**Interstitial Pulmonary Disease Induced by Occupational Exposure to Paraffin**

Jean-Louis Pujol, M.D.; Gilbert Barnéon, M.D.; Jean Bouquet, M.D.; François-Bernard Michel, M.D., F.C.C.P.; and Philippe Godard, M.D.

An occupational interstitial pulmonary disease was observed in a 59-year-old worker after five years of massive exposure to aerosolized paraffin. Histologic studies of open-lung biopsy showed a lipid pneumonia characterized by (1) alveolitis involving large lipid-laden macrophages and (2) interstitial fibrosis. Electron microscopy of AMs disclosed features of paraffin-laden cytoplasmic vacuoles. Successive treatments included prednisolone and cyclophosphamide. Despite these treatments and withdrawal from exposure, the pulmonary function became impaired progressively, resulting in restrictive syndrome and severe exertional dyspnea. Concomitantly, PMNs harvested by BAL increased, whereas initial lymphocytosis decreased. This is the first case observed of occupational interstitial fibrosis in which electron-microscopic findings clearly established a relationship with an exposure to paraffin. This observation also emphasizes the switch from alveolitis to fibrosis in the pathogenesis of interstitial pulmonary disease.

(Chest 1990; 97:324-36)

Paraffin, a mineral oil, can induce alveolitis and interstitial fibrosis, possibly related to the activation of oil-laden AMs. This lipid pneumonia is usually related to repeated aspiration of paraffin-containing laxative or nasal drops. We report the first case of a worker suffering from an interstitial pulmonary disease related to occupational paraffin exposure.

**Case Report**

A 59-year-old worker, a mild smoker, was admitted to the hospital in July 1984 for exertional dyspnea. He had been well until May 1984. He had no previous medical or surgical history and had never received long-term treatment. He had no history of asbestos exposure. Five years ago, he started to work for an automobile dealer. From 1979 to May 1984, the patient was chronically exposed to paraffin in cleaning new cars protected by paraffin, using hot water generated by compressed air jets. This technique aerosolized hot paraffin from car surfaces in a closed workshop (80 m²) without any ventilation and led to massive inhalation. He never used a mask to reduce inhalation, whereas the French legislation requires the use of such protective devices.

The findings from physical examination, cardiac function, routine biologic analyses, and chest x-ray films were normal. A CT scan showed (1) a diffuse interstitial process more pronounced in the periphery of the lower lobes and (2) right paratracheal hypodense (~40 UH) lymph node enlargement (Fig 1).

Hypoxemia and a slight decrease in the DSS were found. In contrast, other pulmonary function tests, including plethysmographic evaluation of compliances, were normal (Table 1).

A BAL was performed and showed an increase in total cell numbers and lymphocyte percentage. Light microscopy of a transbronchial biopsy showedmixed alveolitis involving both normal lymphocytes and AMs, some of them presenting unusual cytoplasmic vacuoles. Diagnostic investigations failed to demonstrate any evidence of systemic disease, of infectious or hypersensitivity pneumonitis, and the patient did not present any evidence of endogenous dislipidosis or gastroesophageal reflux.

In March 1985, a surgical open biopsy of the right middle lobe was performed. Light microscopy following hematoxylin-eosin, PAS, and trichrome stainings disclosed a uniform interstitial pneumonitis with fibrosis. The alveoli were filled with extracellular lipid droplets and large AMs containing lipid vacuoles. Some of them were multinucleated foam histiocytes (Touton giant cells). Lymphocytes were also involved in the alveolitis without granuloma organization. Some histiocytes were present in thickened interalveolar septum in which numerous collagen fibers were seen (Fig 2). Lipid pneumonia was diagnosed.

A new BAL was performed after the open-lung biopsy. Electron microscopy of the AMs disclosed an aspect of foam cells with cytoplasmic vacuoles of various sizes unstained by osmic acid, a specific feature of mineral oil (Fig 3).

