radiation than does phototoxicity. These observations agree with earlier findings that, compared with phototoxic reactions, the eliciting of photocontact allergy requires far lower concentrations of the compounds once photosensitization has developed, and also that it requires less radiation energy (2, 7).

The photoallergic reactions to isobergapten, pimpinellin and sphondin may be explained on the basis of multiple sensitization, but photo-cross-reactions among these closely related agents are indeed likely. The only difference between isobergapten and sphondin is that the methoxy group is located in position 5 for isobergapten instead of position 6 for sphondin, while pimpinellin has two methoxy groups, one in position 5 and one in 6 (Fig. 1).

In conclusion, we have observed that plant products of *Heracleum laciniatum*, probably essentially psoralens, are potentially strong photocontact allergens. It is understandable that the photoallergy is easily overlooked, as the dermatitis is assumed to be phototoxic, which is the common reaction.

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^{65}Zinc Absorption in Untreated and D-Penicillamine-treated Patients with Generalized Scleroderma: Determination by Whole-body Counting Technique

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Abstract. ^{65}Zinc absorption in patients suffering from generalized scleroderma was studied by means of whole-body counting technique following a single dose of ^{65}Zn. In 4 untreated patients the mean ^{65}Zn absorption was calculated to 35% (range 20–59%). Five patients receiving oral D-penicillamine had a numerically higher mean absorption value of 55% (range 37–74%). The results corroborate earlier studies on the effect of D-penicillamine on ^{65}Zn absorption in rats.

Key words: Generalized scleroderma; D-penicillamine; ^{65}Zinc absorption; Whole-body counting

In 1957 Rukavina (8) suggested that the abnormal collagen metabolism in generalized scleroderma (GS) might be due to lack of or excess of certain trace elements or, alternatively, depend on changes in metallo-enzyme function following chelation. Details of such hypothetical mechanisms remain unclarified, but the concept has led to the introduction of various chelating drugs for treatment of GS (1).

D-penicillamine was introduced for GS in 1966 by Harris & Sjoerdsma (4). Later on, Blumenkrantz & Asboe-Hansen demonstrated D-penicillamine in vitro to be a potent inhibitor of collagen synthesis (2).

Recently, Weismann & Knudsen (10) found that oral D-penicillamine increases zinc absorption in rats. This led us to investigate whether therapeutical doses of D-penicillamine for GS exert the same effect in man.

MATERIALS AND METHODS

^{65}Zn absorption studies were performed on patients suffering from GS (i) before any medical treatment was initiated, and (ii) after at least 3 months' therapy with 750 mg D-penicillamine per day. The study was performed from July 1979 to the end of 1980. A total of nine absorption studies

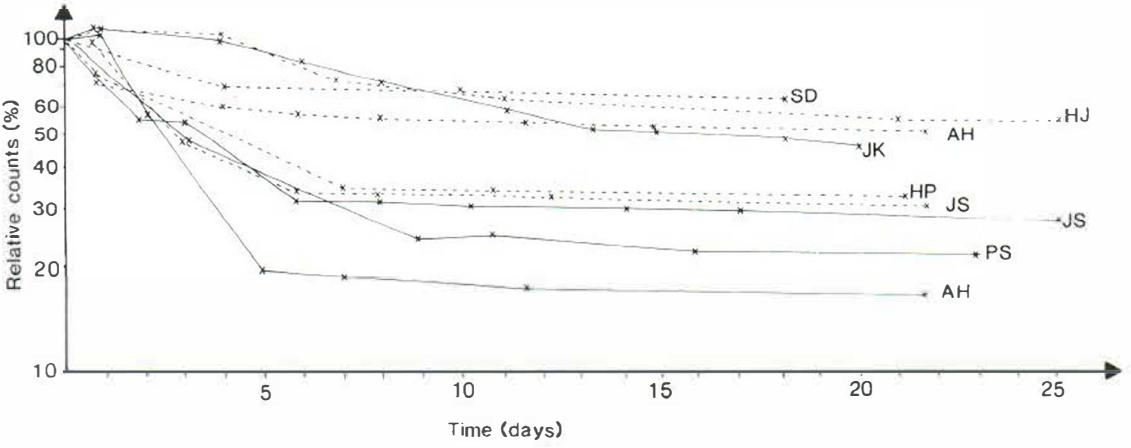

Fig. 1. Retention curves of orally ingested ^{65}Zn in 4 untreated GS patients (——) and in 5 D-penicillamine-treated GS patients (– – –).

were carried out, four in untreated patients and five in D-penicillamine-treated patients. Two patients were studied before and after 3 months' therapy.

