One can only speculate about the possible influence of PUVA therapy on the natural course of a syphilitic infection.

It has been reported that PUVA therapy induces a transient decrease in circulating T-cells (2, 4, 12) and influences possible cell-mediated immune reactions (10, 15). Although in psoriasis patients several functional changes in cell-mediated immune responses have been reported (5, 8), to our knowledge no mention has ever been made of a different course of a syphilitic infection in those patients.

There are very few reports in the literature concerning granuloma formation in secondary syphilis (1, 6) in which no (clear) explanation is given for this phenomenon.

One might hypothesize that PUVA therapy has (transiently) influenced cell-mediated immune reactivity, thereby facilitating granuloma formation in this patient.

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Hair Loss, Depigmentation of Hair, Ichthyosis, and Blepharoconjunctivitis Produced by Dixyrazine

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Abstract. Four patients developed hair loss, depigmentation of hair, ichthyosis, and blepharoconjunctivitis during treatment with large doses of dixyrazine (Esucos®, UCB, Belgium). The hair, skin, and eyes returned to normal within 2 months of withdrawal of dixyrazine, without any other treament.

Key words: Dixyrazine; Hair loss; Depigmentation of hair; Ichthyosis; Blepharoconjunctivitis; s-Cholesterol

Dixyrazine (Esucos®, UCB, Belgium) is a phenothiazine major tranquillizer advocated mostly for the treatment of anxiety and tension in many types of psychiatric disorders, including alcoholism

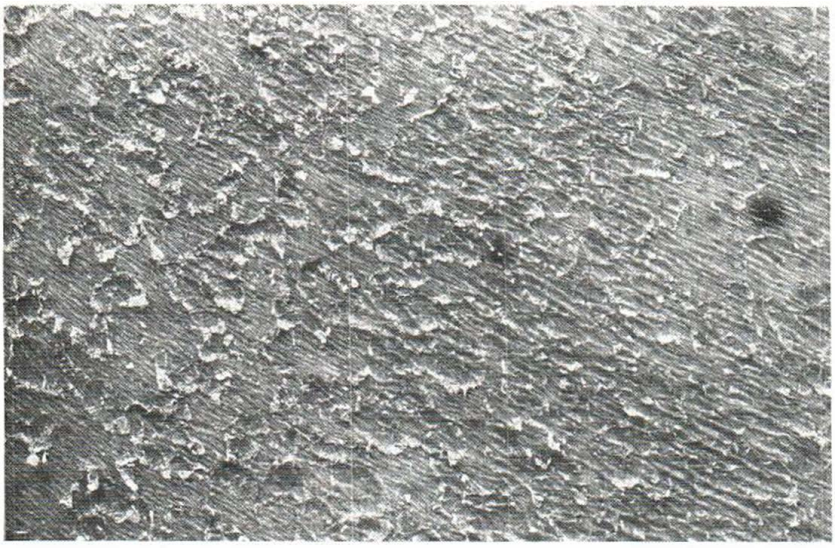

Fig. 1. Case 1. Dixyrazine-induced scaling on the back.

and neurosis. The dosage necessary for patients with different diseases varies greatly, usually ranging from 20 to 150 mg per day, administered orally.

Like other phenothiazine derivatives, dixyrazine has proved to be remarkably safe, compared with previously used sedative and hypnotic drugs. Drowsiness, extra-pyramidal symptoms, elation, fine tremor, and difficulty with balance have been attributed to dixyrazine therapy (3).

After administration of 275 to 300 mg dixyrazine per day for 2 to 6 months, 4 patients, one woman and 3 men, aged 25–35 years, developed hair loss, depigmentation of hair, ichthyosis, and bleparoconjunctivitis.

All were severely mentally retarded and had been hospitalized since childhood. Chromosome analysis and screening tests for metabolic diseases were normal. They ate the usual hospital diet, sufficient in calories, vitamins, and minerals, and were somatically in good health with normal skin, eyes, and hair before the administration of dixyrazine.

CASE REPORTS

Case 1. Woman, aged 27 years, given dixyrazine for 6 months, the first 3½ months, 25 mg three times a day. The dosage was then gradually raised to 75 mg three times a day.

She showed a marked depigmentation of all hair except the pubic and a severe diffuse alopecia on the scalp and in the axillae. The hairs were brittle and could be easily plucked. The trichorhizogram revealed a telogen : anagen ratio of 1 : 1. The scalp was scaling, with patches of erythema. She had a marked blepharoconjunctivitis and scaling on her eyelids. The skin on the forehead, neck, back, and extensor aspects of the arms was xerodermic and scaling with small, fine and translucent scales (Fig. 1). Skin biopsy from the back showed a thin epidermis with moderate degree of hyperkeratosis, a thin granular layer, and keratotic follicular plugs. Examination by direct immunofluorescence technique demonstrated no IgG, IgA, IgM, or C_3 deposition.

