We studied 22 patients with PSS who were treated with nifedipine for more than a year. The mean disease duration was 9.7 ± 7.4 years. Digital ulcers were present in 12 patients when therapy was initiated. We wish to emphasize the dramatic beneficial effects of the drug on digital ulcerations; the ulcers healed, and there were no recurrences.

When nifedipine was first administered, 11 of the 12 patients had esophageal involvement, which was detected by barium esophageal and fiberscopic studies. In 4 patients, there was a marked worsening of the lower esophageal tract function, with the appearance of reflux esophagitis. Therefore, our findings also demonstrate the potential adverse effects of nifedipine on some scleroderma-related symptoms. The severity of esophageal involvement in patients with PSS who are being considered for nifedipine treatment should be considered prior to initiation of the drug.

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Effects of diltiazem versus nifedipine on lower esophageal sphincter pressure in patients with progressive systemic sclerosis

To the Editor:

In the May 1985 issue of *Arthritis and Rheumatism*, Kahan et al (1) reported their evaluation of the effects of nifedipine on esophageal dysfunction in patients with progressive systemic sclerosis (PSS). Their data indicated that nifedipine significantly decreased lower esophageal sphincter (LES) pressure in these patients. Diltiazem hydrochloride is another calcium channel blocking agent that is considered to be effective in the treatment of Raynaud's phenomenon (2,3). With diltiazem, no change in LES pressure in healthy subjects could be substantiated (4). Therefore, to verify whether diltiazem is to be preferred over nifedipine in the treatment of PSS, a randomized, double-blind, double-placebo, crossover comparative study was performed with 10 patients (1 man and 9 women) diagnosed as having PSS and Raynaud's phenomenon. LES pressure was measured before and after a single oral dose of diltiazem (120 mg) and nifedipine (20 mg).

All patients fulfilled the American Rheumatism Association criteria for systemic sclerosis (5). Other symptoms were those of Sjögren's syndrome (7 patients), intermittent dysphagia (1 patient), and "heartburn" (6 patients). Mean age (±SD) was 56 ± 15 years (range 34–75). Mean disease duration was 14 ± 9 years (range 3–30).

Endoscopy was performed in all patients to rule out lower esophageal stricture. Baseline manometric study showed that peristalsis was absent in 4 patients, decreased in 4 patients, and normal in 2 patients. LES pressure was within the normal range (10–30 mm Hg). The three manometric measurements were taken on each patient at 48-hour intervals, according to a previously described method (6).

Patients were given nifedipine and diltiazem at 1.5 hours and 4 hours, respectively, prior to the manometric study, in order to assess the activity close to the time that the peak plasma level is achieved for each drug. Plasma levels were measured by liquid chromatography with ultraviolet detection after extraction. Paired Student's *t*-test was used for statistical analysis of LES pressure.

No interaction could be shown between the drug administration schedule and the drug effect. Compared with baseline values, nifedipine induced a significant decrease in LES pressure ($P < 0.001$) (Table 1); this confirmed the results obtained by Kahan and coworkers. In contrast, with the diltiazem dose, there was a significant increase in LES pressure ($P < 0.05$). The difference between the values obtained with diltiazem and those obtained with nifedipine

Table 1. Lower esophageal sphincter pressure in 10 patients with progressive systemic sclerosis, before and after nifedipine and diltiazem administration*

Patient	Baseline value	Value after treatment with	
		Nifedipine	Diltiazem
1	18.3	14.5	17.4
2	9.9	5.5	20.2
3	22.5	13.8	27.0
4	20.8	16.6	22.4
5	10.2	5.0	10.1
6	11.0	8.8	11.9
7	13.3	9.1	17.2
8	11.9	9.5	13.9
9	21.7	18.3	23.9
10	15.5	15.5	17.8
Mean ± SD	15.5 ± 4.9	11.7 ± 4.7†	18.2 ± 5.3‡

* Values are in mm Hg. Nifedipine (20 mg) and diltiazem (120 mg) were given at 1.5 hours and 4 hours, respectively, prior to manometry so that each drug would reach peak plasma levels by the time of assessment.
†Significant decrease from baseline, $P < 0.001$ by Student's *t*-test.
‡Significant increase from baseline, $P < 0.05$ by Student's *t*-test. Significant difference from values obtained with nifedipine, $P < 0.001$ by Student's *t*-test.

was highly significant ($P < 0.001$). Esophageal peristalsis remained unchanged after administration of each drug.

