drug. This exanthema does not seem related to the "retinoid dermatitis" described by Rüst (1, 2). There is no connection with any other known side effect of retinoids. We cannot give an explanation for the pathogenesis of the case reported here.

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Pemphigus erythematosus Induced by Thiopronine

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Abstract. A patient affected by rheumatoid arthritis developed pemphigus erythematosus after 14 months of treatment with thiopronine. The lesions healed spontaneously after 4 weeks' withdrawal of the drug. Whereas the pemphigus erythematosus induced by D-penicillamine is a quite rare but well documented side effect, we believe our case to be the first one reported as being due to thiopronine. It is very interesting to note that the two drugs are very similar with regard to chemical structure, mechanism of action, therapeutic indications and also side effects.

Key words: Pemphigus erythematosus; Thiopronine; Drug reaction

D-penicillamine and other SH-SS drugs are being used increasingly in the management of rheumatoid arthritis. However, the clinical efficacy of agents such as D-penicillamine, thiopronine and pyrithioxine is often associated with several and relevant side effects (6, 7, 8, 1). As far as the cutaneous complications are concerned it has been noted that treatment with D-penicillamine can induce bullous lesions consistent with pemphigus vulgaris or pemphigus foliaceous and pemphigus erythematosus (10). On the other hand, a review of the pertinent literature has not revealed any case of pemphigus developing during treatment with thiopronine. We therefore deem it important to report a case of pemphigus erythematosus in a patient affected by rheumatoid arthritis as a result of a prolonged treatment with thiopronine.

CASE REPORT

M. M., a 66-year-old man, was found to be affected by serum-negative, polyarticular rheumatoid arthritis, second functional stage, in 1980. In August, 1980, treat-

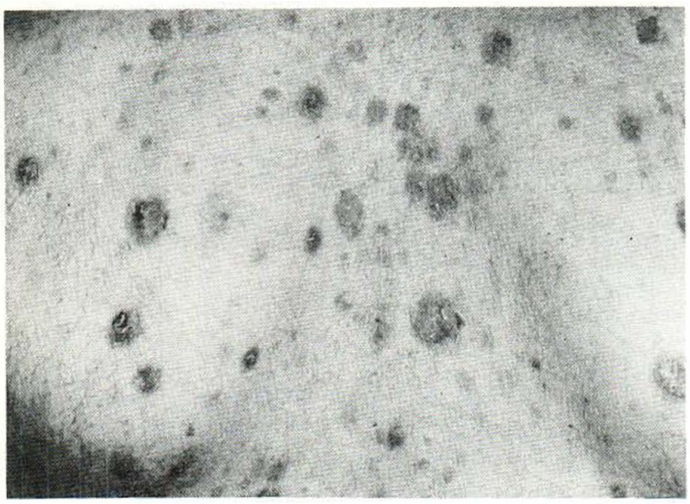

Fig. 1. Clinical picture.

ment with thiopronine (Thiola, Santen Pharm. Co. LTD) was started at the initial dose of 250 mg/day and increased by 250 mg/month to a maintenance level of 750 mg/day. In additional flurbiprofenum (Froben, Boots-GB) 600 mg/day was given. The patient showed marked improvement with no side effects until October 1981, when several lesions appeared on the trunk within few days. On admission, physical examination revealed a few flaccid bullae and several large denuded areas with superficial scaling and brownish crusts on the chest area (Fig. 1). The Nikolsky sign was positive. Mucous membranes proved to be unaffected. Laboratory data included a normal 21-factor automated chemical analysis, a hemoglobin level of 14.6 g/dl, a WBC count of 8700/mm^3, an ESR of 28 mm/h, normal urinalysis test results, LE cell preparation, antinuclear antibodies and antinative-DNA test were negative. X-ray of the hands and feet confirmed changes of rheumatoid disease.

Histologic examination of a skin biopsy showed a superficial intra-epidermal cleft at the level of the granular layer, containing few acantholytic cells and fibrin. A moderate mixed-cell inflammatory infiltrate was seen within the papillary dermis. Direct immunofluorescence studies on the skin biopsy revealed IgG and C3 deposits in the intercellular substance of the epidermis. On two occasions the patient's serum showed no circulating pemphigus antibodies. Treatment with thiopronine was discontinued, but flurbiprofenum was maintained at the same dosage. 4 weeks later the complete remission of the dermatosis was observed and no relapse has occurred since then.

