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# DEPOSITION OF FIBRINOGEN (FR-ANTIGEN) IN SKIN DISEASES

## *II. Pustulosis Palmaris et Plantaris (with Special Reference to Heparin-precipitable Fraction)*

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*Abstract.* Ten out-patients with pustulosis palmaris et plantaris were examined with direct immunofluorescence (IF) technique for deposition of fibrinogen, fibrin or its degradation products (FR-antigen) in affected and unaffected skin, together with heparin-precipitable fraction (HPF), cryoglobulin and total plasma fibrinogen in the blood. FR-antigen was found in all cases in affected skin as a uniform pattern of a continuous ramification below the dermo-epidermal junction. This IF picture was absent in unaffected skin, but in other parts of the dermis in affected and unaffected skin, scattered streaks of IF could be seen. In one case, however, unevenly distributed IF was found in unaffected skin in the junction area. The scattered IF was also present in a minor degree in affected and unaffected skin in a control material of other dermatoses. Only one patient had slightly elevated values of HPF (0.33 mg/ml). Total plasma fibrinogen was insignificantly elevated, and no cryoglobulin could be found.

*Key words:* Pustulosis palmaris et plantaris; Immunofluorescence; Deposition of FR-antigen; Heparin-precipitable fraction

Pustular eruptions in the palms of the hands and the soles of the feet were described in 1930 by Barber (4) as "pustular psoriasis of the extremities". Andrews et al. (2), in 1935, considered some of these to be a secondary reaction to focal infections, and in 1971 (1) divided the phenomenon in two entities: Pustular psoriasis of Barber and pustular bacterid of Andrews. In 1967, Lever (13) classified these as pustulosis palmaris et plantaris (PPP). According to him, the histological picture did not resemble that of psoriasis. Baker et al. (3) could not accept the view that the histological features of psoriasis always were absent, although the picture was seldom typical in all respects, even when typical psoriasis coexisted. Sometimes the histological picture resembled eczema in an early vesico-pustular stage. In another study (19), a biphasic histo-morphological evolution was described, a first phase resembling that of an eczematous dermatitis, and a second phase that of a pustular reaction.

Deposition of immunoglobulins in the pustular area of PPP has been reported (11), mostly within the pustules. This phenomenon is interpreted to be specific of the pustule, rather than of the disease.

Deposition of fibrinogen/fibrin or its degradation products (FR-antigen) detected by immunofluorescent studies (IF) has been found in psoriasis (9, 10, 16) and in other dermatoses (5, 6, 12, 15, 17, 18).

Heparin-precipitable fraction (HPF) in plasma of patients with psoriasis has been reported (8, 9), in psoriasis vulgaris in 6% and in psoriasis arthropathica in 48%. There is a possibility that different types of pustular disease in the skin have a common psoriatic background (7), and because of the probable relation between PPP and psoriasis, and the high degree of deposition of FR-antigen in psoriatic skin, this study was performed to see whether FR-antigen could be detected in affected and unaffected skin in PPP, measured by the IF-technique, together with HPF, cryoglobulin and total plasmafibrinogen in the blood.

## MATERIALS AND METHODS

Ten out-patients from the Dermatological Department, Rikshospitalet, Oslo, were examined. All were female caucasians, between 32 and 60 years of age (mean value 50.7 years). 4/10 had a coexisting mild psoriasis vulgaris. PPP had been present for 1–15 years (mean value 6.3 years) in a relapsing course. Pustule formation was present in palma manuum, except in 3/10 cases where the pustules were found in the planta pedis in addition to erythema and scaling in palma manuum. In addition to pustules, there were always erythema and scaling. Most of the patients had been treated with tar, fluorinated corticosteroids, mostly under occlusive dressings, and subsequently by grenz-ray treatment. Some of

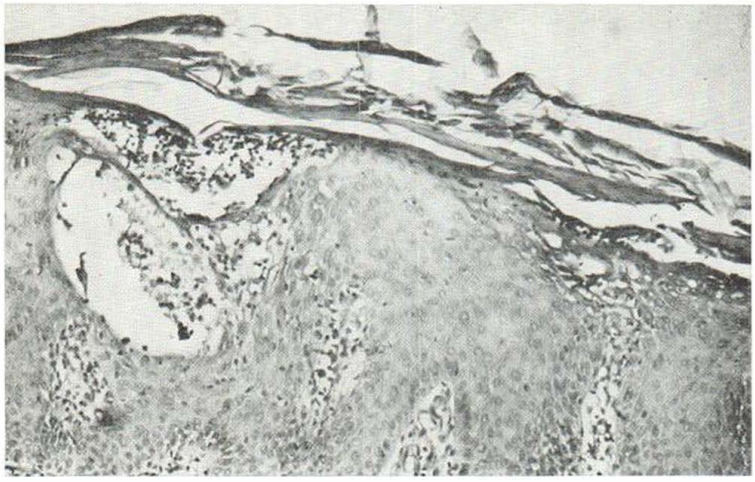

*Fig. 1.* Light micrograph. Pustule formation in pustulosis palmaris et plantaris (× 145).

the patients were in the stage of remission, some in exacerbation of the disease.

