Reply

To the Editor:

Pouchot et al describe an interesting case of Cogan's syndrome that improves following therapy with prednisone and methotrexate. Many features of this case, including the prolonged treatment course, the absence of vasculitis, and the steroid-sparing effect of methotrexate, resemble my earlier report. However, their patient appears to have responded to methotrexate more slowly than my patient, since 2 years and 3 months elapsed between the institution of the methotrexate treatment and the successful tapering of the prednisone, whereas in my report, a substantial improvement was noted after only 3 months of methotrexate treatment. It is possible that some variability exists in patient response to methotrexate.

The Pouchot et al case highlights the chronic course that Cogan's syndrome can follow. Others have reported that Cogan's syndrome can be extremely variable, lasting from several months to more than 15 years (1). Although some patients will respond to relatively short courses of prednisone (2), prolonged treatment is sometimes necessary. In these patients, steroid side effects are likely to become problematic. This report and my previous case report both suggest that treatment with methotrexate may be helpful in this setting.

As noted by Pouchot et al, Cogan's syndrome can be complicated by systemic vasculitis in 15–21% of patients (3,4). The vasculitis often occurs late, 3 weeks to 8 years after the onset of disease, with a mean of 7 months (4). Since the efficacy of methotrexate in Cogan's syndrome–associated vasculitis is unknown, we agree that all patients should be monitored expectantly. More aggressive therapy with drugs such as cyclosporine (5) may be indicated should vasculitis occur.

Finally, in both cases, arguments against natural disease fluctuations were presented. However, spontaneous disease remissions remain possible. I agree with Pouchot et al that additional experiences should be reported before widely recommending methotrexate. Further reports regarding the use of methotrexate or other steroid-sparing agents in Cogan's syndrome, or other forms of autoimmune hearing loss, would be welcome.

Bruce Richardson, MD, PhD
University of Michigan, and
Ann Arbor Veterans Administration Hospital
Ann Arbor, MI

1. Cheson BD, Bluming AZ, Alroy J: Cogan's syndrome: a systemic vasculitis. Am J Med 60:549–555, 1976
2. Haynes BF, Pikus A, Kaiser-Kupfer M, Fauci AS: Successful treatment of sudden hearing loss in Cogan's syndrome with corticosteroids. Arthritis Rheum 24:501–503, 1981
3. Haynes BF, Kaiser-Kupfer MI, Mason P, Fauci AS: Cogan syndrome: studies in thirteen patients, long-term follow-up, and a review of the literature. Medicine (Baltimore) 59:426–441, 1980
4. Vollertsen RS, McDonald TJ, Younge BR, Banks PM, Stanson AW, Ilstrup DM: Cogan's syndrome: 18 cases and a review of the literature. Mayo Clin Proc 61:344–361, 1986
5. Allen NB, Cox CC, Cobo M, Kisslo J, Jacobs MR, McCallum RM, Haynes BF: Use of immunosuppressive agents in the treatment of severe ocular and vascular manifestations of Cogan's syndrome. Am J Med 88:296–301, 1990

Possible role of bone marrow fat in the development of an inflammatory response to sickled erythrocytes: comment on the article by Mann and Schumacher

To the Editor:

We read with interest the report by Mann and Schumacher of inflammation associated with phagocytosis of sickled erythrocytes after a fracture into the knee joint (Mann D, Schumacher HR Jr: Pseudoseptic inflammatory knee effusion caused by phagocytosis of sickled erythrocytes after fracture into the knee joint. Arthritis Rheum 38:284–287, 1995). In 1961, shortly after demonstration of the phlogistic effects of monosodium urate, we aspirated 10 ml of blood from a man with sickle cell anemia, and incubated it under anaerobic conditions for 2 hours, until smears showed that all cells were sickled. With the patient's permission, we injected the blood into one of his knee joints. There were absolutely no signs or symptoms of an inflammatory response within the next 24 hours. Conversely, we have noted intense inflammation after rupture of necrotic fat into a contiguous joint space (McCarty DJ, McCarthy G, Carrera G: Intraarticular corticosteroids possibly leading to local osteonecrosis and marrow fat induced synovitis. J Rheumatol 18:1091–1094, 1991).

Since the patient described by Mann and Schumacher had a fracture into the joint space, could the phagocytosed sickled erythrocytes have been opsonized with lysolecithin or other materials derived from the bone marrow? Were the erythrocyte cell membranes preserved around the crystalline hemoglobin? It may be premature to assign causality to the sickled erythrocytes until Koch's postulates have been fulfilled.

Daniel J. McCarty, MD
Medical College of Wisconsin
Milwaukee, WI
Roland W. Moskowitz, MD
Case Western Reserve University
Cleveland, OH

Reply

To the Editor:

Ms Mann and I thank Drs. McCarty and Moskowitz for their comments. We are pleased that our article elicited their recollection of their interesting unpublished case study. Their failure to demonstrate any inflammation after injecting sickled erythrocytes into a joint is surprising, since even normal blood does cause inflammation in human hemophilia and in animal experiments (1,2). We showed that the cells of normal blood were more phlogistic than the plasma. The failure to demonstrate inflammation might be related to dose, absence of opsonizing material as suggested, or reliance only on clinical examination. Considerable inflammation can be seen in synovium (3), and at least modest inflammation in synovial fluid (4), without clinical signs.

It would have been interesting to know if the sickled cells could have been demonstrated in the joint after 24 hours, and whether there was anything like the extensive phagocytosis of sickled cells that we saw in our patient. Had the patient studied by Drs. McCarty and Moskowitz had attacks of acute inflammatory arthritis, as our patient had?

In response to the specific questions, most of our patient's sickled red cells did have intact cell membranes, and we saw no obvious adherent material. As is known with