If I Had . . .

Severe rheumatoid arthritis

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"Severe RA" usually brings to mind either advanced disease with much crippling, or the less common explosive-onset type. The latter, perhaps because of early vigorous treatment or some inherent difference, often has a reasonably good outcome; the former is at first deceptively mild-looking RA. This account attempts to convey my view that mild RA is better treated as severe.

History (fictitious)

I woke early with pain in my hands. After a restless hour I got up: my hands were puffy and movement was difficult, but, though this made washing and shaving painful, hot water helped and, after a further hour, I could drive to work. During the day my feet hurt and my knees felt stiff and for once I was glad of a committee meeting as an opportunity to sit, and to consider. The symptoms couldn't easily be dismissed; I had not been unusually active the previous day and, anyway, the pains did not resemble postexertional stiffness. With so short a history it seemed wisest to take some aspirin and await the turn of events. Over the next 10 days the pattern changed little though the symptoms gradually worsened despite liberal amounts of aspirin. Each morning I woke with stiffness and pain lasting about two hours, and then gradually improved. I could manage during the day, but by evening I felt weak, tired, and unwell and the pain tended to return. There was now slight swelling of both wrists, the metacarpophalangeal joints of the index and middle fingers, and both knees; walking was painful.

The difficulty I had in doing simple things like tying shoelaces was increasingly frustrating and demoralising. Reconsideration forced me to face the possibility of RA. I had had no recent febrile illness, or any drug other than aspirin; thus a soluble immune complex (serum sickness) -type reaction following a viral or mycoplasma infection, or hypersensitivity to a drug, was improbable. My mother has RA, and this made the diagnosis marginally more likely. Other possibilities—for example, arthropathies associated with inflammatory bowel disease, brucellosis, or sarcoidosis—seemed very unlikely. I decided to talk to my GP.

Early management

Effective symptomatic treatment is the first goal. Rest and non-steroid anti-inflammatory drugs (NSAID) coupled with

a wait-and-see policy is usual. But for how long? Procrastination for, say, six weeks is thought to be reasonable because the disease may not be RA and, if it is, it may remit spontaneously. I want my GP to be more aggressive, and to prescribe bedrest at this stage—at home if possible, but in hospital if not. I also want my GP to be a virtuoso about using NSAIDs. Till recently most people chose soluble aspirin—enough to exert its anti-inflammatory, not just analgesic, properties; this means not less than 4 g daily. Latterly there has been a trend to use other NSAIDs; some are as effective as aspirin, as safe, and fewer tablets need to be taken. My short list includes the drugs with which I am most familiar, but my GP may have other ideas. Response is variable and individual, and if a drug of this group doesn't work in a week, it isn't going to.

Diagnosis next, and the sooner the better. Although on clinical grounds RA is probable, some investigations of exclusion should be carried out. Antibody titres to cytomegalovirus, rubella, mycoplasma, brucella, and *Yersinia* should be measured twice with a two-week interval. Antinuclear factor, by immunofluorescence, might be present as it is in many patients with RA, but anti-DNA antibodies will not be found. The only relevant diagnostic investigation would be for the presence of rheumatoid factor in the blood—if positive the diagnosis is made, if negative it is not excluded.

Prognosis is the third early step. I have a family history of RA; mine began insidiously and has now persisted for three weeks without remission. There are no nodules; if present, that would be ominous, but it is perhaps too early. The Rose-Waaler test is positive at 1:64, blood count shows a slight anaemia, ESR 38 mm in the first hour, serum C-reactive protein (CRP) concentration 44 mg/l, and x-ray films of the joints show periarticular osteoporosis, but there are no erosions. I am resting at home and do not feel or look too bad, but the findings all indicate severe RA.

Second stage management

My GP suggests that we get help. I hope he selects a physician with a particular, but not necessarily exclusive, interest in arthritis and that they will both keep an untiring interest in my follow-up and proceed, if necessary, from one drug to the next in careful progression using objective assessment methods. (I take for granted attention to general problems such as anaemia and depression, and there are other aspects of treatment that I shall omit from this account, which is mainly concerned with medication. I hope too to see, at intervals, an orthopaedic surgeon who has a special interest in RA. If he suggested synovectomy for wrists or tendon sheaths in the hands I would agree with little hesitation, but I would try to avoid other operations in the early stages. If I am one of those unfortunates who do not respond to drug treatment I shall later need much surgery, and I hope I would have the fortitude of some of my patients in facing this; those that do, fare well.) There are enough data to decide about further treatment, but the next step is controversial. Many people persist with aspirin-like drugs and

other supportive treatment for a few more months, reasoning that the dangers of such drugs as gold outweigh the advantages. Nevertheless, I would not be happy to wait any longer. My chances of benign progress are only about one in 10.¹ I have been impressed with the results, in my own patients, of some of the "group 2" drugs (mentioned below), which have not merely alleviated symptoms but can control RA; their hallmark and a good method of assessing their efficacy is that they lower the ESR and serum CRP concentrations.² I hope, therefore, that my physician, like my GP, has a sense of urgency and wide experience of such drugs that I would take without further delay. But which drug?

