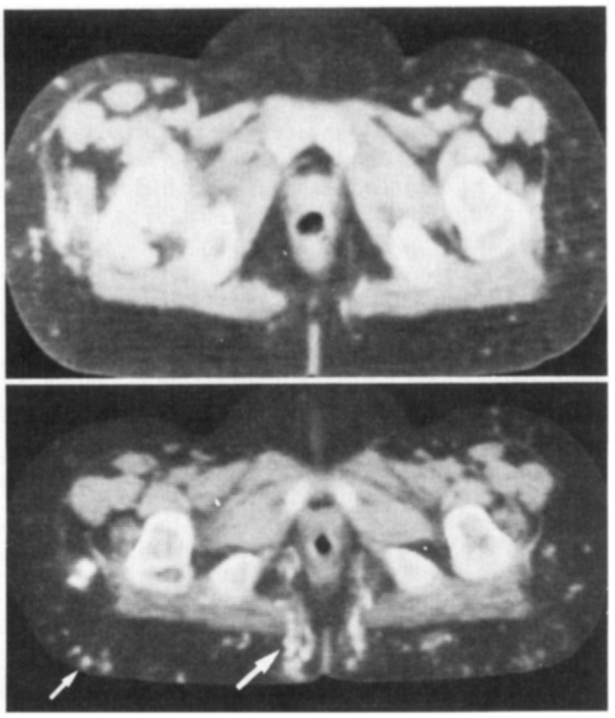

Figure 1. *Computed tomographic scans obtained at the same pelvic level in one patient with dermatomyositis, before (**top**) and 13 months after treatment (**bottom**) with warfarin. The calcifications in soft tissues are more numerous and larger (**arrows**) after treatment.*

of beneficial effect on the progression of calcinosis, especially in patients with mild disease and perhaps in more severe cases.

We report herein our results in treatment of extensive calcinosis with a similar low-dose warfarin regimen in six patients (three males and three females), aged nine to 36 (mean, 22), with dermatomyositis (five patients) or scleroderma (one patient). All patients had extensive calcinosis, graded 4+ according to Berger et al's classification. On entry to this open study, mean duration of calcinosis was 10 years (range, two to 25 years). The primary connective disease was clinically and biologically in remission in four cases, whereas an asymptomatic increase in creatine phosphokinase level was observed in the other two (× 4 and × 6, respectively). All the six patients were treated with 1 mg warfarin per day for a mean period of 14.6 months (range, seven to 28 months). Warfarin was associated with low-dose prednisone (0.15 mg or less a day per kg body weight) in four patients and with higher doses in the two patients who had increased creatine phosphokinase (0.5 and 1 mg/kg per day, respectively). Colchicine (1 mg a day) and penicillin V (1 million units a day) were associated with warfarin and prednisone in four and two patients, respectively.

Response to treatment was evaluated every three months clinically in all cases, and by pre- and post-treatment computed tomography (three patients) or plane radiography (two patients) of a selected involved area. No relapse of dermatomyositis or scleroderma nor adverse drug reaction was observed during the assay. Worsening of calcinosis (increase in the size of previous lesions and/or occurrence of new lesions) was ascertained clinically and radiographically (**Figure 1**) in five patients. In the remaining patient, calcinosis lesions were stable clinically with a follow-up of 28 months.

In our patients, warfarin was clearly ineffective in treatment of extensive soft-tissue calcinosis. Thus, we do not agree with Berger et al's conclusion. In fact, no change in clinical assessment of calcinosis or on plane radiographs was observed in the patients treated by these authors, despite decreased extra-skeletal nuclear tracer uptake and decreased gamma-carboxylation of glutamic acid. These combined facts strongly suggest that low-dose warfarin is of poor therapeutic value in calcinosis universalis.

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The Reply:

Rather than conflicting with our results, Lassoued et al have provided further confirmation that patients with extensive calcinosis (4+ in our grading system included widespread extensive calcific deposits with tumoral areas) do not show response to low-dose warfarin. In our double-blind study, the non-responding patient in the warfarin group had the most extensive calcinosis. The best response, assessed by bone scanning, was in a patient with no clinical evidence of calcinosis. Bone scanning techniques, discussed in our article, are more sensitive in detecting early calcinosis than the plane radiography and presumably computed tomography that were used by Lassoued et al.

We reiterate that the difference between the response to warfarin in mild versus severe disease has a theoretic basis. Excess gamma-carboxyglutamic acid in previously damaged soft tissue may provide a nidus for calcification that is inhibitable by warfarin. However, once appreciable ectopic calcification has occurred, accretion of mineral front in the existing lesion may be independent of gamma-carboxyglutamic acid. We stress that the use of low-dose warfarin had no adverse effects in our patients, and until further controlled studies with larger numbers of patients are done, this therapy would seem reasonable in patients with mild disease.

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