

RESULTS

The 115 men exhibited warts distributed among 159 sites (Table I). Initially, 46% of the men seemed to be cured, but relapse occurred in 16% within 4–12 (mean 7) weeks. 34 men (30%) showed eradication of all warts 3 months after treatment, the effect being best seen with preputial cavity warts. These disappeared in 42 of 102 men (41%) as opposed to other wart types which healed in 13 of 57 cases (23%) ($p < 0.05$). No statistical differences were found between the treatment series.

Absence of side effects was noted in only 27 patients (20%). 67 men (58%) complained of itching, burning or a slight tenderness for a few days; 21 (18%) experienced an intermittent, severe pain up to 7 days, frequently radiating along the shaft of the penis to perineal and inguinal areas. 4 men developed balanoposthitis, which also occurred in 3 of the 136 men in the original series, and consequently preventing a second application. Thus, the latter type of complication developed in 5% of cases painted 1–2 times; caused by 8% solutions in 3, 4% solutions in 4 and 2% solutions of colchicine in one case. In all but one of these cases relatively large numbers of warts were present, frequently confluent in larger plaques.

DISCUSSION

The results from previous studies on penile warts with a single application of colchicine are identical with those achieved when a second treatment was given within 72 hours. This is most clearly evident when comparing the effect on warts affecting the preputial cavity (3). A reassessment of previous series using 8% solutions of colchicine reveals that eradication of preputial cavity warts is obtained in 50% of cases after a single treatment. Applications of identical concentration of the substance twice with a 72-hour interval cured preputial cavity warts in 46% of patients. The latter regimen evokes an intolerable frequency of troublesome side effects.

The cytobiological effect of colchicine is mainly due to binding of the substance to microtubule proteins which constitute ultrastructurally rather complicated building blocks of the spindle structures being involved in chromosome movements during cell division. Colchicine-binding activity may decay due to changes in physical environment, a phenomenon conceivably related to structural changes of microtubules (6). The first colchicine application on

condylomata may alter physical conditions in the cells sufficiently to achieve a temporary block of binding ability when the substance is administered a second time. Lack of therapeutic benefit and intolerable side effects seen with the reported regimen may be concentration dependent.

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Porphyria Variegata: Failure of Chloroquin Treatment

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Abstract. A 27-year-old woman affected by porphyria variegata was treated with chloroquin for 1½ years without any clinical improvement. Urinary excretion of porphyrins was not convincingly altered during treatment.

Key words: Porphyria variegata; Phlebotomy; Chloroquin

Porphyria variegata (PV) was described for the first time in 1924, by Thiele. It is an autosomal dominant trait and the clinical findings are a combination of those occurring in acute intermittent porphyria

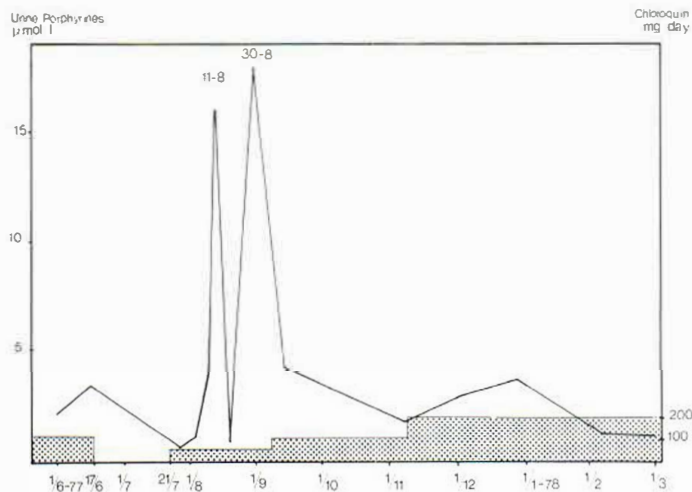


Fig. 1. The full-drawn line indicates excretion of urinary porphyrins (mainly coproporphyrin) and the dotted area shows the dosage of chloroquin during a 9-month treatment period. For the next 10 months, including a break of 6 weeks, the porphyrin excretion varied between 1.02 and 4.8 $\mu\text{mol/l}$. (Urinary analyses were performed by Torben K. With, M.D., Svendborg Hospital, Denmark.)

(AIP) and porphyria cutanea tarda (PCT). The biochemical abnormalities are excessive excretion of coproporphyrin and protoporphyrin in the feces and both of the plus porphobilinogen and delta-aminolevulinic acid (ALA) in the urine.

