hypoxygenia and decrease in diffusing capacity followed by fibrosis, with marked restrictive syndrome and decrease in compliances and a switch from lymphocytes to PMNs in BAL. This suggests that alveolitis leads to fibrosis, despite withdrawal from exposure, and accords with recent concepts of the pathogenesis of interstitial pulmonary diseases.17

Early observations suggested a possible relationship between occupational exposure to mineral oil and respiratory diseases;18 however, this relationship was not clearly demonstrated, and no recent observations confirmed it. The use of mineral oil in industry is prohibited by work legislation, which may explain why occupational pulmonary diseases induced by paraffin are exceptional. Moreover, paraffin inhalation may be underestimated, as it leads to insidious respiratory disorders without acute symptoms. This observation is the first in which a relationship between occupational paraffin exposure and interstitial pulmonary disease has been established by electron microscopy. The impairment of pulmonary function, despite treatment and withdrawal from exposure, emphasizes the importance of prevention for occupational pulmonary disease.

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The Harlequin Nail*
A Marker for Smoking Cessation
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Changes in the human nail frequently serve as an indicator of local and systemic disease. Alterations in the morphology, structure and growth characteristics of the nail accompany chronic cigarette smoking; yellow pigmentation of the nail plate—referred to as the "nicotine sign"—is common. The clubbed yellow nail may indicate the presence of lung cancer. In contrast to the ominous nature of the clubbed yellow nail, we describe a sign that is more propitious: the sudden cessation of smoking due to an intercurrent disease, often a cerebrovascular accident (CVA), leads to the development of a distinct line of demarcation between the distal pigmented nail and the newly emerging proximal nonpigmented nail. We propose the term "harlequin nail" for this curious physical sign. By measurement of the distance between the proximal nail base fold and the line of demarcation, we can deduce the date smoking ceased (and, by inference, the approximate date of a CVA in a patient unable to volunteer this information). This sign also serves as a reminder that the "nicotine nail" remains discolored only because of dynamic restaining of the nail with tobacco by-products.

(Chest 1990; 97:236-38)

The question came up one day, when discussing the grooves left on the nails after fever, how long it took for the nail to grow out from root to edge. A majority of the class had no further interest; a few looked it up in books; two men marked their nails at the root with nitrate of silver, and a few months later had positive knowledge on the subject. They showed the proper spirit.

—William Osler

The bedside clinician, searching for clues to the presence of disease, is often rewarded by careful examination of the patient's hands. The nails offer many clues to the patient's

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physiology and habits. Yellow pigmentation of the nail plate caused by cigarette smoking is especially common (particularly in our Veterans Administration Hospital); clubbing of a "nicotine nail" is an ominous sign.

The process of nicotine staining of the nail is a dynamic one: as new nail appears, it is stained by tobacco by-products from sidestream smoke. Sudden cessation of smoking (which, in a hospital-based practice, is most often due to an acute event such as a CVA) illustrates this point well, because a delicate line of demarcation appears between the pigmented and the newly grown, unpigmented nail. By measuring the distance between the line of demarcation and the proximal nail fold, it is possible to date the onset of the antecedent illness.

We report on two patients who demonstrated this line of demarcation, allowing us to correctly infer on bedside rounds that smoking had ceased. The reason for cessation was an intercurrent illness—a CVA in one case and radiotherapy for lung cancer in another—which made it impossible or unacceptable to smoke. The approximate date of the illness in each case was correctly inferred by measuring from cuticle to line of pigmentation.

CASE REPORTS

CASE 1

A 71-year-old man was brought to the VA Medical Center, Johnson City, by his family, who stated that he had a one-week history of fever, chills, and cough productive of yellow sputum. Prior VA records showed that the patient was a long-term smoker, smoking 1 to 2 packs/day for more than 30 years, and had COPD. The patient was unable to give a lucid history, and records from another hospital where he had been recently treated were not available. On physical examination, the patient had a blood pressure of 120/60 mm Hg, a heart rate of 88 beats/min, and a temperature of 37.7°C. The patient was poorly nourished and ill-looking. The neurologic examination demonstrated a dense left hemiparesis, left cranial nerve 7 weakness, and a positive Babinski reflex on the left side. The patient was able to speak but was not oriented to place or person. The left index fingernail revealed a curious distribution of pigmentation, with the distal nail being yellow and nicotine stained and the proximal portion being pink and pearly. A line of demarcation separated the two halves (Fig 1). The distance between the line of demarcation and the proximal nail fold was 5 mm; we inferred that the patient probably was unable or not allowed to smoke once he became bedridden from the stroke. We estimated that the CVA was between four and ten weeks old (based on a nail growth rate of 0.5 to 1.2 mm/week). A call to the hospital from which the patient was transferred revealed that the stroke had occurred six weeks prior to our seeing the patient. The wife later confirmed that the patient had not been allowed to smoke subsequent to the stroke.

CASE 2

A 70-year-old with a 100 pack-year smoking history and inoperable squamous cell cancer of the lung (diagnosed two months prior to admission) presented for radiation therapy. The extremities revealed bilateral clubbed nails and nicotine staining confined to the distal half of the nail plate of the right hand. (Fig 2.) A line of demarcation was clearly seen 3 to 4 mm distal to the proximal nail fold.