I would not accept the quickest acting, adrenal corticosteroids, as my first choice. In sufficient doses their side effects are too frequent; at lower doses they may control symptoms in a manner similar to aspirin but still constitute a hazard. (An alternative, starting simultaneously with corticosteroids for a rapid effect and gold for more lasting control, and then being weaned off the former, is theoretically attractive but in practice hardly ever works).

The other drugs have various dangers and varying chances of success. The orthodox choice would be gold or penicillamine. Either can lead to striking improvement with a lowering of ESR and serum CRP concentration; both take up to three months to act; both may have dangerous side effects. I would first select a more speculative but safer drug, either dapsone or salazopyrin; of the two, my current favourite for early RA is salazopyrin. First proposed 30 years ago for RA by Svartz,³ it has been little used but I have had some success with it.⁴ If I did not clearly benefit (with a reduction in ESR and serum CRP concentration after six weeks), I would switch to dapsone⁵ for similar reasons and for the same length of time. Failure with this drug too would be my signal to start gold or penicillamine.

I have more experience of gold and would select this. Although there has been a report⁶ that deaths occur with gold more often than with other drugs, I and others⁷ suspect this finding; most people's experience is that, given reasonable safety checks, side effects are common but reversible. I would have 50 mg Myocrisin weekly from the outset, there being no evidence that small starting doses avoid adverse effects, and continue for 20 weeks. Clinical improvement and a fall in ESR to <30 mm in the first hour and in serum CRP concentration to <20 mg/l is the aim; if attained, I would then take 50 mg fortnightly indefinitely. I have too often heard patients say they have had gold previously with great benefit, but that after the course they relapsed; there is no such thing as a course.

If gold failed, penicillamine is indicated. No one yet knows

the right dose of this drug. In general, the incidence of side effects, mostly reversible, appears related to dose and I would start with 125 mg daily increasing slowly to a maximum of 750 mg. Efficacy is judged as with gold. Assuming penicillamine, too, was ineffective and also that I still had considerable pain with a high serum CRP concentration and ESR and, by now, nodules and erosive joint damage on x-ray films, as I suppose would be likely, I depend even more on a vigorous attitude to treatment. Applying the same principles as for gold, I would now take hydroxychloroquine, but with little hope of success. Failure again leaves only immunosuppressants, levamisole, and corticosteroids; my own experience with the first has not been encouraging and adverse effects frightening; as yet the potential of levamisole is unknown. I would start corticosteroids, probably as adrenocorticotrophic hormone, despite the inconvenience of injections, because the risk of the longer-term adverse effects is less than with prednisolone. If this treatment left me with a reasonable CRP concentration and ESR level I should continue adrenocorticotrophic hormone but keep to the lowest dose manageable. If not, as is slightly more likely, the risks of disablement are still higher and I should expect my physician to reconsider using one of the group 2 drugs again—they may behave differently in patients already taking corticosteroids.

I don't think the risks of all these drugs taken serially under careful supervision are greater than the risk of crippling when early indications suggest RA is going to be severe. As Comfort said⁸ in another context, it is essential to be aggressive in guarding one's mobility. Throughout the treatment I would try to set some achievement as an objective—work, sport, a hobby. Success in something would be by far the best way of maintaining morale.

It is right to add, I think, that I have described not only "If I had severe RA" but also a singularly disastrous course; I hope, by a vigorous and enterprising policy, to be one of the patients who do respond—more than half—to one or other treatment and achieve a reasonable, though not ideal, result.

References

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Should measles vaccine be given to children suffering from infantile eczema that is being treated by a topical steroid?

Although the live attenuated measles vaccine should not be administered to people undergoing corticosteroid treatment, this refers to its systemic use, and it is extremely unlikely that the administration of a topical steroid would constitute a contraindication. With regard to infantile eczema, although the manufacturers say that the vaccine should not be given to children with a history of allergic disease, it is unlikely that infantile eczema constitutes a serious contraindication to measles vaccination.

What is a paraganglioma and how should it be treated?

Paragangliomas or chemodectomas are tumours arising in the chemoreceptor organs of the carotid, aorta, and jugular bulb. One variety is the so-called glomus tumour. They are usually small and single and occur in women more often than men, usually in late middle age. Almost always benign, they tend to recur and occasionally may produce distant metastases. They are sometimes familial. Paragangliomas are composed of nests of epithelioid cells surrounded by dense

vascular connective tissue, and are designated non-chromaffin because they do not as a rule secrete catecholamines. They usually come to light when a lump is found in the neck, and excision is the standard treatment.

Is gammaglobulin effective in preventing chickenpox?

There is no evidence whatsoever that normal immune gammaglobulin prevents chickenpox, nor does it prevent encephalitis. It should therefore not be given to babies under 6 months of age.

What are the side effects of propranolol and should it be given to a patient who developed hyperkeratosis while on practolol?

The various side effects have been reviewed.¹ Rashes do occur during treatment with various beta-blockers but cross-reactions are rare. I would not hesitate to prescribe propranolol for this patient, given a sound therapeutic indication, but would ask the patient to report any appreciable deterioration of the skin condition.

¹ Petrie, J C, *et al*, *Postgraduate Medical Journal*, 1976, suppl No 4, p 63.