



Fig. 2. Healing after treatment with triamcinolone intramuscularly monthly for half a year.

healed proximally, regaining their normal appearance.

What is unusual is the appearance of longitudinal bands of melanonychia first after one year's treatment when the nails were almost healed, clinically. In this way it resembles the well-known secondary type of pigmentation which is seen when skin lesions are healing. The occurrence of red lunulae in our patient indicates that the inflammatory reaction had not been completely suppressed. One can therefore speculate that there is a low grade or a specific type of inflammation which induces an optimal stimulation of pigmentation—unless these phenomena are completely



Fig. 3. Nails with longitudinal melanonychia, 2 years later.

independent from the longitudinal melanonychia that appears as a characteristic of healing lichen planus.

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## Nail-changes Induced by Penicillamine

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Peculiar nail-changes in a 70-year-old woman with rheumatoid arthritis occurring after approximately 1 year of penicillamine treatment are described. After cessation of treatment there was a gradual resolution with regain of normal nails after 7 months. Reinstitution of penicillamine treatment caused a recurrence thus proving a causal relationship between penicillamine and the described nail-changes. The fingernails were more affected than the toenails and clinically the changes consisted of absence of lunulae, longitudinal ridging, transverse or longitudinal defects of the nail-

plate and a tendency of onychoschizia. **Key words:** *Rheumatoid arthritis; Side effects of penicillamine.*

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Several drugs have the ability to induce nail-changes (1). Thus pigmentary changes have been reported



Fig. 1. Fingernail-changes after approximately 1 year of penicillamine treatment. Note longitudinal ridging, Beau's lines, onychomadesis (punched out nail keratin at the lunula) on dig IV, longitudinal narrow defect on dig III and onychoschizia.



Fig. 2. Almost normalized fingernails 5 months after cessation of penicillamine treatment. Only minimal distal splitting remains.

with antimalarials, tetracyclines (especially minocycline), phenothiazines, lithium carbonate, heavy metals and several cytotoxic agents such as adriamycin, bleomycin, cyclophosphamide, hydroxyurea, methotrexate and nitrogen mustard. Onycholysis has been described with oral retinoids, thiazide diuretics and some of the cytotoxic drugs. Photoonycholysis is a special form in which a phototoxic substance is activated by sunlight causing phototoxic damage of the nailbed. It is most frequently seen with tetracyclines (especially doxycycline and demethylchlortetracycline) and psoralens. Nail dystrophy occurs with practolol. Several nail reactions are seen with cytotoxic drugs including leuconychia, nail bed splinter haemorrhages, disappearance of lunulae, onychotrophy, Beau's lines, melanonychia and acute paronychia. Several reactions are also seen with the now frequently used synthetic retinoids and includes periungual granulation tissue, proximal onychoschizia, thinning of the nail, onychomadesis and temporary nail shedding. This report describes a case of penicillamine induced nail-changes.

#### CASE REPORT

A 70-year-old woman was referred in January 1985 because of peculiar nail-changes that had appeared approximately 1 year earlier. There were no other complaints than cosmetic. She was suffering from rheumatoid arthritis and had been treated with penicillamine 0.25 g daily since October 1982, increased to 0.5 g in March and 0.75 g in July 1983. During this period she was also taking indomethacine, naproxene and atenolol. The nail-changes were most pronounced on the

fingers and consisted of absence of lunulae, longitudinal ridging, transverse proximal defects of the nailplate on some fingers as onychomadesis (i.e., the nail appears punched out at the lunula), longitudinal narrow defects in the nailplate on some fingers and a tendency of onychoschizia in the part distal to the transversal nailplate defects (Fig. 1).

Penicillamine was suspected as the causative factor and was withdrawn in April 1985. The patient was seen again in September, 5 months after cessation of treatment, and showed almost completely recovered nails with only minimal distal splitting (Fig. 2). She was then lost to follow-up until November 1987 when the following story was told: She had been without penicillamine until May 1986, her nails by then had regained a totally normal appearance. Because of increasing problems with her rheumatoid arthritis she was, however, put on penicillamine again in May 1986 with recurrence of the same nail-changes as before. This could be verified at the clinical examination (Fig. 3).

#### DISCUSSION

Penicillamine has been reported to induce several side effects in the skin (2). Thus both early and late skin reactions have been reported. Among early reactions can be mentioned a local or generalized maculopapular or urticarial rash, pruritus, oedema, eosinophilia and lymphadenopathy. Among late reactions can be mentioned a scaly, itching eruption, abnormalities due to production of poor collagen and elastin leading to, e.g., bullous epidermolysis, systemic lupus erythematosus, a pemphigus-like condition, lichen planus and alopecia.

Nail-changes induced by penicillamine have been reported previously. Thus, Thivolet et al. described a



Fig. 3. Nail-changes of the same type as in Fig. 1 appearing 1.5 years after reinstitution of penicillamine.

14-year-old girl with Wilson's disease who, after 1 year of penicillamine treatment, developed lichenoid skin changes on her hands, legs and feet, nail-changes and stomatitis (3). The lesions disappeared when penicillamine was withdrawn. Because of a deterioration of the underlying disease, penicillamine had to be reinstited whereupon the oral lesions as well as nail-changes recurred. The nails showed ridging, white streaks, fragmentation of the free end and pseudoseparation of the nailplate. Another type of nail-changes, "Yellow nail syndrome", has been reported

with penicillamine by Lubach & Marghescu (4). Their patient had been treated with penicillamine for 2 years because of chronic polyarthritis when she developed a Yellow nail syndrome. Penicillamine was withdrawn and the nails were normalized about 6 months later. The causal relationship between the medication and the nail-changes was not tested with provocation.

The nail-changes in the present case thus show some resemblance to the changes described by Thivolet et al. (3) with longitudinal ridging, fragmentation and separation of the nailplate. In the present case a causal relationship has been proved since the same changes reappeared when penicillamine was reinstited.

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## Localized Bullous Pemphigoid, a T Cell-mediated Disease? Electron Microscopic and Immunologic Studies

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Two new cases of the rare, nonmucosal and nonscarring localized variety of pemphigoid are described. With reference to the data in the recent literature, the disease was classified as Localized Bullous Pemphigoid (LBP). The ultrastructural and immunologic findings are described and are briefly discussed in the context of the possible mechanisms leading to local subepidermal tissue injury in LBP. Although classical features of humoral responsiveness (in vivo bound IgG and complement at the epidermal basal membrane-zone (BM-zone)) were observed, a possible additional

role of T cell mediated immunity in generating this local disease is considered.

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It is established that the nonmucosal forms of the localized varieties of pemphigoid can occur in two