steroidal anti-inflammatory drugs; more effective and earlier use of disease-modifying drugs such as gold and penicillamine; and major improvements in orthopaedic procedures, particularly in joint replacement. Two other factors are more speculative: a considerable reduction in the use and dosage of corticosteroids and the greater availability of doctors skilled in managing rheumatic diseases.

Principles of management

The rate of introduction of new non-steroidal anti-inflammatory drugs (NSAID) is such that not even rheumatologists can claim to be familiar with each and every one, a far cry from the days when the choice lay between aspirin and phenylbutazone. Most have an appreciable anti-inflammatory effect as well as an analgesic effect: they will reduce the duration of morning stiffness, decrease joint swelling, and lower the erythrocyte sedimentation rate. In particular, the newer NSAID produce a satis-

factory anti-inflammatory effect with fewer side effects, and almost every patient can be effectively treated with one or other. This is perhaps the one factor that has reduced long-term disability in rheumatoid arthritis, for it is now rare to see patients with persistently swollen and tense joints, irreversibly stretching the joint capsule to such an extent that subluxation and deformity must follow.

Timing of daily medication is often incorrect. The symptoms of inflammatory joint disease occur principally as morning stiffness, as immobility after varying periods of sitting and lying, and lastly at night, interfering with sleep. Medication is usually given thrice daily in the daytime, when symptoms are least. Ideally, the patient should be given a rapidly acting preparation in the morning, with another dose at tea-time or after work, and a long-acting preparation at night, which will ensure effective sleep and reduce morning stiffness. Side effects of drugs, so prominent in rheumatoid arthritis, may often be minimised by reducing the dosage.

Careful counselling of the patient and reassurance about prognosis are as important as effective treatment. Rheumatoid arthritis is sufficiently common for new sufferers to know of someone severely disabled, often one whose disease has been complicated by iatrogenic problems. Reassurance that the disease is only rarely disabling and the early identification of domestic or work handicaps may produce as much relief for the mind as tablets do for the joints.

Management of the early case

The various established proppionic acid derivatives (fenoprofen, ibuprofen, ketoprofen, and naproxen) seem ideal for the early case as the ratio of therapeutic effect to toxicity is high. Of the four, naproxen scores because of its twice-daily dose: most patients will be clearly improved by one or other of these drugs.

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An initial prescription of two weeks will be long enough to tell whether the drug will be effective, if not another is indicated. The patient should be told early on that a period of trial and experiment may be necessary to find which one of several medications may be the most suitable (table I). Once that drug is identified, change just for the sake of change is unnecessary.

TABLE I—My commonly used NSAID and their dosage

	Usual dose	Duration of activity	Cost per day*
Starters:			
Fenoprofen	300-600 mg four times daily	Short (4-5 h)	13-26p
Ibuprofen	200-400 mg four times daily	Short (4-5 h)	10-19p
Ketoprofen	50 mg twice to four times daily	Medium (6-8 h)	11-22p
Naproxen	250 mg twice daily	Long (12 h)	18p
Major anti-inflammatory effect:			
Aspirin	Soluble 8-12 x 300 mg by day. Enteric coated 3-4 x 325 mg at night	Short (4 h) Medium (6-8 h)	3-5p
Indomethacin	25-50 mg in morning 50-100 mg at night	Long (12 h +)	13-26p
Naproxen	250 mg in morning 250-500 mg at night	Long	18-27p
Phenylbutazone	100 mg twice daily 100 mg at night	Long (12 h +)	4p†

*Approximate "basic" NHS prices based on MIMS.
†As Butazolidin.

Aspirin in one of its many forms is still best for many patients, particularly those with more severe and acute onset of disease, and I find the combination of an adequate daily dose of soluble aspirin by day and long-acting aspirin at night very successful. The therapeutic ratio of aspirin is low so that patients must often take a daily dosage (around 4 g) close to the toxic dose to gain full anti-inflammatory effect. The best dose is one aspirin tablet a day less than tinnitus or deafness levels, and in many patients, especially very young and old, salicylate blood concentrations need to be checked. Some patients with side effects on aspirin will cheerfully tell you that they gain major relief from Anadin or Veganin, and I find a change in brand of aspirin usually gets around gastrointestinal upset.