In PV there is an increase in ALA-synthetase activity (ALAS) (2, 5, 7). This enzyme is the rate-controlling enzyme for porphyrin biosynthesis which, according to the model of Jacob & Monod (4), is controlled by a feedback mechanism via heme. Drugs and hormones are capable of affecting its regulation.

Chloroquin was primarily developed for the treatment of malaria. In 1975 (6) it was tried out on and found to clear the lesions in porphyria cutanea tarda. In 1977 it was tried and reported successful in PV (3) but was administered for a short period only. We have tried the same treatment in one patient with PV for approximately 1½ years (including two short breaks) with a less favourable result.

CASE REPORT

A 27-year-old female with a family history of porphyria, suffered episodes of acute abdominal pain following pregnancies in 1971 and 1973. Since 1973 she has also displayed bullous eruptions on light-exposed areas and later developed facial hypertrichosis together with an increased skin fragility. The skin symptoms were aggravated after use of hormonal contraceptives. Because of this aggravation she was seen by a dermatologist, who stopped the hormonal treatment and referred her to our department.

We found increased amounts of ALA and porphobilinogen in the urine and copro- and protoporphyrins in the feces, indicating a mixed porphyria, most likely a porphyria variegata. During the first 5 months she received three phlebotomies and also sunscreens, but with-

out any clinical effect. Subsequently she was treated with chloroquin in varying dosages (Fig. 1), but this treatment, too, failed to improve her skin symptoms.

Laboratory data. A permanently, slightly elevated sedimentation rate of 22–46 mm/h. Se-transferrin and serum iron were normal prior to the phlebotomies; later she showed signs of iron deficiency. Leukocytes, thrombocytes, se-creatinine, se-electrophoresis, se-transaminases, alkaline phosphatases and urine microscopy were all normal. A liver biopsy before treatment proved normal.

DISCUSSION

The clinical response of chloroquin is excellent in PCT, apparently unlike in PV. The mechanism, however, is still not understood. Cohen et al. (1) found a water-soluble complex formation in vitro between chloroquin and ferrichemic acid.

Scholnick et al. (8) found that in porphyric rats, chloroquin causes massive porphyrinuria, associated with a markedly decreased hepatic porphyrin level, but without any elevation of ALAS, and without any hepatotoxicity. They confirmed the above-mentioned in vitro findings of a molecular interaction between chloroquin and porphyrin.

In our patient, neither phlebotomy nor chloroquin treatment resulted in any improvement of the cutaneous manifestations. Nor did the urinary excretion of porphyrin alter convincingly. Excretions ranged from high to low levels, irrespective of the chloroquin dose. Assuming that the effect of chloroquin, as suggested above, is due to the formation of a complex with porphyrin in the liver, the absence of any effect of chloroquin in PV might indicate a lack of hepatic porphyrins, as found in acute intermittent porphyria (2).

If this theory is valid, one could propose the same therapy for an acute crisis in PV as for an AIP in relapse, that is, infusions of hematin (4, 9).

It has been stated that crises in PV are provoked by medicinal alcohol, starvation, or infections (5, 10). This was also the case in our patients.

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Dimethyl Sulphoxide and Macular Amyloidosis

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steroids. The demonstration by Ravid and others (1) of the solubilization of amyloid fibrils by dimethylsulphoxide (DMSO) led us to try it topically in these patients. Two of five gave us their informed consent.

The first patient, a 79-year-old woman, had a 5-year history of macular amyloidosis of the back, confirmed by histological, histochemical, and ultrastructural analysis (2). Topical steroids were partially effective on pruritus. Pure DMSO was applied weekly from September to December, 1977, then, during the next 9 months, twice a week in a 50% lotion with betamethasone dipropionate. The pruritus improved slightly but pigmentation persisted. A biopsy was then performed. The deposits of amylosis observed by thioflavine T persisted but some of these appeared to be fibrillar.

The second patient, a 70-year-old woman, had had typical but mild macular amyloidosis of the back for 15 years, as demonstrated by histological and histochemical studies (Thioflavine T, Congo Red). DMSO was applied in a 50% solution as in case 1, every 2 days, from March to September 1978. During the 9 months since therapy was stopped, pruritus has not recurred, but the pigmentation has persisted. However, the patient refuses a biopsy.

DMSO is a substance which crosses the skin quite rapidly. It has been tried in a great number of dermatological conditions, with greater or lesser success, or as a vehicle for active molecules. The favorable though subjective effect observed in our second patient, prompted us to report it. Moreover, since macular amyloidosis is not a particularly rare disease and in view of the ability of relieving pruritus in some patients by topical DMSO, therapy must be investigated more extensively.

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Macular amyloidosis is a chronic pruritic disease which is only partially controlled by topical