Besides dixyrazine, she took an oral contraceptive (Follinet®, levonorgestrel 0.25 mg + ethynyloestradiol 0.05 mg; Recip, Sweden) once a day, diazepam (Stesolid®, Dumex, Denmark) 5 mg three times a day, and amitryptyline (Saroten®, Lundbeck, Denmark) gradually decreasing from 100 to 0 mg a day over the first 3 months.

One week after withdrawal of dixyrazine without other treatment, eye examination showed normal conditions. Within 2 weeks, skin was normal. After 4 weeks, she had no extraordinary loss of hair, and repigmentation was observed.

Case 2. Male, aged 25 years, presented with a marked depigmentation of hair, eyebrows, and eyelashes; a marked blepharoconjunctivitis, dryness of the skin, and a slight telogen defluvium. A definite line was visible on his scalp hair showing where the sudden change of colour had occurred.

For the past 6 months, he had been treated with dixyrazine: the first 2 months, 25 mg three times a day, then gradually increasing for a further 2 months to 100 mg three times a day. Over the last 5 years, he had taken levomepromazine (Nozinan®, Rhone-Polenc, France) 100 mg three times a day.

One week after withdrawal of dixyrazine, the eye examination revealed normal conditions. Repigmentation of the hair commenced within a few weeks (Fig. 2).

Case 3. Male, aged 35 years. Treated with clopenthixol-chloride (Sordinol®, Lundbeck, Denmark) 50 mg three times a day and haloperidol (Haldol®, Jansen, Belgium) 2

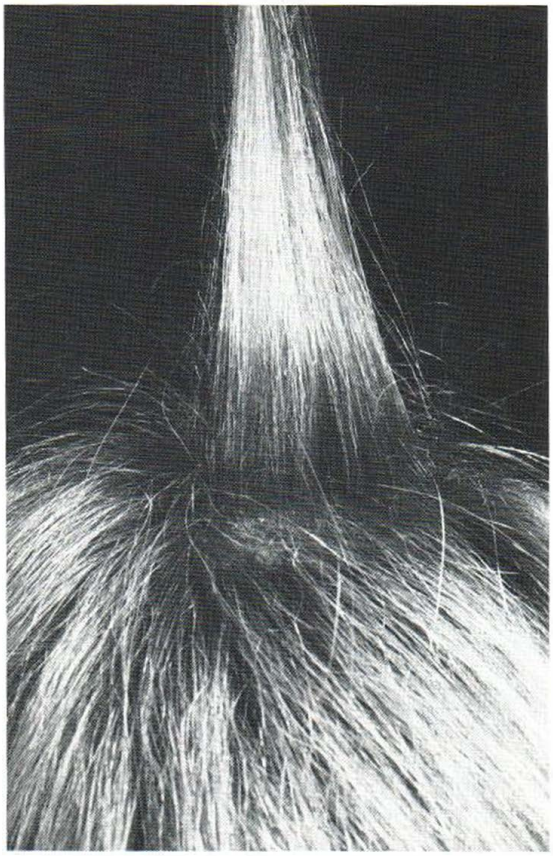

Fig. 2. Case 2. Repigmentation of the hair 3 months after withdrawal of Dixyrazine.

mg three times a day for 11 and 6 years, respectively. Clopenthixolchloride treatment was then discontinued and dixyrazine 25 mg three times a day was added and successively increased until by the end of four months he was receiving 100 mg three times a day.

Six months after the addition of dixyrazine, his eyelashes and eyebrows had turned white and his previously black mustache was tinged with white hairs. A definite line was visible on the scalp hair, showing the time of onset. The hair was brittle and could be easily plucked. In the trichorhizogram, the ratio telogen : anagen was 1 : 3. The skin on the forehead, eyelids and the extensor aspects of the arms showed marked dryness and scaliness. A grey-brownish discolouration was present on the upper back where there was most scaling. He had a marked blepharoconjunctivitis.

After withdrawal of dixyrazine but without other treatment, the blepharoconjunctivitis cleared up rapidly. After 2 weeks, he had no sign of ichthyosis. Regrowth and repigmentation of the hair began within 2 months.

Case 4. Male, aged 25 years. Given dixyrazine 75 mg three times a day for 2 months. Treatment was then discontinued because of a 2×5 cm alopecia patch on the top of the vertex, irritation of the eyes, and dryness of the skin.

Examination 4 weeks after withdrawal of dixyrazine showed regrowth of hair on the previously bald scalp area. During and after the treatment with dixyrazine, he also received fenytoin (Difhydan®, Leo, Sweden) 0.2 g three times a day and sodiumvalproate (Erginyl®, Erco, Denmark) 300 mg three times a day.

ESR, blood counts, b-glucose, s-iron, s-TIBC, s-zinc, s-T_4, s-TBP, s-cobalamines, b-folate, s-FFA, WR, and VDRL were in all cases within normal limits.