Indomethacin is a remarkably effective NSAID such that many patients will wish to risk a return to it despite serious gastrointestinal problems. I often prescribe 25 mg in the morning, 25 mg (optional) at 1800, and 75-100 mg at night. As indomethacin suppositories do not avoid gastrointestinal problems and the dose cannot be tailored to the patient's needs, I rarely prescribe them. Phenylbutazone is now grossly under-used and at 200-300 mg a day its therapeutic index is high. The addition of phenylbutazone or indomethacin to an adequate dosage of aspirin will often change a therapeutic failure to success. Distalgesic may usefully complement the more potent drugs. The place of alclofenac, azapropazone, and the newcomers flurbiprofen, indoprofen, and sulindac is not yet established, but the individual responses of patients will certainly ensure them a useful place for non-responders to other drugs (table II).

TABLE II—Scheme for managing rheumatoid arthritis

Early or mild disease	Naprosyn 250 mg twice daily If no improvement try other propionic acid derivatives If no improvement aspirin in high dosage with long-acting aspirin at night or Indomethacin 25 mg thrice daily with 75-100 mg at night or Phenylbutazone 100 mg twice or thrice daily Radiographs of hands and feet at six-month intervals
Progressive or unresponsive rheumatoid arthritis	Refer for specialist advice regarding disease-modifying drugs—antimalarials for "mild" cases, gold or penicillamine, or cytotoxic drugs
Localised disease	Intra-articular steroid; if no improvement consider intra-articular radioisotope or synovectomy

As important as matching drug to patient is matching dose to patient. The pharmaceutical companies can establish a usual dosage range, but many patients suffer from side effects while obtaining complete relief of symptoms with a standard dose, and here I find the paediatric suspensions of the various drugs allow an effective method of reducing the dose. Other patients need more than the recommended dosage.

Management of established and progressive rheumatoid arthritis

Some patients with rheumatoid arthritis come late to medical care, often when some particular handicap has forced their attendance. In other patients, seemingly well controlled on NSAID, serial six-monthly radiographs of hands and feet will show new erosions or progressive joint space loss, indicating the presence of progressive and potentially disabling disease. In such patients, and particularly in those with established disease, I encourage the patients to list their problems in order of severity and complete a one-page assessment sheet. On one side the patient's present clinical state is detailed—the duration of morning and immobility stiffness, the joints that are currently painful or swollen, and the measurements of grip strength and walking time. On the other side the patient completes a simple assessment of daily living activities.

The problem list and this assessment provide a useful record, and often unsuspected problems are uncovered which may be improved by physiotherapy, occupational therapy, by appliances such as wrist splints, or with local surgery. All patients at this stage are taught a daily exercise regimen. The NSAID is usually changed also, particularly to try those previously beneficial or others not previously used, and I discuss with the patient the use of disease-modifying drugs and their possible advantages and disadvantages, so that if there is no improvement within a finite period, a mutual decision to start one can be made.

DISEASE-MODIFYING DRUGS

The indications that I use for disease-modifying drugs—antimalarials, gold, penicillamine, and cytotoxic drugs—fall into four categories. The most common group includes those patients with widespread active disease, usually in the first year of disease, whose disease activity cannot be controlled despite the trial of several NSAID in effective dosage. Some patients have been reasonably controlled with NSAID, but serial radiographs of hands and feet show new erosions or further loss of joint space. A few patients have systemic features of chronic disease such as weight loss, general weakness, and anaemia, and benefit little from NSAID. The most controversial group, but one in which considerable benefit may often be derived, includes those patients with long-standing disease with evidence of continuing disease activity, in whom further joint damage would convert minimal incapacity to major incapacity.

