

## PUSTULOSIS PALMARIS ET PLANTARIS TREATED WITH METHOTREXATE

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**Abstract.** Twenty-five patients with pustulosis palmaris et plantaris were treated with methotrexate in weekly oral doses of 25 mg for 2 months. Based upon the presence of psoriatic lesions in other sites and/or psoriasis of the nails, the material could be divided into a psoriatic group of 12 patients and a non-psoriatic group of 13. Methotrexate had a beneficial effect upon 6 patients of the psoriatic and upon 2 patients of the non-psoriatic group. This difference is not significant ( $0.5 < P < 0.1$ ). There were no definite histological differences between the two groups. Mild side effects occurred in 18 patients (aphthous ulcers, gastrointestinal symptoms, elevated SGOT). It is concluded that methotrexate is worth trying in severe cases having psoriatic lesions in other sites.

Pustulosis palmaris et plantaris (ppp) is a well-known disease, characterized by a protracted course with recurrent eruptions of sterile, yellow pustules, brown crusts, erythema, and exfoliation, situated symmetrically on the palms and soles and accompanied by itching and pain. The condition is further characterized by its stubborn resistance to treatment.

Classification and aetiology are still disputed. Andrews & Machaček (3) called the disease pustular bacterid to signify that it was unrelated to psoriasis, but was a bacterid secondary to focal infection. Histologically, pustules were found deep in the epidermis with but few inflammatory changes in the dermis.

Barber (4), claiming that the disease was a pustular variant of psoriasis vulgaris, called it pustular psoriasis of the extremities. The histological changes were said to be the same as in psoriasis, except for a denser leukocytic infiltration of the dermis and more marked abscess formation in the epidermis.

Andrews & Domonkos (2) suggested a division into two sub-groups: Pustular psoriasis of Barber

and pustular bacterid of Andrews. They say: In the former group there are pustules and patches of psoriasis in the palms and soles, while pustules in pustular bacterid of Andrews occur on normal skin. The histology is distinctive, since pustular psoriasis is psoriasis with Munro abscesses, while pustular bacterid of Andrews shows vesico-pustules deep in the epidermis, surrounded by scarcely any inflammation and resembling the findings in dyshidrosis and vesicular trichophytid.

Ingram (5) speaks of one entity, interpreting acrodermatitis continua, pustular bacterid, and pustular psoriasis as variants of a single pattern of reaction. They are, he says, combined eczematous and psoriatic reactions and like so many other combinations owe their recalcitrance to that fact. He calls the disease pustular psoriasis.

Wilkinson (11) felt that it was difficult to deny that the disease is a form of psoriasis. He reported a wide range of histological changes, from eczema to multilocular pustules or Munro micro-abscesses.

Veltman & Schuermann (10) as well as Pierard & Kint (9) considered that pustular bacterid and pustular psoriasis differed clinically and histologically. In pustular bacterid the fingers, toes, and interdigital spaces are spared and so is the anterior one-third or one-quarter of the soles. In pustular psoriasis, on the other hand, the fingers and toes are often involved. The pustules of pustular bacterid occur on normal skin, while the psoriatic pustules occur in erythematous patches. In pustular psoriasis there are intra-corneal Munro abscesses, while in pustular bacterid there are large sub-corneal pustules.

Lever (6) emphasized that the disease was not related to psoriasis and that the histological pic-

Table I. *Pustulosis palmaris et plantaris*, material sub-divided into psoriatic and non-psoriatic patients, showing results of treatment with methotrexate, 25 mg weekly for 2 months

	Psoriatic (no. of pats.)	Non-psoriatic (no. of pats.)
Number of patients	12	13
♂/♀	5/7	5/8
Age, years		
average	53.2	56.9
range	32-73	48-69
Duration of disease, years		
average	3.2	7.2
range	0.5-14	0.2-21
Family history of psoriasis	5	1
<i>Effect of treatment on lesions</i>		
Complete resolution of lesions	3	1
Almost resolution, except for a few pustules	3	1
Improvement, but still pustules, erythema, scaling	2	3
No effect	4	8

ture does not resemble that of psoriasis, presenting large intra-epidermal unilocular pustules. In a recent discussion in the New England Dermatological Society (7), however, Lever stated that the condition was psoriasis, as he had found spongiform pustules. At the same meeting Samuel L. Moschella pointed out that the Barber type could be distinguished from pustular bacterid of Andrews by its therapeutic response to methotrexate.

