systemic therapy (9) could support the notion of systemic immunologic mechanisms of the disease. Alternatively, the minimal absorption of the drug through the skin may not be sufficient to achieve a response. The undetectable levels of CS in the blood may confirm such an assumption.

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Prostaglandin E_1 and Prostaglandin $F_{2\alpha}$ in Exudate in Nickel Allergy

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Ten nickel-allergic patients and 5 healthy control subjects participated in a study of the kinetics of the flux and concentration of migrated leukocytes and extracellular PGE_1 and $PGF_{2\alpha}$ during a 48 h period, using a skin chamber technique. The patients were provided with two skin chambers, one with and one without nickel challenge. A higher flux of leukocytes, PGE_1 and $PGF_{2\alpha}$ was observed during the second day of allergen exposure, while the concentrations probably due to dilution were unchanged or diminished, indicating an unspecific role of the prostaglandins during the contact allergic reaction. No correlations were found within the groups between the migration of leukocytes and the prostaglandin content. *Key words: Leukocyte migrations; PGE_1; $PGF_{2\alpha}$;* Skin window technique.

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The main alterations of the arachidonate metabolism in delayed hypersensitivity consist of (*a*) inhibition of PGD_2 synthesis, (*b*) a switch from predominantly PGD_2 to a predominance of PGE, (*c*) an increased lipoxygenase activity (1), (*d*) an inhibitory effect of the immune response of PGE by inhibition T-lymphocyte activation (2). Furthermore, PGE inhibits the leukocyte inhibitory factor (LIF) production (3), exhibits a negative inhibitory chemotactic activity and $PGF_{2\alpha}$ exhibits a positive chemotactic activity (4). The purpose of the present study was to measure the release of PGE_1 and $PGF_{2\alpha}$ and leukocyte migration in exudate during the evolution of a delayed hypersensitivity reaction (DHR) in human skin, when using a skin chamber technique.

METHODS

Subjects

The control group consisted of 5 healthy controls (all females, mean age 28 years, age range 23–32), with no eczema or history of allergic contact dermatitis.

The patients studied (8 females, 2 males, mean age 37 years, age range 20–65) all had allergic contact dermatitis to nickel, verified by anamnesis and by patch testing (5). At the time of investigation the eczema was inactive or mildly active and the patients were without medication. All participants had normal blood values. Informed consent was obtained from all subjects, in accordance with the principle of the Helsinki Declaration.

Skin chamber technique, chamber media and collection procedure

A dermabrasion was made with surgical scalpel on the inner surface of both forearms of patients with nickel hypersensitivity and on the right forearm of controls, as previously described (5). A sterile chamber of epoxy material was sealed over the skin window. The chamber applied to the right

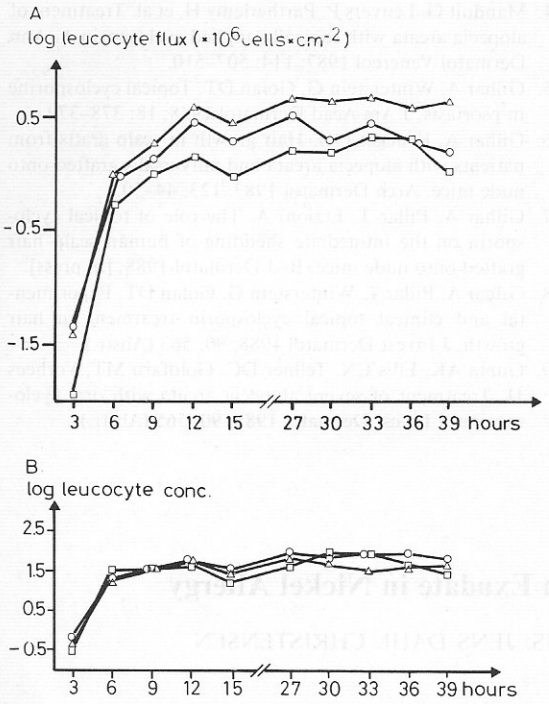

Fig. 1A. Logarithm of mean flux of migrated leukocytes (10^6 cells$\times$cm^{-2}) in skin window exudate during a 30 h period. □—□, Controls; ○—○, patients allergic to nickel, not exposed to nickel in the chamber medium; △—△, patients allergic to nickel, exposed to nickel in the chamber medium. *B.* Logarithm of mean concentration of migrated leukocytes during the observation period. For symbols, see Fig. 1*A*.

