is rare, and that enrolling mothers during a subsequent pregnancy is therefore a challenging task.

The rarity of disease notwithstanding, there remain concerns, especially with regard to the use of corticosteroids. Evidence to date supports the notion that corticosteroids do not appreciably alter titers of anti-SSA/Ro and anti-SSB/La (1), in contrast to the experience with anti–double-stranded DNA antibodies. Overall, the data presented by Kaaja and Julkunen are not in accordance with the literature, although in 3 of their patients the changes in titer did not exceed more than 1 dilution (actually increased in 1). Serial measurement by enzyme-linked immunosorbent assay with paired samples run simultaneously could further strengthen Kaaja and Julkunen's unexpected, but potentially important, observation. Determination of total IgG levels would be helpful to gauge an effect on hemodilution. Since nonfluorinated glucocorticoids are inactivated by placental 11β-hydroxysteroid dehydrogenase (2–4), the reasons for the use of prednisone rather than dexamethasone in their study are unclear. Importantly, there have been cases of CHB despite antecedent use of prednisone by the mother (generally as therapy for systemic lupus erythematosus [5,6]). The use of prophylactic steroids is not without potential risk to the mother and fetus. With regard to the mother one needs to consider infection, hypertension, diabetes, and osteoporosis. Based on the CHB recurrence risk recorded to date (see below), >80% of these women would be unnecessarily exposed. For the fetus the major concerns are oligohydramnios and intrauterine growth retardation, specifically with the use of dexamethasone.

The use of IVIG to potentially eliminate maternal anti-SSA/Ro and anti-SSB/La antibodies via idiotype–antiidiotype regulation is of interest and might account for the reduction in antibody titers as discussed above. If a decrease in placental transport is also hypothesized, then cord blood could be tested to demonstrate that the anti-SSA/Ro and anti-SSB/La titers were lower than expected, as assessed by comparison with the maternal:fetal ratio of total IgG. This would indeed be very exciting. Finally, there is the consideration that IVIG induces surface expression of the inhibitory Fc receptor, Fcγ receptor IIB, on macrophages. Modulation of inhibitory signaling could be a potent therapeutic strategy for attenuating autoantibody-triggered inflammatory diseases (7). Disappointingly, however, the 1 mother who did have a second baby with CHB in Kaaja and Julkunen's study had received only IVIG.

Effectiveness of treatment in their study is difficult to assess. The 1 recurrence in 8 (12.5%) is close to that predicted based on our recent data from the Research Registry for Neonatal Lupus, in which there were 15 recurrences of heart block (inclusive of 3 with first-degree) in 88 births (17.0%) immediately subsequent to the birth of the child with CHB. In addition, an estimate of the CHB recurrence rate from their data would be extremely imprecise because of the small sample size. Based on their results, we have computed the 95% confidence interval for the recurrence rate to be 0.3–53%. This implies that rates as high as 53% cannot be ruled out from their findings, because of the limited data.

To formally evaluate the efficacy of treatment, a randomized placebo-controlled trial would have to be conducted. As discussed above, however, this would be challenging given the rarity of the disease and the difficulty in achieving the sample size necessary for an adequately powered study. For example, nearly 70 patients would be needed in each arm to detect a decrease in the recurrence rate from 17% to 3% with sufficient power.

Clearly, the ideal approach to CHB, as considered by Kaaja and Julkunen, is prevention, since available histologic data demonstrate that the atrioventricular node is replaced by fibrosis and not likely to regain function. Therapy should either be targeted to eliminating the "necessary" factor (no antibody, no disease) or modifying the inflammatory component before it provokes an irreversible scarring phenotype of the fibroblast (8). This remains a challenging task.

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Use of sildenafil citrate in Raynaud's phenomenon: comment on the article by Thompson et al

To the Editor:

Raynaud's phenomenon, or temperature-sensitive vasospasms of the hands and feet, is commonly encountered by the practicing rheumatologist. Symptoms may be mild, but it

can also be a serious problem resulting in digital gangrene. Raynaud's phenomenon may occur independently or in conjunction with another disease, such as systemic lupus erythematosus (SLE), CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, interstitial dysmotility, sclerodactyly, telangiectasias), or systemic sclerosis. To date, no reliable and consistently effective treatment has been described. For instance, in a review of all studies of Raynaud's phenomenon in patients with systemic sclerosis treated with calcium-channel blockers, Thompson et al (1) reported only modest improvement. Other treatment modalities, including oral and topical vasodilators and central and peripheral sympathetic blockade, have not been reliably effective.