Skin sections from 10 patients routinely investigated for depositions of immunoglobulins in the skin, served as a control (pemphigus vulgaris, bullous phemphigoid, dermatitis herpetiformis and systemic lupus erythematosus).

The biopsies were taken from affected and unaffected skin under local infiltration anaesthesia. Affected skin from PPP was mostly taken from palma manuum, always from pustular areas (7/10), or from planta pedis (3/10), mostly at the border of the lesion. Unaffected skin in PPP was taken from the middle of the anterior aspect of the underarm, at least 15 cm from active lesions. The biopsy of affected skin was divided in two; one part was sent with the biopsy of unaffected skin in physiological saline solution within hours for IF studies. Frozen sections were produced as previously described (9), and examined with rabbit anti-fibrinogen anti-serum labelled with fluorescein isothiocyanate. As these antibodies react with fibrinogen/fibrin and degradation products, it is not possible to decide which one of these related substances act as antigen in the tissue sections in our IF studies, and therefore the term FR-antigen (Fibrinogen/fibrin related antigen) (14) has been used. The other part of the affected skin was sent in 4 % formaldehyde solution for examination by light microscope.

HPF, cryoglobulin and total plasma fibrinogen were examined as previously described (8, 9).

## RESULTS

*Cryoglobulin* was not present in the serum of the patients examined.

*Total plasma fibrinogen* was, on average, 415 mg%, ranging from 335 to 521 mg%, insignificantly elevated above the normal range of 200–400 mg%.

*HPF* was not present in the plasma of 4/10 patients. In 5/10 patients traces of HPF were present with a mean value of 0.11 mg/ml. The pattern and the quantity of the cryoprecipitation did not differ from that of healthy persons (8), and was therefore not

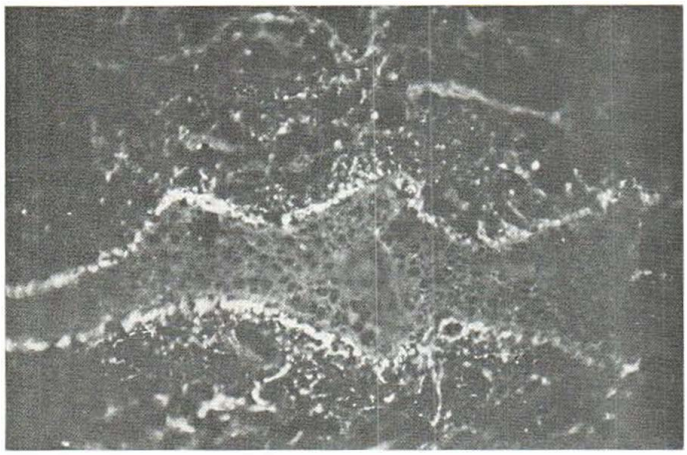

*Fig. 2.* Fluorescence micrograph. Continuous deposition of FR-antigen at the dermo-epidermal junction, and traces of scattered FR-antigen in dermis, in affected skin in PPP (× 155).

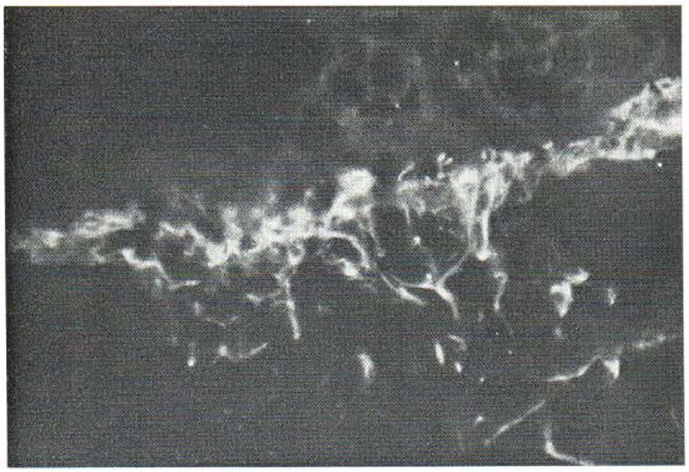

*Fig. 3.* Fluorescence micrograph. Higher magnification of the ramified pattern of FR-antigen at the dermo-epidermal junction as a continuous network in affected skin in PPP (× 770).

considered as pathologic. 1/10 patients had a pathological formation of HPF of 0.33 mg/ml.

