

quently during the various stages of the disease. DIF investigations were performed at comparable sites of the skin (Table I).

Immediately after withdrawing sulfone therapy, the DIF test on newly appearing lesions revealed unchanged IgA fluorescence. The complement staining at the BM was also still clearly visible, though possibly a little weaker. Other classes of immunoglobulins were still absent.

DIF examination performed during the stage of complete remission (3 weeks after oral prednisone therapy) at a comparable site on the skin (healed lesions) revealed an unchanged linear IgA staining, but the complement staining had disappeared completely at this stage.

DISCUSSION

In the present case, clearing of the skin lesions was immunologically accompanied by the complete disappearance of complement (C3), while IgA deposition remained apparently unchanged. This might indicate a primary pathogenic role for complement in tissue injury, leading to blister formation in this case. It can be speculated that IgA deposition might, however, play an indirect pathogenic role in the induction of alternative complement activation. It is of interest that evidence in favour of both classical and alternative pathway activation of complement in BP has been reported (5). In the present case the indirect IF observation indicates the presence of free circulating BM antibodies, as in BP. The antibody appears to be of the IgA class and seems to be highly specific for patient's own (autologous) skin.

It should be noted that apart from the existence of microabscesses, the exact cellular composition of the infiltrate in the papillary regions might be of importance for differences between BP and DH. It has been reported that, in contrast to BP, the number of eosinophils in cases of DH can be relatively large, though never predominant (7). From this point of view the histopathology in the patient described might be better interpreted as BP. Increased incidence of HLA-B8 has been reported in patients with DH (4). In neither of two cases with linear *in vivo* staining of IgA, recently described (6), could HLA-B8 be demonstrated.

Although it can be said generally that classification based on clinical and laboratory finding and on therapeutic response is hazardous as long as the aetiology of the disease is unknown, the data in the present case with linear IgA deposition might well favour the diagnosis Bullous Pemphigoid.

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Treatment of Generalized Scleroderma: Updated Results

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Abstract. Long-term treatment of patients with generalized progressive scleroderma by means of inhibitors of connective-tissue biosynthesis brings about total or subtotal regression of dermal sclerosis in 40.8%, partial regression in 33.1%, arrest of progression without regression in 14.8%, while in 11.3% it had no effect whatsoever. The drugs used were D-penicillamine, benzylpenicillin-diethyl-aminoethyl-esterhydro-iodide, glutamine, hydralazine, chlorpromazine, L-dopa, diphenylhydantoin, and corticosteroids. Disease activity before, during and after treatment was indicated by the urinary frac-

Table I. *Treatment of generalized scleroderma with inhibitors of collagen biosynthesis (1975)*

	0	1	2	3	4	Total
PA only	3	6	14	8	3	34
PI only	1	3	6	3	3	16
CS only	6					6
DT only		1				1
Hy only			1	2		3
Mixed	9	10	11	3		33
Total	19	20	32	16	6	93
%	20.4	21.5	34.4	17.2	6.5	100

tions of high-molecular hydroxyproline and hydroxylysine containing peptides and of uronic acid, break-down products of collagen and acid glycosaminoglycans of connective-tissue ground substance.

The prospects were better for young patients than for old, for those with a short history than for the longstanding disease cases, and for those having a large total dose than for those who had less. If left untreated, scleroderma progresses inexorably.

In 1975, in this journal, an account of studies on 114 patients suffering from generalized scleroderma was given in detail (2). Ninety-three patients were treated with drugs which, *in vitro*, inhibit collagen and/or ground substance glycosaminoglycan biosynthesis. The group of drugs included D-penicillamine (dimethylcysteine, PA), benzyl-penicillin-diethylamino-ethylester hydro-iodide (PI), adrenal glucocorticoids (CS), dextro-thyroxine (DT), and hydralazine (Hy), administered separately, concurrently, or as two or several drugs in consecutive courses (mixed). The effect of dextro-thyroxine could not be evaluated, no improvement was observed with adrenocortical therapy. D-penicillamine improved 25 of 34 treated patients, penicillin hydro-iodide 12 of 16. The dermal sclerosis of 6 patients treated with one of the two drugs regressed completely. In 16, the sclerosis regressed entirely, with the exception of finger sclerosis. In 32, partial regression was noted. Twenty patients had their progression arrested, while no regression occurred. In 19 cases, there was no effect whatsoever (Table I). The prognosis of the disease seemed to be more favourable for young than for old patients. In the better groups, the age at onset was relatively low. The higher the total dose, the better were the results. The length of the treatment course seemed to be of some significance. The total dose of penicillamine must exceed 1 kg to promise true regression.

