Hypersensitivity Pneumonitis Associated with Environmental Mycobacteria

Citation

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Accessibility
A previously healthy man working as a machine operator in an automotive factory developed respiratory symptoms. Medical evaluation showed abnormal pulmonary function tests, a lung biopsy showed hypersensitivity pneumonitis, and his illness was traced to his work environment. His physician asked the employer to remove him from exposure to metalworking fluids. Symptoms recurred when he was later reexposed to metalworking fluids, and further permanent decrement in his lung function occurred. Investigation of his workplace showed that five of six large reservoirs of metalworking fluids (cutting oils) grew Mycobacterium chelonae (or Mycobacterium immunogenum), an organism previously associated with outbreaks of hypersensitivity pneumonitis in automaking factories. His lung function remained stable after complete removal from exposure. The employer, metalworking fluid supplier, union, and the National Institute for Occupational Safety and Health were notified of this sentinel health event. No further cases have been documented in this workplace.

Key words: atypical mycobacteria, extrinsic allergic alveolitis, hot tub, hypersensitivity pneumonitis, metalworking fluids, Mycobacterium chelonae, Mycobacterium immunogenum, nontuberculous mycobacteria, occupational lung disease. Environ Health Perspect 113:767–770 (2005).

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Case Presentation
A 57-year-old nonsmoking auto-parts machine operator presented in 1995 because of shortness of breath on exertion, cough, fatigue, and chest congestion. In his job he operated a machine that cut metal parts using a semi-synthetic metalworking fluid (Figure 1) that was collected and recycled through large tanks holding > 1,000 gal fluid. A chest radiograph showed a generalized increase in interstitial markings. He was treated with empiric antibiotics on two occasions. Later, his treating physician suspected occupational asthma due to exposure to oil mist, and asked the employer to remove him from exposure to metalworking fluids. A trial of bronchodilator medications was not effective in improving his symptoms, which were worse after work. Spirometry was performed by the factory’s medical department just before and after a 5-day work week; no change in spirometry was noted. A measurement of total metalworking fluid aerosol done in the patient’s work area showed that the mass of aerosol was 0.42 mg/m³ of air sampled, which was below the recommended limit of a recent advisory committee.

When the physician’s recommendations to remove the patient from all metalworking fluids was not followed and symptoms persisted, the patient was referred to a pulmonary specialist for further testing. Pulmonary function tests showed a reduced diffusing capacity of 67% predicted with oxygen desaturation on ambulation (Table 1), and a carbachol challenge (a test for airway hyperreactivity in asthma) was negative. Bronchial alveolar lavage showed 90% lymphocytes and 10% macrophages in alveolar lining fluid, with negative smear and culture for acid fast bacilli (mycobacteria) and fungi. A transbronchial lung biopsy (Figure 2) showed interstitial chronic inflammation and collections of epithelioid cells suggestive of granulomas with negative stains for acid-fast bacilli and fungus and, on review, diagnostic of hypersensitivity pneumonitis. Several years later, testing of the preserved tissue block by polymerase chain reaction was negative for sequences found in Mycobacterium chelonae. The patient’s treating pulmonologist suspected that the hypersensitivity pneumonitis was due to bacteria growing in the metalworking fluid. Serum-precipitating antibodies to a standard panel of nine substances, including bacteria, several fungi, and pigeon serum, were all negative. The pulmonologist gave the patient a brief note for his employer restricting exposure to metalworking fluids; the company physician misinterpreted the message as indicating that the patient had chronic obstructive pulmonary disease made worse by metalworking fluid exposures, and changed his work location but did not fully restrict him from exposure to metalworking fluids.

No specific interventions were made in the workplace with regard to the metalworking fluids, although a plantwide program of reduction of fluid aerosol exposures for all workers was already in progress. Several months later the patient had an uncomplicated myocardial infarction, and after 3 months returned to work with continued exposure to metalworking fluids. Three years later, in 2000, he noted daily nasal congestion associated with work, and worsening dyspnea...
on exertion. His pulmonologist repeated lung function tests, which showed a further decline in diffusing capacity to 44% predicted (Table 1), and a thin-section computed tomography (CT) scan of the chest (Figure 3) showed “ground glass” opacities indicating interstitial lung disease and mild bronchiectasis. A visit to the patient’s residence by a treating physician trained in occupational and environmental medicine did not reveal any exposures suggestive of contributing to his hypersensitivity pneumonitis.

With the assistance of the county health department, samples of metalworking fluid were obtained for culture from the large reservoir supplying metalworking fluids to the patient’s work area. Standard bacterial and fungal counts were below the level of detection of 10 organisms/mL, unusually low for industrial metalworking fluids, which are usually contaminated by microorganisms. Stain of the centrifuged fluid pellet for acid-fast bacilli was qualitatively “very high,” and culture grew $1.6 \times 10^5$ mycobacteria/mL, which were identified as M. chelonei. This mycobacterium, although similar to the M. chelonae-acctabula group, has been proposed as a new species, Mycobacterium immunogenum (Brown-Elliott and Wallace 2002). Additional, separate fluid specimens were sent to another laboratory, which cultured and identified the same organism. Samples of fluid from five reservoirs, a blank of “virgin” metalworking fluid, and a tap water control were for a third time tested and showed > 2,500 mycobacteria/mL, with single-stranded conformational polymorphism analysis showing M. immunogenum in the used fluid samples, and none in the virgin fluid or tap water. Endotoxin, the active agent in the walls of gram-negative bacteria, was measured in the five samples from the five reservoirs at from $2.4 \times 10^2$ to $2.5 \times 10^4$ endotoxin units per milliliter of fluid by the Limulus assay. Based on these findings, the patient was removed completely from exposure to metalworking fluids.