DISCUSSION

Following embryonic differentiation, the human nail grows continuously throughout life at a rate of about 0.5 to 1.2 mm per week, slowing down with age.1,4 Trauma appears to stimulate growth, while immobilization retards the process.4,5 Toenails appear to grow at a third to a half the rate of fingernails, and full replacement from base to free edge might take anywhere between 12 and 18 months.5 Slowing of nail growth is also a feature of malnutrition, arterial insufficiency, systemic infections, and intercurrent acute illness; the latter typically produces metabolic growth arrest, or Beau's lines.5

Cigarette smoking affects nail growth and morphology in several ways: the most common manifestation is the yellow nail or the nicotine sign. Such a yellow pigmentation, though more generalized, has been seen in the endogenous dyschromias due to toxic reaction (long-term tetracycline therapy), infectious (scopulariopsis), metabolic (amyloidosis, diabetes, jaundice), and idiopathic (yellow nail syndrome) causes.1,5 The yellow nail syndrome describes a yellowish green discoloration of the nails associated with lymphedema, facial edema, lymphatic hypoplasia, and a characteristic slowing of nail growth. A host of pulmonary abnormalities has been described with the syndrome, including pleural

![Figure 1: Case 1: Note line of demarcation between distal nicotine-stained nail and proximal pink (new) nail (original magnification × 5).](image1)

![Figure 2: Case 2: Nicotine staining and line of demarcation involving several fingers (original magnification × 3). The finger is also clubbed.](image2)
effusions, bronchitis, bronchiectasis, and malignant pulmonary neoplasms.\textsuperscript{3,4,7} When the yellow staining is accompanied by clubbing in a long-term smoker, a diagnosis of broncho-pulmonary suppurative or malignancy is suggested. Long-term smokers can also develop a progressive curving of their fingernails associated with pulp atrophy, to which the term "breaking," or claw nail, has been applied,\textsuperscript{6} not to be mistaken for clubbing.

An acute illness, such as a CVA, interrupts the process of nicotine staining, and with continuing nail growth, a line of demarcation forms between the distal, pigmented, yellow nail and the proximal, newly formed, pink nail with a white lunule. We propose the term "harlequin nail" for this curious physical sign. The word "harlequin" has at least five meanings;\textsuperscript{8} we prefer the meaning "fancifully varied in color, decoration, etc." the "half-and-half" nail described by Lindsay\textsuperscript{9} is superficially similar, occurring in patients with chronic renal failure and rarely in patients receiving cytotoxic therapy. The pigmentation in this condition, unlike that in the "harlequin nail," appears to be located in the nail bed rather than the nail plate and hence does not grow out with the nail.\textsuperscript{9}

In this era of increasingly complex diagnostic technology and therapeutic intervention, there continues to be interest and a growing literature on bedside diagnosis. The "harlequin nail" is a simple clinical sign that provides useful information on the patient and underscores the rewards of careful bedside examination.

\textbf{References}


\textbf{Leukocyte Migration Inhibition in Propranolol-induced Pneumonitis*}

\textbf{Evidence for an Immunologic Cell-Mediated Mechanism}

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About 20 cases of beta blocker-associated pneumonitis have been published in the mid-70s, and a case of interstitial pneumonitis has been attributed to propranolol. The pathogenesis of these cases of pneumonitis with or without pleural effusion is not clear. A 59-year-old man developed pneumonitis which showed all the characteristics of a drug-associated pneumonitis due to propranolol: BAL demonstrated a lymphocytosis, the variations of which closely correlated with a provocation test. The LIF appeared to be released by the patient's peripheral blood lymphocytes when cultured with optimal doses of propranolol. Production of LIF by the patients' lymphocytes suggests the existence of a drug-specific cellular immune response in propranolol-associated pneumonitis.

\textit{(Chest 1990; 97:238-41)}

\textbf{BAL} = bronchoalveolar lavage; \textbf{LIF} = leukocyte inhibitory factor; \textbf{PaO}_2 = arterial oxygen pressure; \textbf{FCS} = fetal calf serum; \textbf{LMI} = leukocyte migration inhibition

\textbf{Bronchospasm in patients with chronic bronchitis or asthma}\textsuperscript{4,5} is the most frequent adverse respiratory effect of beta-blockers. However, a few cases of pneumonitis with or without pleural effusion also have been described.\textsuperscript{4,5} The case reported herein is, to the best of our knowledge, the second case of pneumonitis due to a widely used beta blocker, propranolol. Clinical and radiologic data, results of pulmonary function tests and BAL, as well as the outcome of the disease, were in favor of an immunologic mechanism of cell-mediated hypersensitivity.

A sensitive photoelectric method for measuring cell migrations\textsuperscript{5} was used to assess leukocyte migration inhibition in presence of the drug; the patient's lymphocytes appeared to produce a factor inhibiting the migration of peripheral blood leukocytes (LIF) when cultured with optimal drug concentrations, suggesting the existence of a cellular response which could possibly play a role in the pathogenesis of the lung disorder.

\textbf{CASE REPORT}

\textbf{Clinical History and Findings}

A 59-year-old man, formerly a smoker, complained of exertional dyspnea and was found to have interstitial pneumonitis. He had been receiving treatment with propranolol for 30 months, 40 mg per day (cumulative dose, 36 g). The roentgenogram showed small opacities disseminated over both lungs. A chest x-ray film taken

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\textit{Leukocyte Migration Inhibition (Gauthier-Rahman et al)}

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