The short-lasting cases had better prospects than the long-standing. Side effects leading to a change of treatment were relatively common. Twenty-one untreated patients showed continued progression. It is generally agreed all over the world that, although static periods occur, untreated scleroderma will progress inevitably.

MATERIAL AND METHODS

By the end of 1978, the total number of patients treated with inhibitors of collagen biosynthesis for more than one year was 115.

The group of inhibitors of connective-tissue synthesis has subsequently been supplemented with glutamine (Glu, 3), L-dopa (5), diphenylhydantoin (6) and chlorpromazine (4), while corticosteroids (8) were only exceptionally used, and dextro-thyroxine (1) was abandoned. At present, dimethylcysteine free base together with glutamine in daily doses of 750 mg and 300 mg, respectively, is considered the most efficacious choice. The "mixed" treatment includes the above-mentioned group of drugs.

Treatment was maintained for a minimum of one year, mostly for several years, and the period of observation was at least one year. The disease activity was evaluated clinically, light- and electron microscopically, and biochemically. Earlier experience indicated that a high-molecular collagen peptide fraction in the urine indicates the activity of scleroderma with considerable accuracy (7) and the same is true of the urinary excretion of acid glycosaminoglycans (9).

The results of the treatment are listed in Table II, while Table I reviews the situation at the end of 1975.

It appears that 11.3% showed no improvement of their dermal sclerosis; 14.8% had their progression arrested, though there was no evidence of regression; 33.1% were definitely improved; in 24.3% the sclerosis of the skin had regressed to normal, with the sole exception of the fingers;

Table II. *Treatment of generalized scleroderma with inhibitors of collagen biosynthesis (1978)*

	0	1	2	3	4	Total
PA only	2	2	12	10	3	29
PI only	1		3	3	4	11
CS only	3					3
DT only		1				1
Hy only				3		3
PA + Glu			5	2	8	15
Mixed	7	14	18	10	4	53
Total	13	17	38	28	19	115
%	11.3	14.8	33.1	24.3	16.5	100

and 16.5% experienced complete regression of their cutaneous sclerosis.

DISCUSSION

In contrast to what has been achieved with other kinds of treatment, the treatment with drugs inhibiting connective-tissue formation has been shown to bring about partial or complete regression of the dermal sclerosis and a restitution of normal conditions seems to take place. Recent research has provided evidence that sclerodermal collagen is pathological, insofar as the characteristic amino acid of collagen, hydroxyproline, is underhydroxylated in comparison with the normal. Recent studies, yet unpublished (10), failed to demonstrate any restitution of the degree of hydroxylation of proline to hydroxyproline, which would mean that even after treatment the skin collagen remains abnormal.

Although there is some evidence of improvement of the sclerosis of internal organs, e.g. oesophagus, lungs, along with that of dermal sclerosis (2), this problem needs further investigation. The sclerosis of fingers was relatively recalcitrant, probably because of cartilage destruction and fusion of dermis with tendon, joint capsule and periosteal connective tissue. These changes appear to explain why the condition of some patients with severe acrosclerosis does not proceed from grade 3 to grade 4.

The difference between the 1978 and the 1975 results confirms the usefulness of extending the treatment over a long period of time and/or of selecting and combining the most potent drugs.

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Severe Skin Pain after Puva Treatment

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Abstract. Severe skin pain lasting one or two months occurred in 8 of 210 patients treated with PUVA. The pain started 4-8 weeks after the initial dose, mostly about one week after discontinuation of the treatment. It was a prickling, burning pain, usually coming in bouts and confined to limited areas "deep under the skin". In some respects the pain was related to itching, but the patients could easily distinguish between the two sensations. A variety of drugs was tried, but none had any noteworthy effect on this peculiar pain.

Key words: Pain; PUVA treatment

Oral psoralen photochemotherapy (PUVA) can control psoriasis effectively (3, 6, 7) and sometimes ameliorate atopic dermatitis (4), vitiligo (5), and mycosis fungoides (1). During the last 3 years PUVA has been used according to the principles of the European Cooperative Clinical Trial as described by Wolff et al. (7) in the treatment of 210 patients, mostly psoriatics, seen at our department.

The same side effects were observed as those described in other studies on PUVA treatment, viz. erythema, nausea and pruritus (3, 7), as well as less common untoward reactions, such as herpes labialis, hypertrichosis and bleeding beneath the finger nails (2, 4). A further troublesome side effect