any clear way with other ophthalmologic signs of toxicity (3). It will be important to learn whether these electrical changes represent effects of the underlying rheumatoid disease, pharmacologic (but not toxic) actions of the drug, or toxicity. A new technique called multifocal electroretinography can measure local electrical activity across the central retina, and may prove a powerful tool for following patients on HCQ (4).

The message for rheumatologists: be aware of the proper dose levels for "lean" body weight -- and get the assistance of your ophthalmology colleagues for screening.

MICHAEL F. MARMOR, *M.D.*
Professor of Ophthalmology
Stanford University School of Medicine
Boswell Building, Room A-157, 300 Pasteur Drive,
Stanford, California 94305-5308, USA

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This evidence-based section was prepared by A. Del Rosso, MD, Department of Medicine, University of Florence, Italy

ERRATUM CORRIGE

In our last issue the cited references were omitted from the comment of Prof. M. Cutolo on the paper by A. Weinblatt *et al*. We apologize for the oversight and herewith re-publish the comment in its entirety.

The addition of adalimumab to methotrexate reduces rheumatoid arthritis activity in patients with longstanding disease

Author: A. Weinblatt *et al*.
Title: Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: The ARMADAtrial.
Source: *Arthritis Rheum* 2003; 48: 35-45.

Comment

This study by Weinblatt et al. *on the fully human monoclonal TNFα antibody adalimumab presents further confirmation that TNFα blockade in rheumatoid arthritis (RA) is efficacious and well tolerated. The improvement was dose-related (i.e. 40 mg every other week seemed to produce better results than 80 mg); however, the best results once again were achieved when treatment was combined with methotrexate (MTX low-dose, average 16 mg/week). The side effects appeared to be less severe with adalimumab than other available monoclonal antibodies; however, further comparisons will be necessary. The study seems to demonstrate that MTX is less effective alone than in combination with adalimumab in long-lasting RA. However, given its complex role as an antiproliferative/antiinflammatory agent, MTX remains the fundamental "gold standard" for RA treatment, although other agents such as leflunomide (LFN) (or even cyclophosphamide) may play a similar role (1).*

The main question that now arises is: "When is the best time during the course of RA to add the TNFα blockade to the antiproliferative/antiinflammatory agent (and to the frequently associated low-dose prednisolone)?" Various treatment algorithms have recently been proposed (2).

Since TNFα is one of the earliest and most active mediators of RAsynovitis and since articular damage starts soon in the disease course, it would now appear sensible to consider early intervention with TNFα blockade (3). Of course, both antiproliferative/antiinflammatory agents (MTX or LFN) and prednisone also act as anti-TNFα agents since they start the blockade at the level of inflammatory cell production, but their action may be better sustained by the concomitant directly targeted effect of true TNFα blockers (i.e. adalimumab) (4).

The second problem is for how long and with what frequency the RA patient should be treated with the TNFα blocker (apart from such obvious considerations as the well-known differing half-lives of etanercept and infliximab). It is evident that the combination of different drugs such as MTX and prednisolone, plus TNFα blockers, after some time will reduce the body fluid concentrations of TNFα from the levels seen at the beginning of therapy, as well as the activity of the primary TNFα-producing cells (monocytes and macrophages). During this period severe side effects linked to the excessive perturbation of TNFα synthesis might arise and the frequency of the dosage should be reduced. In addition, neither TNFα nor IL-1 blockade will resolve the disease progression in all RA patients and new combination strategies will still be needed (5). Keeping these caveats in mind, adalimumab seems now ready to play a key role in RA treatment.

MAURIZIO CUTOLO, *MD*
Director, Research Laboratory and Division of Rheumatology
Department of Internal Medicinem University of Genova
Genova, Italy

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