*Light microscope examination* was performed on biopsies from 8/10 patients; 2/10 were technically insufficient to be evaluated. 5/8 of the cases showed a histological pattern resembling psoriasis with parakeratosis, deep rate pegs, invasion of granulocytes in the papillae and into the epidermis, sometimes with intra-epidermal pustule formation (Fig. 1). Edema and vasodilatation in the papillary bodies could also be observed in 4/8 of the cases. 3/8 displayed the picture of chronic unspecific dermatitis.

*Immunohistochemical detection of FR-antigen* showed that all patients (10/10) with PPP had depositions of FR-antigen in affected skin. In these cases, the IF picture was rather uniform, consisting of a medium strong to strong (2 +/3 +) deposition, judged by the degree of IF in the tissue. No deposition could be observed in the epidermis, but in the dermis, below the dermo-epidermal junction, FR-antigen was found as a continuous ramificating network (Figs. 2, 3). In other parts of the dermis, scattered streaks of FR-antigen (2 +) evenly distributed, were observed. In unaffected skin in PPP, the sub-junctional deposition of FR-antigen was absent in 9/10 cases; in 1/10 cases it was present in some areas. As in affected skin, the scattered depositon of FR-antigen could be observed in other parts of the dermis (Fig 4).

In the control group, the subjunctional deposition of FR-antigen was totally missing, whereas the same scattered deposition of FR-antigen was present in the dermis in affected and unaffected skin areas. This deposition was weaker than the one observed in PPP.

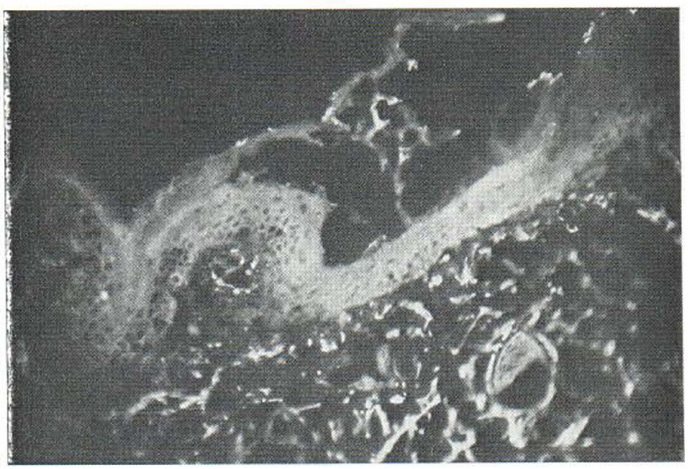

*Fig. 4.* Fluorescence micrograph. Deposition of FR-antigen as scattered streaks in dermis in unaffected skin in PPP (× 155).

## DISCUSSION

Deposition of FR-antigen has been demonstrated by the IF-technique, in dermatological affections such as lichen ruber (5, 18), dermatitis herpetiformis (12, 15, 17) and contact dermatitis (6). In psoriasis, conflicting studies have been reported (9, 10, 16). In one study (9), deposition of FR-antigen could be found in psoriasis vulgaris and psoriasis arthropathica in unaffected skin in 50% and 72%, and in affected skin in 64% and 84% respectively. The IF-picture of the FR-antigen depositions showed almost uniformly a pattern of ramification just below the dermo-epidermal junction in affected and unaffected skin in psoriasis, as in affected skin in PPP in the present study. The scattered deposition of FR-antigen in other parts of the dermis observed in this study, in both affected and unaffected skin in PPP and in the controls, was missing in the above-mentioned study (9) in psoriatics. Whether this is due to a different sensitivity of the new conjugate used, or whether it reflects real differences in the deposition of FR-antigen in the dermis, is hard to say. The subjunctional deposition of FR-antigen is, however, strikingly similar in psoriatics and in affected skin in PPP. Until further groups of dermatological affections have been systematically investigated by the same technique of IF against FR-antigen, the specificity of this deposition cannot be conclusively evaluated.

Light microscope examinations demonstrated a histological picture resembling psoriasis in 5/8 of the cases. Of these, 3/8 had a mild psoriasis at the time of the examination. The remainder 3/8 showed the picture of chronic unspecific dermatitis, one of these also having a mild psoriasis vulgaris. These histological results are in agreement with other studies reported (3, 19).

HPF is an acute phase reactant. Its presence in plasma is not disease-specific, and can be found in diseases with inflammatory changes like arthritis or cases of tissue destruction. HPF has been found in psoriasis vulgaris in 4–6%, and in psoriasis arthropathica in 48–80% (8, 9). In this study, only one patient (1/10) had pathological values of HPF in whole blood. (0.33 mg/ml). As in psoriasis (9), no direct correlation could be found between the deposition of FR-antigen in the skin on the one hand, and HPF and total fibrinogen on the other.

A systematic examination of deposition of FR-antigen measured by the IF technique in affected and unaffected skin in different dermatoses is presently being performed, the results of which will be reported later. The significance of the depositions of FR-antigen in PPP is unknown.

## ACKNOWLEDGEMENT

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