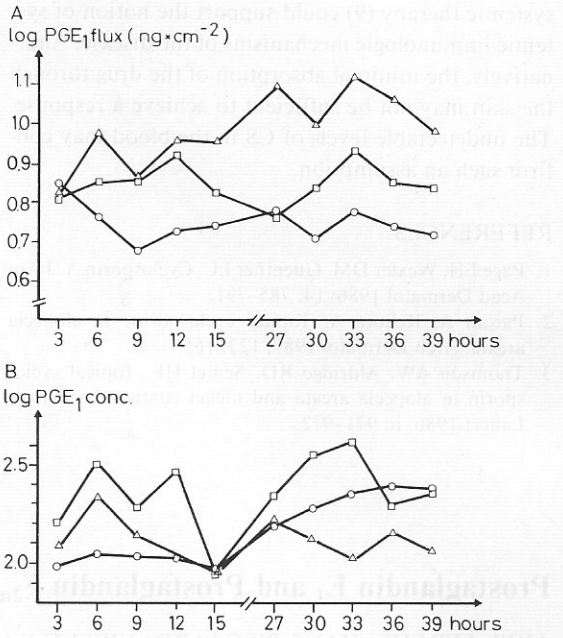

Fig. 2A. Logarithm of mean concentration of PGE_1 (ng$\times$cm^{-2}) in skin window exudate during a 39 h period. *B.* Logarithm of mean concentration of PGE_1 (ng$\times$ml^{-1}) in skin window exudate during a 39 h period. For symbols, see Fig. 1*A*.

forearm of the eczema patients and controls was filled with 0.5 ml autologous serum containing 10 mM EDTA immediately after application and after each collection. The chamber medium used on the left arm of the nickel allergic patients consisted of 0.5 ml autologous serum with 10 mM EDTA and 10 mM nickel sulphate. After each collection the cells were harvested, studied for morphology and total number, as previously described (5). The migration of leukocytes was expressed as the mean of the logarithm to the leukocyte migration during the 3 h collection period related to the skin window area, i.e. leukocyte flux. At each collection, the concentration of migrated cells was expressed as the cell number in the exudate volume minus the chamber volume (0.5 ml serum).

PGE_1 and $PGF_{2\alpha}$ determinations

Cell-free exudate were extracted and PGE_1 was converted to PGB_1 by alkalization before entering the radio-immunoassay as previously described (6). The concentrations and the fluxes of PGE_1 and $PGF_{2\alpha}$ at each collection were corrected for the PG content in the chamber medium and expressed as ng per ml exudate volume and ng per cm^2. The flux of PGE_1 and $PGF_{2\alpha}$ describes the total content of each PG in exudate across 1 cm of the skin window area.

The concentrations and fluxes of leukocytes, PGE_1 and $PGF_{2\alpha}$ were evaluated by two-way analysis of the logarithmic observations. Comparisons between patients and controls were done by Wilcoxon's two-sample test.

RESULTS

Leukocyte migrations, PGE_1 and $PGF_{2\alpha}$ in exudate fluid

The mean leukocyte flux and leukocyte concentrations in exudate cells of controls and patients showed a time-dependent increase during the first day (Fig. 1). On the second day, the leukocyte flux was higher ($p<0.05$) for the allergics exposed to nickel compared with the same patients without nickel addition and compared with the control group. No difference in leukocyte concentrations was seen between the groups. Controls and patients showed a time-dependent fluctuation in the flux and the concentration of both PGs (Figs. 2 and 3). However, a significantly increased flux of PGE_1 and $PGF_{2\alpha}$ ($p<0.05$) and a decreased concentration of PGE_1 and $PGF_{2\alpha}$ ($p<0.05$) were found on the second day in allergen-challenged patients, compared with the same patients without.

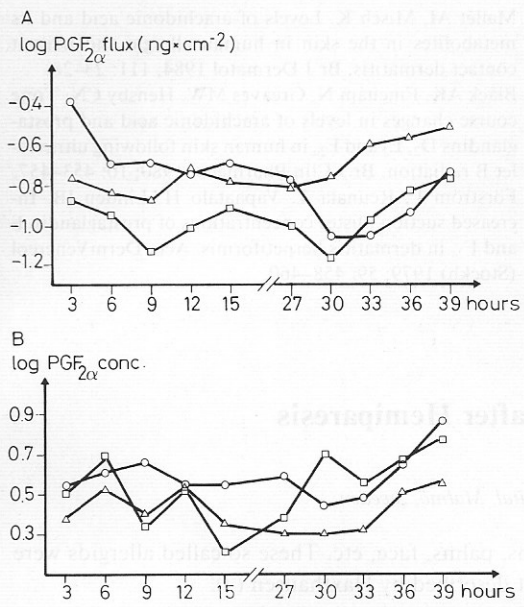

Fig. 3A. Logarithm of mean flux of $PGE_{2\alpha}$ ($ng \times cm^{-2}$) in skin window exudate during a 39 h period. *B.* Logarithm of mean concentration of $PGF_{2\alpha}$ ($ng \times ml^{-1}$) in skin window exudate during a 39 h period. For symbols, see Fig. 1*A*.