A daily dose of prednisolone (1.5 mg/kg) was begun in March 1985. Then dosage was slowly decreased until a daily maintenance dosage of 0.5 mg/kg was reached. In November 1985, corticosteroids were discontinued because of clinical impairment. An immunosuppressive treatment by cyclophosphamide (2 mg/kg daily per os) was begun and maintained for four months. Cyclophosphamide induced neutropenia with digestive candidiasis. Despite therapy, dyspnea and pulmonary function became worse, and a restrictive syndrome occurred (Table 1). Diffusing capacity (49 percent) and static compliance (0.25 L/cm H₉O) decreased concomitantly. Serial cyto logic studies of BAL fluid demonstrated the progressive decrease of total cells and lymphocyte counts, which returned to subnormal values, whereas PMNs increased (Table 1). As no clinical benefit justified further active therapy, cyclophosphamide was discontinued, and only long-term oxygen therapy was maintained.

**Figure 1.** Computed tomographic scan shows diffuse interstitial process more pronounced in periphery of lower lobes.
**Table 1—Follow-up Data of Pulmonary Function Studies and Cytologic Analysis of BAL.**

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<td>July</td>
<td>Oct</td>
<td>March</td>
<td>June</td>
<td>Nov</td>
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<tr>
<td>PaO₂, mmHg</td>
<td>60</td>
<td>60</td>
<td>57</td>
<td>59</td>
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<td>VC, percent of predicted</td>
<td>95</td>
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<td>TLC, percent of predicted</td>
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<td>94</td>
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<td>FEV₁, percent of predicted</td>
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<td>96</td>
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<td>D-SS, percent of predicted</td>
<td>68</td>
<td>68</td>
<td>53</td>
<td>49</td>
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<tr>
<td>BAL</td>
<td></td>
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<tr>
<td>Total cells (× 10⁶/ml)</td>
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<td>200</td>
<td>—</td>
<td>372</td>
<td>525</td>
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<td>AMs, percent</td>
<td>48</td>
<td>27</td>
<td>—</td>
<td>41</td>
<td>32</td>
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<td>Lymphocytes, percent</td>
<td>52</td>
<td>73</td>
<td>—</td>
<td>47</td>
<td>64</td>
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<td>Neutrophils, percent</td>
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Treatments
- Prednisolone (1.5mg/kg)
- Cyclophosphamide (2mg/kg)
- Long-term oxygen therapy

*PaO₂: Partial pressure of oxygen (while patient was breathing room air); VC, vital capacity; TLC, total lung capacity; and FEV₁, forced expiratory volume in 1 s.

**DISCUSSION**

The diagnosis of paraffin-induced interstitial pulmonary disease was established by (1) evidence of massive exposure to aerosolized hot paraffin, (2) interstitial pulmonary disease with progressive constitution of restrictive syndrome, (3) CT scan demonstrating interstitial syndrome and hypodense mediastinal lymph nodes suggesting fat density, (4) light microscopy of open biopsy showing features consistent with lipid pneumonia and fibrosis, and (5) demonstration of paraffin-laden AMs by electron microscopy.

Mineral oil is a well-known cause of lipid pneumonia. Paraffin resists common hydrolysis and acts as a foreign body when aspirated during treatments with laxatives or nose drops. Lipid pneumonia is usually restricted to exogenous causes; however, many pulmonary diseases are associated with lipid-laden AMs, in particular, obstructive cholesterol pneumonia, long-term amiodarone treatment, and lipid accumulation in the reticular endothelial system.

Pathologic findings in these diseases are almost similar to those of exogenous lipid pneumonia. Many studies have suggested that electron microscopy or biochemistry of BAL and lung biopsy are useful tools for diagnosis. Thus, electron microscopy of mineral oil-laden vacuoles shows an "empty" appearance, as these vacuoles are not stained by osmic acid. In contrast, vegetable or animal oil-laden vacuoles are strongly stained by osmic acid, and lamellar mild osmophilic vacuoles suggest amiodarone-induced pneumonia.

The diagnosis of paraffin-induced lipid pneumonia requires both long-term exposure and suggestive histologic features. It has been suggested that BAL and transbronchial biopsy should be sufficient for diagnosis; however, a recent study found that lipid-laden AMs are not specific markers, as they are observed in non-lipid pneumonia. On the other hand, open biopsy can establish the definitive diagnosis of lipid pneumonia. Moreover, open biopsy is the only technique staging inflammation and assessing fibrosis.

Follow-up of this observation disclosed two clear-cut steps: alveolitis involving lymphocytes and AMs associated with...
hypoxemia 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
Abraham Verghese, M.D., F.C.C.P.; Guha Krish, M.D.; Donald Howe, M.D.; and Marcus Stonecipher, M.D.

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 unpigmented 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.

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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