Over a 3-year period, I have successfully treated >10 patients (9 women, 1 man) with Raynaud's phenomenon, using sildenafil citrate (Viagra), a phosphodiesterase inhibitor used for erectile dysfunction. All 10 patients were treated with a 50-mg tablet, given once orally at bedtime. Included in this group were patients with idiopathic disease, SLE, CREST syndrome, and systemic sclerosis. Most patients had previously failed prior treatment with calcium-channel blockers and other modalities. In all patients, the results ranged from an excellent response to complete relief of symptoms. Digital ulcers on the hands and feet healed after treatment with sildenafil citrate, and symptoms relapsed after sildenafil citrate was withdrawn.

Multiple side effects, such as hypotension, arrhythmias, heart attacks, strokes, flushing, headaches, dizziness, blurred vision, and altered color vision, have been reported with the use of sildenafil citrate for erectile dysfunction (2,3). Surprisingly, no side effects (including unwanted sexual side effects) from sildenafil citrate occurred among the patients described here. This absence of side effects is likely attributable to the small number of patients treated. I suspect that sildenafil citrate works for Raynaud's phenomenon as it does for erectile dysfunction: as a potent peripheral vasodilator. Regardless, sildenafil citrate is a safe and effective treatment for Raynaud's phenomenon.

I would like to initiate an interest in using sildenafil citrate to treat patients with Raynaud's phenomenon. One of the problems hampering such treatment has been the lack of reimbursement by insurance companies for the medication. Insurance companies will reimburse only for use in the treatment of erectile dysfunction. I believe that if this treatment becomes accepted by the medical community, patients with Raynaud's phenomenon would have reimbursable medication available to them. Hopefully, this report will stimulate more interest and studies into the use of sildenafil citrate in patients with Raynaud's phenomenon.

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Reply

To the Editor:

We read the letter by Dr. Lichtenstein with great interest. Using a literature search on Medline, we were unable to find any trials or reports of treatment of Raynaud's phenomenon using Viagra. There has been interest in sildenafil citrate and other drugs like it (e.g., cGMP-specific phosphodiesterase inhibitors) for the treatment of pulmonary hypertension, because of the vasodilatory effects of such agents.

A well-conducted randomized, controlled trial could certainly help to confirm the suspicion that sildenafil citrate may, indeed, be beneficial in patients with Raynaud's phenomenon secondary to scleroderma.

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A further note on testing for a birth order effect in ankylosing spondylitis

To the Editor:

There has been brisk, but inconclusive, research regarding the possibility that the risk of ankylosing spondylitis (AS) is related to birth order (or maternal age). In a recent letter (1), I noted that the method of testing used by Baudoin et al (2) is almost certainly invalid. That method depends on the intuitively appealing idea that if an individual is ascertained randomly from a sibship of size n, then he or she has equal probabilities (1/n) of being first-, second-, third-, . . . nth born. In fact, this is so only in a population in which the family size distribution has remained constant for many years. For example, if an adult were to be ascertained today from a sibship of size 12, then he or she would be more likely to be later-born, because such sibships have become more rare over the last century (and the older, earlier-born sibs are more likely to have died). To take this into account, a control sample of nonaffected, unrelated adults with the same age distribution should also be ascertained. Such a procedure would have the further advantage of facilitating testing of whether only-born individuals are also at enhanced risk.

Unfortunately, this precaution was not taken in more recent investigations. I suggest that the conclusion of Said-Nahal et al (3) and Brophy et al (4) (that there is no birth order effect) is no more valid than that of Baudoin et al (who concluded that there is an effect). The notion that there is a real birth order effect is potentially important. Therefore, I urge investigators who have published data on the birth order of patients with AS to assemble data on the birth order of age-matched controls.