No cataract formation has been observed.

COMMENTS

Hair loss, depigmentation of hair, and disturbed epidermal differentiation are non-specific effects resulting from a variety of mechanisms. Many chemical agents are capable of producing either hair loss, depigmentation of hair, ichthyosis, or ocular changes; but it seems that only two drugs are known to produce the combination of alopecia, depigmentation of hair, ichthyosis, and blepharoconjunctivitis. Triparanol, an anticholesterol agent, was reported to produce hair loss, change in hair colour, and ichthyosis (1, 5). Meibomianitis, blepharoconjunctivitis, and cataract formation (2) were later described. Similar cutaneous and ocular changes developed during the routine evaluation of a new antipsychotic butyro-phenone drug (4). During therapy, the s-cholesterol values were significantly decreased compared with the values after therapy had been discontinued.

Although dixyrazine, triparanol, and butyrophenones are not chemically related, the cutaneous effects bear a close resemblance. The 3 patients reported (cases 1, 2 and 3) who were still on dixyrazine at first examination revealed an increase in s-cholesterol of 24%, 24%, and 28%, respectively, 4 weeks after withdrawal of dixyrazine, compared with the values during dixyrazine treatment. This increase remained remarkably stable during the post-drug observation. There were few patients, admittedly, and the increase could be accidental, but as the syndrome can be produced by agents that inhibit the synthesis of cholesterol, it does suggest that large doses of dixyrazine could interfere with the synthesis of cholesterol.

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Erythema Multiforme Due to Methaqualone

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Abstract. A 23-year-old white man developed erythema multiforme after ingesting methaqualone "lude and coke".

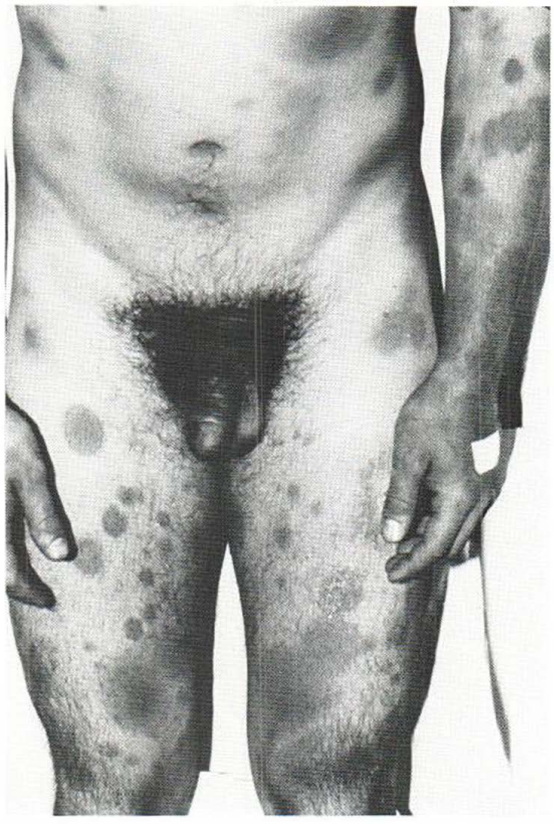

Fig. 1. Diffuse target lesions on the patient's body.

A 23-year-old white man presented in the Emergency Room with a temperature of 103°F and rose-colored bumps over his body. Forty-eight hours before he had taken 150 mg of methaqualone with Coca-Cola. We identified the drug by its code number of 714. Within an hour, he described his skin as having claws climbing over it. Fever and sweats soon developed, and he felt so poorly that he stayed in bed over the next 2 days. An hour before examination diffuse erythematous lesions became apparent over his entire body.

Past history revealed that the pateint had had a similar episode 2 years before, when he had also taken "lude and Coke". Erosive lesions also developed over his body. Eight months ago, he had had a bout of hepatitis, precipitated by shooting a variety of street drugs. He had since recovered and denied using any habituating substance since that time. He has no known allergies.

Physical examination revealed erythematous, macular-to-large, iris-shaped and target-shaped lesions enveloping his entire body. Tense bullae were also seen on his shoulder, palms, soles, and penis. Some erosions were visualized on his penis and lips but the buccal mucosae were clear. CBC with differential, urinalysis, and SMA 12 were within normal limits.

He was treated with 100 mg of prednisone daily for 5 days followed by a tapering dose for the next 7 days. The lesions resolved rapidly and no scarring was evident.

DISCUSSION

Methaqualone was initially synthesized in 1951 as a potential antimalarial agent. It was later found to be a central nervous system depressant. At first, addiction was not thought possible but by 1970 the drug was being abused both legally and illegally in a number of countries. Methaqualone is popularly thought to be an aphrodisiac. This action, however, has not been proven. The drug is metabolized by