An analysis of the leukocyte flux and the flux of PGE_1, respectively $PGF_{2\alpha}$ in exudate from allergics and controls did not show any correlation. Nor was any correlation found between the leukocyte concentration and the concentration of PGE_1, or of $PGF_{2\alpha}$.

DISCUSSION

Epidermal abrasion induces leukocyte flux and subsequent release of PGE_1 and $PGF_{2\alpha}$. However, in nickel-allergic reaction a higher flux was observed due to release of chemotactic agents such as lymphokines (7) or products released from the skin (8). The increased diffusion of cell-free fluid into the chambers resulted in an unchanged or reduced concentration of leukocytes and PGs during this period. In contrast to our findings, increased concentrations of PGE_1 and $PGF_{2\alpha}$ have been described in DHR after 24 h and 48 h (3, 9) using the suction bulla technique. The concentrations of PGE_1 in suction bullae of control subjects were one-tenth of those obtained by the skin window exudate (3), while the $PGF_{2\alpha}$ concentrations (9) were identical by both methods. It is likely that the difference in PG concentration is due to: difference in mechanical trauma, collection intervals and exposure of antigen. The present study gives information on the early events and the kinetics of the DHR.

The content of the PGs in exudate could not be correlated to the migrated cells, so it is likely that the origin of PG stems primarily from the inflammatory infiltrate in dermis and diffusion from skin and vessels induced by dermabrasion. The contribution from inflamed abraded skin areas in nickel-allergic exposed subjects was significantly increased on day 2. In summary, identical levels of PG were found in all groups during the first day, indicating the PG release to be triggered by mediators produced during the inflammatory process regardless of its nature. Similarly an increased PG content has been reported in suction fluid of various dermatoses with differing pathogenic origins (10–12), indicating an unspecific induced PG release during the initial phase of inflammation. The increased PG flux in exposed allergics on the second day could be caused by an unaltered release of PG per migrated cell combined with a high cellular recruitment.

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Unilateral Eruption of Endogenous Eczema after Hemiparesis

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Five patients with cerebrovascular hemiplegia developed an endogenous eczema (nummular eczema, pompholyx, allergids, atopic dermatitis). In all cases the dermatitis was mainly confined to the healthy side.

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Nummular eczema is an endogenous disease characterized by coin-shaped eczematous patches mainly occurring on the extensor aspects of extremities. The eczema often starts on the legs but usually spreads to arms and trunk. In the acute phase the lesions are pruritic and oozing, later become chronic and scaling. The clinical picture and presumed etiopathogenesis have been discussed for decades. The following etiologies have repeatedly been suggested: asteatosis, bacterial allergy, focal infection, venous insufficiency, ethylism, external irritants and infected wounds. The reader is referred to several good reviews (1–4).

Pompholyx or vesiculosis is another endogenous eczema in which, however, the itching and periodic eruptions are localized to the palms and/or the soles. Since in many cases the etiology is never demonstrated, they are often considered idiopathic; some, however, are attributed to atopy or "endogenous contact eczema" (5, 6). In our experience, pompholyx often accompanies an active nummular eczema, although this is seldom mentioned in text-books or reviews.

Deterioration of a hypostatic eczema of the lower leg, whether complicated by contact allergy or not, occurs primarily by local extension. Often this is followed by dissemination of papules or vesicles to arms, palms, face, etc. These so-called allergids were first described by Haxthausen (7).

The symmetric distribution of the eczematous eruption is very characteristic of endogenous eczema, be it nummular or atopic eczema, pompholyx or allergids. It therefore seems warranted to report 5 cases of different types of endogenous eczema with a unilateral distribution following hemiparesis.

CASE REPORTS (Fig. 1)

Case 1

Female, 94 years old. Cerebrovascular insult twice the same year, resulting in left hemiparesis. In this connection an itching nummular eczema developed on extensor aspects of extremities, predominantly on the right leg. One month later, residual patches were observed, mainly on the right leg. Grasset's sign was positive on the left side but neurologic examination was otherwise normal.

Case 2

Male, 64 years old. Left-sided cerebrovascular infarction, confirmed by computer tomography, resulting in right hemiparesis. A few months later, incipient nummular eczema on left arm and left side of the back. Follow-up 4 years later still showed active eczematous patches on both sides of extremities and trunk, but predominantly on the left side. Neurologic findings on the right side, but not on the left: diminished muscular power in arm and leg; exaggerated biceps reflex; absent brachio-radialis reflex; dig.I–III in flexion; diminished sensitivity with regard to vibration, pin-prick pain and stereognosis.

Case 3

Male, 62 years old. Multiple sclerosis including right-sided hemiparesis since 35 years. Venous insufficiency of right foreleg with ulcer on right lateral malleol for one year. Progressive eczema around the ulcer and extending to the same foreleg during the last month, and exudative eczematous