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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
1-33. PACHYONYCHIA CONGENITA

**SYNONYM**
Jadassohn–Lewandowsky syndrome.

**DEFINITION**
Pachyonychia congenita is a rare autosomal dominant disorder characterized by remarkable thickening of the nails, palmar and plantar hyperkeratoses, oral leukokeratosis, and follicular hyperkeratoses on the elbows and knees.

**HISTORY**
Jadassohn and Lewandowsky first described pachyonychia congenita in 1910. The patient was a 15-year-old girl who was severely affected by what has come to be regarded as the classic findings of the disorder. Her younger brother had only follicular hyperkeratoses of his elbows and knees. In 1968, Moldenhauer and Ernst reviewed the 93 cases reported in the world literature. They found that 90 patients had pachyonychia, 57 had plantar keratoderma, 44 had palmar keratoderma, and 50 had oral leukokeratosis. There were 35 patients with bullae, 22 with hyperhidrosis, 11 with sparse thin hair, 11 with premature dentition (natal teeth), and 4 with granulosis rubra nasi.

**INCIDENCE**
Over 100 cases have been reported. Males seem to be affected more often than females, and the disorder may be more prevalent in Jews. Kupper and Loos classified the disorder into three types: type I there are symmetrical keratoses of the hands and feet with follicular keratoses of the body; type II is like type I but with leukokeratosis oris (Riehl type) (this is the most common type); and type III is like type I but with corneal changes.

**ETIOLOGY**
The disorder is inherited in an autosomal dominant fashion with high penetrance and variable expression. Several patients have been reported in whom there is no positive family history.

**CLINICAL MANIFESTATIONS**
The most prominent feature of this disorder is congenital pachyonychia in which all 20 nails are thickened, tubular, and extremely hard, with raised distal margins (Figs. 1 and 2). The ventral nail surface is filled with a thick horny mass of keratotic material. The fingernail and toenail changes are frequently present at birth and are nearly always present during the first year of life. Recurrent episodes of paronychial inflammation associated with *Candida albicans* infections are frequent, as is episodic shedding of nails (Fig. 3). The nail plates are generally darkened and yellowish brown distally, with less discoloration of the proximal portions. Painful ventral incurvation of the lateral nail margins may occur. There is abnormal hyperkeratosis and hypertrophy of the ventral nail surface, which is normally much thinner than the nail plate itself. The process of incurvation by the turning inward of lateral nail edges tends to be progressive so that a cylinder or conelike change occurs in the nails. The free distal end of the nail is pushed upward and outward, away from the nail bed. Keratinous debris from the nail bed then accumulates under the raised-up nail (Fig. 4). In essence, the nails grow up instead of out. When the nail plate becomes separated from the nail bed, the epithelium of the nail bed keratinizes into loose, irregularly arranged clumps of keratin rather than forming a compact, continuous layer.

The oral lesions may be focal, with the appearance of white, opaque plaques, involving only a portion of the buccal mucosa or lateral tongue, or they may be generalized, involving the entire mucosa of the cheeks, lips, and tongue. Angular cheilosis is often present. The plaques are frequently superinfected by *Candida*. The leukokeratosis of the oral, nasal, and otic mucosa is commonly present by adolescence. Unlike the changes found in dyskeratosis congenita, the leukokeratosis of pachyonychia congenita is not premalignant. In many cases, oral lesions are present at birth. Hoarseness caused by thickening of the posterior laryngeal commissures has been reported.

Hyperkeratotic lesions tend to occur on the weight-bearing surfaces of the feet as an affected
child starts to walk (Figs. 5 and 6). Similar hyperkeratotic lesions occur on the thenar and hypothenar eminences of the pams (Fig. 7) and on the palmar surfaces of the fingers. Large, painful bullae may occur on the plantar feet, especially during summer. The lesions can be painful enough to discourage walking. Hyperhidrosis and bromhidrosis are common. The palmoplantar lesions tend to remain stable over time.