Allenby (1) has successfully used methotrexate, applied topically in an aqueous solution under polythene. On the other hand, there do not appear to have been reports of the effect of systemic methotrexate in ppp. Since systemic methotrexate is effective in psoriasis, we felt it important to investigate the effect of this treatment in ppp—also with a view to establishing the relation of the condition to psoriasis.

#### MATERIAL AND METHODS

Twenty-five consecutive in- and out-patients from the Finsen Institute with ppp were treated with systemic methotrexate. The diagnosis was based on a protracted course with crops of yellow pustules, brown macules, erythema, and scaling on the palms and soles. Histological examination was made in 8 cases. All the patients

were subjected to mycological examination with microscopy and culture and to our standard patch tests.

By clinical criteria the patients could be divided into two sub-groups, a psoriatic and a non-psoriatic group, according to the presence or absence of psoriatic lesions on other areas of the skin. Patients of the psoriatic group had one or more plaques of psoriasis on other sites and/or psoriasis of the nails, while patients of the non-psoriatic group had cutaneous changes only on the palms and soles. Both groups were of approximately the same size, there being 12 patients in the psoriatic and 13 in the non-psoriatic group.

There were 10 males and 15 females, equally distributed on the two groups. The age distribution was the same in both groups, the average age in the psoriatic group being 53.2 years and in the non-psoriatic group 56.9 years. The duration of the disease in the non-psoriatic group was more than twice that in the psoriatic group, 7.8 years as compared with 3.2 years. Five of the patients in the psoriatic group had a family history of psoriasis. Only one patient of the non-psoriatic group gave a history of psoriasis in the immediate family. No patient of either group showed signs of focal infection.

Methotrexate was administered in weekly oral doses of 25 mg for 2 months. In 2 cases the dose was increased to 50 mg for 2 weeks. Vaseline aquosum (Ph. Dan.) was applied as the only topical agent. Every week, or every second week, the condition was checked by clinical examination and laboratory tests. The patients were questioned and examined for side effects such as nausea, abdominal pain, diarrhoea, and aphthous stomatitis. The following laboratory tests were performed: Hb, ESR, erythrocytes, reticulocytes, WBC and differential count, prothrombin time, S-GOT, alkaline phosphatase, serum creatinine, urine for protein, and urine microscopy.

#### RESULTS

##### *Histology*

Biopsies of pustules on the palms or soles were performed in 4 cases of the psoriatic and 4 of the non-psoriatic group. Only one patient showed histological changes compatible with psoriasis, there being parakeratosis, intracorneal pustules, and elongated oedematous dermal papillae with dilated capillaries. This patient belonged to the psoriatic group. One patient of the same group exhibited histological changes which were characterized as chronic dermatitis, while the remaining 6, non-psoriatic as well as psoriatic, exhibited identical histological changes in the form of major subcorneal or intra-epidermal pustules. The stratum granulosum was present except above the pustules, the papilla of the dermis were plump, but small and non-oedematous, and the vessels were not dilated. Mild perivascular lymphocytic infiltration was found in the dermis.

### *Clinical signs*

The two groups differed somewhat from each other, primarily in a tendency to more serious lesions in the psoriatic group. In the non-psoriatic group the localization was more often posteriorly or medially on the sole. Only 3 patients of the non-psoriatic group, as compared with 7 of the psoriatic group, had involvement of the toes and fingers. Four patients of the psoriatic group had psoriasiform plaques studded with pustules, while the remaining patients of both groups had yellow and brown pustules with some erythema and scaling.