Diltiazem does not show a tendency to lower LES pressure, which is the major drawback with nifedipine. Therefore, diltiazem is to be preferred over nifedipine in the treatment of Raynaud's phenomenon in patients with PSS.

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Successful treatment of Raynaud's phenomenon with pentoxifylline

To the Editor:

Raynaud's phenomenon (RP) is a common feature of many rheumatic diseases. Although the pathophysiology of RP remains unclear, many theories have been proposed: local digital vascular abnormalities, an "overreactive" sympathetic nervous system, desensitization of alpha receptors, circulating vasoconstrictor substances, abnormal synthesis or release of prostacycline or prostaglandins, and abnormalities of blood viscosity or plasma proteins (1). RP may be primary or it may be secondary to other diseases, particularly rheumatic diseases.

Red blood cell rigidity may be important to blood viscosity (hence small vessel blood flow) and may amplify the so-called inversion phenomenon, a complex alteration of cellular elements of blood flow through the circulation, which effectively decreases viscosity with the reduction in vessel diameter (2). Increased blood cell rigidity has been found in renal failure, in hemolysis, and in some cases of Raynaud's phenomenon (3).

We have observed a systemic lupus erythematosus (SLE) patient with RP that was characterized by 12–15 attacks per day, digital ulceration, and accompanying dysesthesias. While this patient was inadequately responsive to conservative methods of controlling RP, she had a marked and sustained clinical response to pentoxifylline.

The patient, a 37-year-old woman, had SLE of 5 years duration, which was characterized by antinuclear antibody (ANA) positivity (titer 1:320, speckled pattern), arthralgias, arthritis, pleurisy, fever, and subacute cutaneous lesions, without evidence of renal involvement. She presented with a 1-year history of 12–15 episodes of RP per day, and frequent small, painful digital ulcerations. There were no detectable levels of anti–native DNA (by *Crithidia* assay) or cryoglobulin. Anti-Ro, anti-La, and circulating immune complexes were not sought. Drug therapy at the time of presentation included piroxicam and hydroxychloroquine. Despite avoidance of precipitating stimuli and trials of calcium channel blockers (nifedipine and verapamil), her daily painful attacks persisted. She was empirically begun on a regimen of oral pentoxifylline, 400 mg, 3 times a day. Within the first 2 weeks, the number of episodes of RP decreased to 2 per day. Within 1 month, episodes diminished to 1–2 per week, and her digital ulcerations healed. She experienced no adverse effects from the pentoxifylline and has continued treatment with it. She has experienced no further rash or digital ulcerations, and her disease has otherwise remained under adequate clinical control.

Treatment of RP is often unsuccessful. Avoidance of the cold, smoking, and emotional stress, coupled with biofeedback or hypnosis, may be of variable effectiveness. Plasmapheresis is of questionable value except in those patients who have clearly documented hyperviscosity. Digital sympathectomy is clinically effective, but requires operative intervention with attendant risks. Chemotherapeutic intervention with oral or intraarterial vasodilating agents has been variably helpful. Side effects such as hypotension, light-headedness, and/or diarrhea, which indicate intolerance to calcium channel blockers, are common.

There is a subset of patients with RP who have increased red cell rigidity and may respond to pentoxifylline, a newly approved medication for the treatment of nonoperative ischemic claudication. Pentoxifylline is a methylxanthine with vasoactive properties. It changes rheologic properties of blood secondary to an increase in the flexibility of red cells. In addition, pentoxifylline may induce vasodilation by inhibiting cyclic adenosine monophosphate phosphodiesterase and relaxing vascular smooth muscles (4). A decrease in platelet hyperactivity due to pentoxifylline has also been described (5). The therapeutic profile of pentoxifylline is remarkably free of adverse effects (6).

While this report describes only 1 patient, it presents an interesting approach to the treatment of RP. Pentoxifylline could possibly be used with or without calcium channel blockers in a larger clinical trial in the treatment of RP. We