The treating occupational physician scheduled a meeting with the plant occupational physician, industrial hygienists, and the contracting supplier of the metalworking fluids to recommend a) a survey of symptoms and chest X rays of workers exposed to metalworking fluids to identify any additional cases and b) testing of all metalworking fluid reservoirs in the facility for mycobacteria. In addition, the disease occurrence was reported to the Division of Respiratory Disease Studies of the National Institute for Occupational Safety and Health (NIOSH) and the New York State Health Department Occupational Lung Disease registry.

### Discussion

Metalworking fluids may be pure petroleum oils (“straight oils”), emulsions of petroleum in a water base (semisynthetic fluids), or emulsions of synthetic oils in water (synthetic fluids). Because they contain biologically available carbon (in the form of lipids) and water, water-based metalworking fluids routinely sustain microbial growth, but excess growth degrades the fluids and leads to loss of usefulness. Thus, standard use of these metalworking fluids in industry often includes routine testing for bacteria counts (without identification of all organisms) and the use of microbicides with the objective of suppressing, although not necessarily sterilizing, microbial growth.

A variety of respiratory illnesses have been reported to be associated with occupational inhalation of metalworking fluids, including bronchitis, asthma, and lipoid pneumonia (Cullen et al. 1981; Kennedy et al. 1989; Leigh and Hargrave 1999), and their toxicology has recently been reviewed (Gordon 2004). Currently there is no specific Occupational Safety and Health Administration (OSHA) standard for metalworking fluids, although guidance in prevention of health hazards is provided in an NIOSH criteria document.

### Table 1. Patient’s pulmonary function laboratory data.

<table>
<thead>
<tr>
<th>Date</th>
<th>FEV₁ (%)</th>
<th>FVC (%)</th>
<th>D₂CO (%)</th>
<th>O₂ saturation (%)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rest</td>
<td>Exercise</td>
</tr>
<tr>
<td>June 1985</td>
<td>2.70 (88)</td>
<td>3.0 (70)</td>
<td>—</td>
<td>—</td>
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<tr>
<td>January 1996</td>
<td>2.77 (94)</td>
<td>3.47 (95)</td>
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<tr>
<td>January 1996</td>
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<td>3.40 (93)</td>
<td>—</td>
<td>—</td>
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<tr>
<td>September 1997</td>
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<td>—</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>January 1998</td>
<td>—</td>
<td>—</td>
<td>(67)</td>
<td>—</td>
</tr>
<tr>
<td>April 2000</td>
<td>2.52 (89)</td>
<td>3.14 (89)</td>
<td>9.8 (44)</td>
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<tr>
<td>June 2000</td>
<td>1.86 (60)</td>
<td>2.55 (65)</td>
<td>—</td>
<td>89</td>
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<tr>
<td>April 2004</td>
<td>2.42 (89)</td>
<td>3.15 (92)</td>
<td>11.5 (45)</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: —, not measured; D₂CO, diffusing capacity for carbon monoxide (percent predicted); FEV₁, forced expiratory volume in 1 sec in liters (percent predicted); FVC, forced vital capacity in liters (percent predicted).
Hypersensitivity pneumonitis may be associated with exposure to various metalworking fluids, such as Mycobacterium avium complex (MAC), which can cause inflammation and cell proliferation with the presence of inflammatory and epithelial cells. 

There is no standard approach to treatment of hot tub lung. Case reports describe significant improvement with removal from exposure to the hot tubs. Oral corticosteroids, antimycobacterial therapy, or both have also been used. The expected course of this disease after the above measures is recovery without relapse. Measures proposed as being helpful in prevention include better ventilation of the hot tub room, frequent cleaning of the hot tub, frequent change of hot tub water, and use of disinfectants such as chloramines, bromine, and ultraviolet light. These measures are similar to those usually proposed for prevention of hypersensitivity due to exposure to mycobacteria in metalworking fluids.

**Conclusions**

Environmental mycobacteria have been associated with a serious lung condition, hypersensitivity pneumonitis, when inhaled as part of liquid droplet aerosols generated from large volumes of liquids serving as a culture medium. These organisms are found commonly in nature and are able to grow in sufficient quantities to cause disease. The case reported here involved an occupational source of such an exposure (aerosolized metalworking fluid in a machining environment), although aerosols containing mycobacteria have been described in other settings as well (aerosolized water from hot tubs). For this reason, specific investigation of sources of aerosols in the work or home environment of patients with this condition should consider the growth of mycobacteria as one of the potential sources of disease. As with other causes of hypersensitivity pneumonitis, removal from exposure and remediation of exposure are the first approaches to treatment.

**References**