### *Patch tests*

In the non-psoriatic group the following positive patch tests were found: Neomycin 1 patient, rubber 2 patients, dichromate 1 patient, nickel 1 patient, cobalt 2 patients, and primula 1 patient. In the psoriatic group the findings were: Neomycin 1 patient, nickel 1 patient, and cobalt 1 patient. None of these allergies was found to be relevant.

### *Mycological examination*

Scrapings for fungus were negative in all patients.

### *Effect of methotrexate*

As is apparent from Table I, methotrexate had a favourable effect upon 2 patients of the non-psoriatic group and upon 6 patients of the psoriatic group, with complete or almost complete clearing of lesions. In the non-psoriatic group there was no or questionable effect in 11 cases, in the psoriatic group in 6. Moreover, this difference is not significant ( $0.05 < P < 0.1$ ). If an effect was obtained, it was evident quite soon, as a rule within 2 weeks. No rebound phenomenon occurred when the treatment was discontinued.

### *Side effects*

Side effects occurred in 18 patients. Three developed aphthous ulcers in the mouth, 8 fairly mild gastrointestinal reactions in the form of nausea and epigastric pain. One patient exhibited, after each dose of methotrexate, a peculiar reaction, viz. fever, pain, swelling, erythema, and scaling of the hands and feet, leaving excoriations.

Twelve patients showed a transient increase in

the SGOT during the medication. This increase was moderate, exceeding 6 units (normal below 1.8 units) in only 4 cases. The highest value was 11 units. No signs of impaired bone-marrow function were found.

The frequency of side effects in the two groups did not differ.

## DISCUSSION

According to the present study, ppp must still be considered a highly recalcitrant disease, even after the advent of methotrexate, since only 8 out of 25 patients responded satisfactorily to methotrexate in weekly oral doses. This is a considerably poorer response than in psoriasis vulgaris in which most investigators have found the lesions to clear in about 60% of the patients (8). The explanation might be that ppp is not psoriasis, but it might also be that this entity is not homogeneous, thus including cases which respond to methotrexate and others which are resistant. Further, the localization to the palms and soles might render the disease difficult to treat. This latter possibility can probably be rejected, as ordinary psoriasis of the palms and soles responds to methotrexate parallel with the lesions in other sites. Lastly, the dose of methotrexate might be too low. In 2 patients of the non-psoriatic group, who did not respond to 25 mg methotrexate, the dose was increased to 50 mg weekly for 2 weeks, but without any effect. Therefore, this possibility may probably also be rejected.

As regards the first possibility, the present study might indicate that ppp is in fact two diseases, one of which at least is psoriasis. By clinical criteria (psoriatic lesions elsewhere, psoriasis of the nails) the patients could be divided into a psoriatic and a non-psoriatic group. This classification was supported by a more common family history of psoriasis in the psoriatic group. The psoriatic group responded better to methotrexate than the non-psoriatic group, 6 patients as compared with 2. However, this difference is not significant, perhaps because the material is too small. Moreover, it was our impression that the more distinctly psoriatic the lesions in the palms and soles, the better the response.

On the other hand, the histological findings militate against this classification into two subgroups. Histological signs of psoriasis were found

in only one patient, while the other biopsies showed large, solitary, subcorneal, or intra-epidermal pustules, small, plump dermal papillae, and moderate cellular infiltration of the dermis. These are approximately the same changes as described by Lever (6) in ppp and by Veltman & Schuermann (10) and Pierard & Kint (9) in pustular bacterid. The solution of this problem must presumably await further histological studies.

However, the present material is large enough to warrant the conclusion that methotrexate is not to be recommended for routine treatment of ppp, but is worth trying in severe cases having psoriatic lesions elsewhere.

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