Usually by 3 or 4 years of age the patient has follicular hyperkeratotic lesions on the elbows and knees (Fig. 8), and frequently these lesions appear on the extensor surfaces of the extremities, the buttocks, the popliteal fossae and occasionally they are found on the face and scalp. The lesions tend to be worse in winter, and they may coalesce to form verrucous papules or plaques (Fig. 9). The keratotic papules can be picked out, leaving a small bleeding point that will eventually be filled again with a keratotic plug.

Murray first described the association between pachyonychia congenita and natal teeth. Soderquist and Reed studied a family with pachyonychia congenita in which affected family members developed epidermal cysts. They raised the question of whether cystic lesions previously found to be associated with pachyonychia congenita were really steatocystomas (Figs. 10 and 11), as had been reported. Corneal dyskeratosis and cataracts of varying severity are sometimes seen. Hair is generally described as dry, lusterless, sparse, or kinky. Varying degrees of congenital alopecia are reported.

Schonfeld has suggested the following classification based on the clinical syndromes:

I. Jadassohn-Lewandowsky syndrome: characterized by symmetrical, hard, thickening of all fingernails and toenails; palmoplantar keratoses; follicular keratoses; blisters; leukokeratosis; hoarseness; hair abnormalities; and palmoplantar hyperhidrosis.
II. Jackson-Sertoli syndrome: type I plus natal teeth and multiple cysts (leukokeratosis of the oral mucosa has not been reported in type II).

III. Schaffer-Brunauer syndrome: type I plus corneal dystrophy (extremely rare type).

Anneroth and associates pointed out that natal teeth and oral leukokeratosis may constitute the earliest clinical signs of paronychia congenita and that they may be present before nail lesions occur. Therefore, when there is a family history of pachyonychia congenita, it is important that the child have an early examination of the oral cavity.

Fig. 3. Pachyonychia congenita: nail shedding.

Fig. 4. Pachyonychia congenita: keratinous subungual debris.

Fig. 5. Pachyonychia congenita. (A) Plantar hyperkeratosis of forefoot. (B) Plantar hyperkeratosis of heel.
Lesions can be a serious clinical problem for affected persons but should not lead to increased mortality. Blindness can occur in patients as a consequence of corneal dyskeratoses. Mental and physical retardation are not normally a part of the syndrome.

**PATHOLOGY**

Forslin and co-workers reported that the pathologic nail changes were exclusively local-ized in the nail bed (the ventral nail plate) and possibly in the connective tissues supporting the ventral nail plate. They found an increase, at least threefold, in the thickness and dry mass of the affected nail bed. The hard nail plate proper showed no pathologic changes. Thormann and Kobayasi, using electron microscopy, found abnormalities in the keratinization process in pachyonychia congenita. These abnormalities included lacunae in horny cells, lack of separation of desmosomes between horny cells, large

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**Fig. 6.** Pachyonychia congenita: painful hyperkeratosis on soles.

**Fig. 7.** Pachyonychia congenita: hyperkeratosis on palms.

**Fig. 8.** Pachyonychia congenita. (A) Hyperkeratotic lesion on elbow. (B) Hyperkeratotic lesions on knees.
Fig. 9. Pachyonychia congenita: verrucous papule on dorsal foot.

Fig. 10. Pachyonychia congenita: nail changes and steatomatosis on forehead.

Fig. 11. Pachyonychia congenita: steatomatosis on chest and nail lesions.


distinct keratinosomes, increased numbers of keratohyaline granules, and thick tonofilament bundles.\textsuperscript{14}

Witkop and Gorlin examined oral mucosal lesions histopathologically.\textsuperscript{10} They described intracellular vacuolization and edema, as well as pyknotic cells in the superficial layers of the epithelium and in the spinous layer. Schonfeld examined involved plantar skin histopathologically and found that cells in the upper squamous cell and granular layers develop increased intracellular edema in their migration toward the surface, with a progressively increasing perinuclear vacuolization, leading to vesicle formation and loss of keratohyaline granules.\textsuperscript{11} At sites without vesicle formation, there were abundant keratohyaline granules with a mild perivascular lymphocytic infiltrate in the dermis. The histopathologic picture seen in bulla formation in skin, in oral and laryngeal mucosal leukokeratoses, and in corneal leukokeratoses were similar with respect to their intracellular vacuolization.\textsuperscript{6, 13, 15}

