the second and fifth elements, we cannot exclude a possible role of cryoglobulins in the development of MMN in our case, because demyelinating polyneuropathies have been described in association with mixed cryoglobulinaemia [9]. The fourth element is not available to study because infliximab was not reintitated. However, temporal association and dechallenge (improvement in symptoms following discontinuation of the drug) suggest that infliximab, rather than cryoglobulin, is related to the development of the neurological complication in our case. Hepatitis C infection and cryoglobulins were recognized at least 5 and 2yr respectively before the demyelinating event occurred, and after only four doses of infliximab. Furthermore, the levels of cryoglobulins decreased after infliximab infusions. On the other hand, discontinuation of infliximab therapy was followed by a quick recovery of the muscle strength. Thus, we conclude that infliximab is probably the agent responsible for the development of MMN in this patient.

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FIG. 1. Changes in measures in 100 patients with rheumatoid arthritis over 5yr determined by effect sizes. From Callahan et al. [6], with permission.

How aggressive should initial therapy for rheumatoid arthritis be?

SIR, The report of Matteson et al. [1] concerning their experience with 111 rheumatoid arthritis (RA) patients who were treated primarily with hydroxychloroquine continues a long line of careful clinical investigation by the authors. We were surprised, however, by their characterization of patients with a mean value of 25 swollen joints, 23 tender joints and HAQ disability score of 1.1 as having ‘mild’ RA, most of whom could be treated with hydroxychloroquine for 2yr. We would regard mean values after 2yr of nine swollen joints, seven tender joints and HAQ disability scores of 0.4, along with an increase in the percentage of patients with erosions from 26 to 59%, as unacceptable at this time [2].

Severe long-term outcomes of RA including functional declines, work disability and increased mortality were recognized in the 1980s [3, 4]. Many reports recognize that patients whose inflammatory activity, measured as joint tenderness, swelling and erythrocyte sedimentation rate (ESR), was only partially improved over several years had progression of damage, measured as joint
deformity and radiographic scores [5]. For example, in 100 patients over 5 yr, joint tenderness, swelling and ESR were partially improved while joint deformity and scores for radiographic damage indicated disease progression (Fig. 1) [6].

Statistical significance of improved measures of inflammatory activity does not necessarily indicate clinical significance of the observations [7]. Aggressive treatment strategies for early RA have been advocated, with a goal beyond statistical significance toward remission [2, 8–10]. We would have treated most of these patients with methotrexate and anticipated many fewer swollen and tender joints. Methotrexate is the disease-modifying anti-rheumatic drug (DMARD) that is significantly more likely to be continued at 5 yr because of greater efficacy and tolerability and fewer adverse events than any other DMARD [11, 12], including hydroxychloroquine. Methotrexate appears the ‘anchor drug’ of choice for most patients with early RA [13], including those with a level of severity described in the cohort of Matteson et al. [1].

At this time, evidence of improved long-term outcomes in RA with aggressive treatment strategies is emerging, including radiographic damage [14], functional capacity [15], work disability [16] and survival [17, 18]. However, these reports remain unusual, and many patients continue to experience ‘side-effects’ of the disease [19].

We certainly admire the effort of Matteson et al. to collect rigorous data in standard clinical care, which we have advocated [20]. However, we suggest a reassessment of the hydroxychloroquine treatment strategy in these patients with early RA.

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How aggressive should initial therapy for rheumatoid arthritis be? The Finnish experience

Sir, We read with interest the report of Matteson et al. [1] concerning 2-yr results of hydroxychloroquine (HCQ) treatment in 111 patients with early rheumatoid arthritis (RA). After 2 yr of follow-up, inflammatory activity decreased statistically significantly, but the percentage of patients with erosions increased from 26% to 59%. At 2 yr the mean number of swollen joints was nine, and 38 patients (40% of 94 who completed 2 yr) did not apparently have an ACR50 response. Despite these findings, the authors suggest that treatment with HCQ is ‘greatly beneficial in patients with early RA’.

A Finnish cohort from Heinola was one of the first prospective cohorts of patients with recent-onset (<6 months) RA. One hundred and three RF-positive patients were enrolled in this cohort in 1973–1975. At the time of diagnosis, 31% of patients began HCQ, 51% gold sodium thiomalate, 5% a combination of these, and 2% penicillamine; 85% were taking these drugs at the 1-yr visit and 76% at the 3-yr visit [2]. However, these treatments did not