Of the four disease-modifying regimens, I tend to use anti-malarials for patients with non-erosive disease and gold for the more severe. I prefer gold to penicillamine; firstly because I get better results with gold and secondly because the list of side effects with penicillamine,¹ even in the hands of its greatest advocates, frightens me more than those of gold. Once again, dosage tailored to the patient's need is important.^{2 3} Gold is no longer given in courses, and I use 50 mg injections weekly until major improvement occurs. At this stage injections are given fortnightly, and then an individual maintenance level is found, which varies from 50 mg fortnightly to three-month intervals.³

LOCAL TREATMENT

At various stages of rheumatoid arthritis, and particularly when compiling a problem list, one or two joints may seem to cause a greater problem than the others. Here judicious use of

intra-articular steroid injections (usually hydrocortisone acetate) may work wonders, especially when combined with muscle exercises. Intra-articular steroids work particularly well in the knee, shoulder, and in tenosynovitis of the flexor tendons of the hand, and my use of them increases year by year, but never at more than three-month intervals. If repeated injection is needed I tend to use intra-articular radioisotopes to ablate the synovium in older patients and surgical synovectomy in younger ones.

Misuse or severe damage of one joint often leads to problems in nearby joints. Subluxed and painful metatarsal heads often predispose to knee or ankle problems, or a flexion deformity of the knee leads to hip or ankle problems in the opposite side. Identification of the problem and correct treatment will reduce the need for unnecessary tablets.

Systemic corticosteroids

The vogue of systemic steroids in rheumatoid arthritis is long over. No one will deny the temporary benefit given to patients, but their long-term side effects outweigh their advantage, even in low dosage. Long-term trials show this effect to be lost after the first year, after which steroid-treated patients do worse. Most rheumatologists feel they see less "vasculitis" and less amyloidosis now that systemic steroids are used less, and the higher rate of wound infections, vertebral collapse, and skin fragility in steroid-treated patients deters me from using them.

Besides, many patients spontaneously request me not to start steroids. I do use them for two groups: firstly in wage-earners about to lose their job and housewives unable to cope while I wait for the gold or penicillamine to take effect; and secondly in patients in whom all else has failed and whose quality of life is poor. Ideally I try to use them on an alternate-day basis or as a morning daily dose of not more than 5 mg, as both of these minimise the steroid side effects more commonly seen with thrice daily or night-time regimens.

Remissions

Remission of inflammation may occur spontaneously or with disease-modifying drugs. At this stage NSAID may be reduced or stopped, or conversion to pure analgesic drugs such as Distalgesic may relieve the pain of damaged joints.

I acknowledge much valuable discussion with my colleagues, and the assistance of the Pharmacy at Northwick Park Hospital in the preparation of table I.

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Epidemiology for the Uninitiated

Repeatability and validity

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An ideal survey technique is repeatable (it gives the same answer when the subject is re-examined) and also valid (it measures what it purports to measure). Poor repeatability implies poor validity, because only one answer can be the right one. But a consistent answer may also be wrong: a laboratory test might yield persistently false-positive results, or a highly repeatable psychiatric questionnaire might be an insensitive measure of, for example, "stress." To assess how much weight to attach to epidemiological results calls for numerical estimates of both their repeatability and their validity.

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Repeatability

The principles of repeatability testing were described in last week's article. Results for numerical variables such as blood pressure may be expressed as the *standard deviation* of replicate measurements or as the *coefficient of variation* (standard deviation ÷ mean). Separate estimates may be given for within and between observers, or for variability between measurements made consecutively and those made on separate occasions.

For qualitative attributes, such as clinical symptoms and signs, the results are first set out as a contingency table:

		Observer 1	
		Positive	Negative
Observer 2	Positive	a	b
	Negative	c	d

The overall level of agreement could be represented by the proportion of the total falling in cells a and d. This measure unfortunately turns out to depend more on the prevalence of the condition than on the repeatability of the method. This is