Measurements were performed with a whole-body counter consisting of a plastic scintillator system (NE 8114 3π, Nuclear Enterprises) and a multichannel analyser (ND 660, Nuclear Data). The scintillation unit is shielded in a steel room with 15 cm thick walls, internally lined with 2 cm lead.

The patients were given an oral dose of 0.21–0.36 μCi $^{65}ZnCl_2$ (Amersham, ZAS 1, specific activity 0.36 μCi per μg). The maximal absorbed dose for the patients in this study has been calculated to less than 25 mrem to the liver and less than 10 mrem to the body as a whole (5).

Retention of the isotope was recorded at regular intervals for more than 3 weeks. Retention values corrected for physical decay were plotted on a logarithmical scale against time on a linear scale. The ^{65}Zn absorption was calculated by linear regression of retention values forming an approximate monoexponential curve back to time zero.

Table 1. *^{65}Zn absorption in generalized scleroderma (GS) patients*

	^{65}Zn absorption (% of ingested dose)
Untreated GS patients	
P. S.	26
I. K.	59
A. H.	20
J. S.	34
D-penicillamine-treated GS patients	
H. J.	63
H. P.	37
S. D.	74
A. H.	63
J. S.	37

RESULTS

Retention curves are shown in Fig. 1 and the calculated absorption values in Table 1.

The average absorption of ^{65}Zn in the untreated group was 35% (range 20–59%) which was numerically lower than the value of the D-penicillamine-treated group showing an average absorption of 55% (range 37–74%).

Two patients were studied before and after D-penicillamine treatment was initiated. One patient demonstrated a considerable rise in ^{65}Zn absorption, from 20 to 63%, whereas the other patient showed a slight increase, from 34 to 37%.

The serum zinc levels and the activity of serum alkaline phosphatase were within normal limits in all patients, both before and after initiation of D-penicillamine therapy.

DISCUSSION

Using the same whole-body counting technique as here Weismann et al. (11) reported ^{65}Zn absorption among 8 healthy adults to an average of 43%, ranging from 27 to 65%. The present study shows a numerically lower absorption in untreated GS patients, viz. 35% and a range from 20 to 59%. This apparent discrepancy could be explained by a rela-

tive malabsorption of zinc as a consequence of intestinal involvement in GS. In accordance with this view, D-penicillamine was found to increase zinc absorption in our GS patients. A study of GS patients receiving D-penicillamine in identical therapeutical doses as here, revealed normal levels of serum zinc, but an increasing urinary output of zinc, presumably reflecting an increased intestinal absorption of zinc during D-penicillamine treatment (5). Experimental studies in young rats receiving from 63 to 625 mg D-penicillamine per kg per day by gavage showed a dose-dependent significant increase in the ^{65}Zn absorption as compared with untreated controls (10). The therapeutical doses in our patients were considerably lower than in the experimental rats, about 10 mg per kg per day, which may explain the difference between the two studies.

The role of zinc in collagen metabolism is only fragmentarily known. Zinc deficiency induced in rats impairs collagen biosynthesis significantly, probably via nucleic acid dependent processes (3). Whether low or high concentrations of zinc interfere with the establishment of intramolecular crosslinking by means of the copper-containing enzyme lysyl oxidase is still a matter of contention (8).

One direct effect of zinc on collagen metabolism may be on its degradation, since it has been demonstrated that mammalian collagenase is a zinc metalloenzyme (9).

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Low Molecular Weight Dextran in Systemic Sclerosis and Raynaud's Phenomenon

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There have been several reports of improvement of peripheral circulation in patients with systemic sclerosis by infusions of low molecular weight dextran (LMWD) (1, 2, 3, 4, 5). A pilot study by us of 12 patients given a single infusion of LMWD failed to show any significant change in digital temperature when compared with an infusion of 5% dextrose. Some authors (1) have suggested that repeated infusions are necessary, so it was decided to conduct a double-blind trial comparing 10% LMWD in 5% dextrose with 5% dextrose alone, giving three infusions at 8-week intervals.

PATIENTS AND METHOD

Twenty-one patients with systemic sclerosis took part in the trial. Clinical details are shown in Table I. They all suffered from severe Raynaud's phenomenon and 2 patients had had previous digital amputation for gangrene.

Each patient received intravenous infusions on three occasions at 8-weekly intervals. On admission to the