An electron microscopic study of the involved skin of two patients revealed an increased number of desmosomes throughout the epidermis, increased number and thickness of tonofibrils, intracellular and intercellular edema, and large abnormal keratohyaline granules,\textsuperscript{16} consistent with a defect in keratinization. After the patients received oral isotretinoin therapy, electron microscopy demonstrated increased intercellular and intracellular edema and decreased density of tonofibril bundles, consistent with suppression of abnormal keratinization.
DIFFERENTIAL DIAGNOSIS

Pachyonychia congenita is frequently confused with dyskeratosis congenita (Table 1).

COMPLICATIONS

Pain and infections of hyperkeratotic feet are the most common complications. The most severe complications are opacities and partial or total blindness due to corneal dyskeratoses.

TREATMENT

Topical keratolytic agents, hypnosis, superficial x-ray and grenz ray therapy, and high doses of vitamin A and vitamin E have been used with varying degrees of success. Specially designed rubber-base foot mold inserts in shoes have been beneficial. For bullous lesions and ruptured bulbar sites, appropriate dressings and trauma avoidance are necessary. Thomas and colleagues treated a father and son with severe, disabling pachyonychia with oral isotretinoin in dosages of 2 to 3 mg/kg/day. The keratotic papules on the knees cleared within 1 month, and the leukokeratotic plaques on the father’s oral mucosa cleared. There was no objective clinical improvement in the palmoplantar keratoderma of either patient. The son underwent a full 16-week course of isotretinoin therapy at 2 mg/kg/day, and he had no clinical improvement of his nails or keratoderma. The father’s course was complicated by hypertriglyceridemia, and there was little improvement during two 8-week trials at 3 mg/kg/day and 1 mg/kg/day, respectively.

White and Noone treated a 15-year-old boy with severe nail changes. The nail bed and nail plate were elevated and removed from the wound, leaving a cavity lined by the germinal matrix. The skin proximal and dorsal to the nail bed was reflected, the entire germinal matrix was sharply excised down to the extensor tendon, and the surgical wound was covered by a split-thickness skin graft. The cosmetic and functional outcome was good. It appears that all of the nail matrix must be removed to prevent nail regrowth. Cosman and co-workers performed a deep surgical excision of the nails in a 4 1/2-year-old girl with pachyonychia congenita. The exposed phalanx was curetted, only a small distal portion of matrix was left, and the defects were covered with full-thickness skin grafts. Ten months after the surgery, nail again formed.

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<th>TABLE 1. Characteristics of Dyskeratosis Congenita and Pachyonychia Congenita</th>
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<td><strong>Inheritance</strong></td>
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<td><strong>Gender</strong></td>
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<td><strong>Pigmentation</strong></td>
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<td><strong>Palmoplantar Hyperhidrosis</strong></td>
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<td><strong>Palmoplantar Bullosae</strong></td>
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<td><strong>Hyperkeratoses</strong></td>
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<td><strong>Verrucous Lesions</strong></td>
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There matrix had been left.\(^4\) Thomsen and associates treated the fingernails of a 37-year-old woman with pachyonychia congenita by vigorous curettage and electrofulguration of the nail matrices and beds.\(^2\) Treatment sites were not sanded, and healing occurred by secondary intention. They report that this is an effective and easily performed technique for permanent nail correction. There are reports of amputation of the distal phalanx in order to correct the nail defect. Such potentially mutilating surgery does not seem warranted in light of the efficacy of other less radical surgical techniques by which the nail matrix can be satisfactorily ablated. Patients and their families can benefit from genetic counseling.

**PROGNOSIS**

Lesions persist for life. Blindness can occur in patients who have corneal dyskeratosis. Growth and development are normal, and intelligence is usually normal.

**JAMES B. PATTERSON**

**REFERENCES**

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