doses, pulse methylprednisolone therapy may continue to be a useful rheumatological tool.

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1 Smith M D, Ahern M J, Roberts-Thomson P J. Pulse methylprednisolone therapy in rheuma-
7 Garrett R, Paulus H. Complications of intra-

Response criteria for slow acting antirheumatic drugs

Sir: With great interest we read the recent article by Scott et al on response criteria for slow acting antirheumatic drugs.1 We fully agree with the concept of development of an index of response to slow acting antirheumatic drugs. The authors emphasise the development of a single index and its relation to clinical practice. The basis for this index was a consensus meeting of 16 rheumatologists. Later the response index was used in the evaluation of penicillamine and sulphasalazine. As the authors explained, however, the index has not been validated.

We have attempted to determine which variables are most useful for measuring disease activity. We evaluated, therefore, the judgment of doctors in clinical practice for high and low disease activity.2 The study group comprised 113 patients with recently diagnosed rheumatoid arthritis who were studied prospectively. The follow up ranged from two to 39 months (1816 check ups). We thus obtained a disease activity score (DAS) composed of the Ritchie articular index, the number of swollen joints, erythrocyte sedimentation rate, and general health (a 5 point scale). Subse-
sequently, the DAS was validated by comparison with various single and composite indices used to measure disease activity, with attention to their correlation with radiographic damage and functional capacity (in preparation).

This validation was made with an extended group of patients from the same prospective study (follow up range eight to 58 months, 6011 check ups). The DAS and the Mallya index were found to be the most valid variables for measuring disease activity. In comparison with the response index proposed by Scott et al, the DAS has several advantages and one disadvantage. The disadvantage is that the DAS is not as simple to compute as the response index. The advantage, however, is that the DAS needs no further validation and is ready to use.

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Correlation of iron exchange between the oral iron chelator 1,2-dimethyl-3-
hydroxypyrid4-one (L1) and transferrin and possible antiaemic effects of L1 in rheumatoid arthritis

Sir: Iron and ferritin are probably able to stimulate local free radical damage in joints of patients with rheumatoid arthritis (RA) by forming hydroxyl radicals3 and in this way contribute to persistence of synovitis.4 In the anaemia of chronic disease in RA iron saturation of transferrin generally is low5 so it is possible that iron exchange between ferritin and transferrin mediated by L1 takes place, explaining the haemoglobin increase after iron chelation in these patients.6 7 It has also been found that L1 diffuses easily through the erythroblast membrane8 and thus it may incorporate iron into erythroblasts and hence the possible deleterious effects of iron stores on RA activity the treatment of RA with desferrioxamine is controversial.8 9 We confirmed their findings using a new oral iron chelator—1,2-dimethyl-3-hydroxypyrid4-one (L1).9 L1 has been shown to be an effective iron chelator10 with promising potential in the treatment of haemosiderosis and, possibly, RA. If increased bone marrow iron availability is the mechanism through which a haemoglobin increase occurs after iron chelation it can be assumed that this takes place through a higher iron saturation of transferrin, which indeed was the case in our study.

Hewitt et al found that L1 released 90% of iron59 (Fe) bound to transferrin.11 This implies that after L1-iron chelation a high proportion of iron may be bound to L1, instead of transferrin, suggesting a decrease rather than an increased amount of iron bound to transferrin available for bone marrow. We therefore examined both the ability of L1 to chelate iron from human transferrin and of human transferrin to remove iron from L1.

The following method was used: 388 μL of L1 (0-1 mg/ml) was added to 100 μL of Fe-
transferrin (transferrin 9-7 mg/ml). After incubation for 24 hours the elution was carried out by gel permeation chromatography (Sephadex G 50; pH 7:4 with an elution velocity of 32 ml/h, recovery 76-6%). In the second experiment 20-4 μL (272 μg/ml) of FeCl3 and 148 μL (2 mg/ml) of FeCl2 were added to 1 ml of Fe-L1 solution, after which fractionation was performed similarly (Sephadex G 50; pH 7:4; velocity of 32 ml/h; recovery 75-8%). The table shows the results obtained. Activity was measured with a Packard-autogamma 500 C.

The results obtained indicate that L1 is able to remove a substantial amount of iron from transferrin, confirming findings of Hewitt et al,11 depending on the time of incubation and the amounts of L1 and transferrin added. It was also found, however, that after fractionation was performed similarly (Sephadex G 50; pH 7:4; velocity of 32 ml/h; recovery 75-8%), this removal did not occur in the case of transferrin.

Iron-59 exchange after incubation of (A) L1 and (B) Fe bound to transferrin and (B) apotransferrin and (A) Fe bound to L1.

Iron-59 exchange after incubation of (A) L1 and (B) Fe bound to transferrin and (A) Fe bound to L1.