DISCUSSION

In this paper we have described a case of pemphigus erythematosus induced in a patient after 14 months of treatment with thiopronine. The diagnosis was supported by clinical, histologic and immunopathologic data. We ruled out any causal effect of flurbiprofenum, since the administration of this anti-inflammatory drug did not prevent the regression of the lesions. It is our opinion that the spontaneous resolution of pemphigus erythematosus 4 weeks after the suspension of thiopronine clearly shows that the dermatosis was iatrogenic. This is, to our knowledge, the first reported case of pemphigus erythematosus induced by thiopronine, recently used also in the treatment of rheumatoid arthritis, where it has demonstrated the same effect and toxicity as D-penicillamine (6, 7, 8, 1). Clinical observations and experimental studies have supported the role of autoimmunity in the pathogenesis of pemphigus. The coexistence of pemphigus with other autoimmune diseases, like myastenia gravis (4), lupus erythematosus (3) and pernicious anemia (2) conceivably indicates a latent predisposition to develop autoimmune diseases. Pemphigus erythematosus is a well recognized side effect of therapy with D-penicillamine which has been reported more frequently in connection with rheumatoid arthritis. When considering the analogous effect of thiopronine and D-penicillamine in inducing pemphigus erythematosus the similarity of the two drugs in chemical structure, mechanism of action, therapeutic indications and side effects should be noted. Pemphigus erythematosus resulting from D-penicillamine has been proposed to be due to the capacity of the SH-SS groups of the drug to bond to the intercellular cement of the epidermis and to form antigen complexes which lead to the formation of autoantibodies (5). Moreover Ruocco in 1979 (9) also considered an interaction of D-penicillamine with circulating normal human immunoglobulins capable of eliciting IC antibodies. Similar mechanisms might be attributed to the pemphigus erythematosus provoked by thiopronine. In conclusion, we underline that pemphigus erythematosus should be included in the list of the side effects of thiopronine and that extensive investigations should be performed to clarify its pathogenesis.

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Demodex folliculorum hominis (Simon): Incidence in a Normomaterial and in Patients under Systemic Treatment with Erythromycin or Glucocorticoid

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Abstract. A study was made of 20 cilia and sebum from 20 nasal follicles from each of 86 persons. In a normomaterial aged 20–30 years, Demodex folliculorum was present in the nasal follicles in 25% and in the cilia in 29% of the subjects. This is consistent with the very high incidence we found 10 years ago. Systemic erythromycin treatment did not erradicate the mite, but the incidence decreased in both regions. Systemic glucocorticoid treatment lowered the incidence in the nasal region, whereas the incidence increased in the ciliary region.

Key words: Demodex folliculorum; Erythromycin; Steroids

The hair follicle mite Demodex folliculorum is rare in humans, according to most reports in the literature. Some authors consider it to be the causative organism in a series of diseases, e.g. blepharitis, chalazion, meibomitis, rosacea (3 (review), 4).

In 1969, one of the authors of the present paper (M. S. Norn) found the incidence of Demodex in a clinical material to be very high and to increase with age. Moreover it was concluded that the mite does not cause ocular disease (3).

In 1979, conflicting results were presented by Liotet et al. (2), who found an incidence of only 3%. Furthermore, they claimed that Demodex played a pathogenic role in blepharitis, and they recommended mite killing therapy, especially in persons wearing contact lenses. This promted us to investigate whether the high incidence of Demodex demonstrated in Copenhagen 10 years ago might now have decreased. We also investigated whether systemic antibiotic treatment (erythromycin) damages the mite by altering the bacterial flora and thereby the properties of sebum on which it feeds. Likewise we investigated the incidence of Demodex in patients receiving systemic glucocorticoid treatment, in order to establish whether the changed resistance of the host affects the occurrence of the mite.

METHOD

Sebum from 20 expressed nasal follicles, and a minimum of 20 cilia were obtained from each subject. After expression of the nasal follicles with a pair of tweezers or the like, the sebum was transferred to a slide with a small stick or a knife.

Following epilation, the cilia were arranged in parallel in a row on clear adhesive tape which was subsequently fixed on a slide. Both slides were placed immediately in a moist chamber (airtight plastic container with a soaked tuft of cotton wool, and after max. 4 hours microscopy was done.

One drop of immersion oil between tape and slide (respectively between slide and coverslip) served as clarifier. The oil was distributed carefully over the entire area in order to avoid air bubbles. For further details, reference is made to (ref. 3, p. 13). The cilia were counted and an area containing 20 cilia was scanned for Demodex.

The statistical method used was the studentized extreme range, accepting 2 $a<0.05$ as deviation from the nil-hypothesis. The density of Demodex in cilia and nose follicles was calculated by the following formula:

$$\text{Demodex index:} \frac{\text{Number of Demodex} \times 100}{\text{Number of pilosebaceous units studied}}$$

Informed consent was obtained after explaining the nature of the procedure.

MATERIAL

The normomaterial consisted of 28 students between the ages of 20 and 30 (mean age 23.5 years). All patients were in-patients in the departments of Medicine, Dermatology, Otology, Ophthalmology, and undergoing systemic treatment with either erythromycin or glucocorticoid. The erythromycin group comprised 24 patients (mean dose 1.2 g/day, range 1–3 g/day for 7.5 days, range 3–30 days). The glucocorticoid group comprised 34 patients (mean dose 28 mg/day, range 5–80 mg/day of prednisone for up to one year)

These series from 1980 were compared with previous ones (M. S. Norn) which have been statistically proc-