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Hypersensitivity Pneumonitis Due to Metal Working Fluids: Sporadic or Under Reported?

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Background *Occupational exposure to metal working fluids (MWF) is common with over 1.2 million workers in the United States involved in machine finishing, machine tooling, and other metalworking operations. MWF is a known cause of hypersensitivity pneumonitis (HP). Recent reports of outbreaks of hypersensitivity HP secondary to exposure to MWF are reported.*

Design *Cases were identified through the Occupational Disease surveillance system in the State of Michigan and from referrals for evaluation to the Division of Occupational and Environmental Medicine at Michigan State University (MSU). Each patient underwent a clinical examination including an occupational history, lung function studies, radiographic imaging, and in some cases lung biopsies. Following the diagnosis of definite HP, an industrial hygiene investigation was carried out, which included a plant walk-through, and review of the "Injury and Illness" log. Air monitoring and microbial sampling results were reviewed.*

Results *As part of Michigan's mandatory surveillance system for occupational illnesses, seven cases of suspected HP were identified in 2003–2004 from three facilities manufacturing automobile parts in Michigan. Each plant used semi-synthetic MWFs, and conducted a MWF management program including biocide additions. Two facilities had recently changed the MWF before the cases arose. Growth of mycobacteria was found in these two MWFs. Breathing zone samples for particulates of two employees in plant A (two cases) ranged from 0.48 to 0.56 mg/m^3. In plant B (four cases), two employees' sampling results ranged from 0.10 to 0.14 mg/m^3. No air sampling data were available from plant C.*

Conclusion *Hypersensitivity pneumonitis due to exposure to MWFs is under-recognized by health care providers, and current surveillance systems are inadequate to provide a true estimate of its occurrence. HP arose from environments with exposures well below the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for MWF, and in one case from exposures well below the National Institute of Occupational Safety and Health (NIOSH) recommended exposure limit (REL). The sporadic nature of reports of HP in relationship to MWF probably represents a combination of workplace changes that cause the disease and inadequate recognition and reporting of the disease when it does occur. Physician awareness of HP secondary to MWF and an effective medical surveillance program are necessary to better understanding the epidemiology and prevention of this disease* Am. J. Ind. Med. 49:423–433, 2006. *© 2006 Wiley-Liss, Inc.*

KEY WORDS: hypersensitivity pneumonitis; metal working fluids; mycobacteria

Abbreviations: HP, hypersensitivity pneumonitis; MWF, metal working fluids; OSHA, Occupational Safety and Health Administration; MSU, Michigan state university; PFT, pulmonary function test; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; D_LCO, diffusion capacity of carbon monoxide; MIOSHA, Michigan Occupational Safety and Health Administration; MDLEG, Michigan Department of Labor and Economic Growth; BAL, broncho-alveolar lavage; PEL, permissible exposure limit; AFB, acid fast bacteria.

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INTRODUCTION

Hypersensitivity pneumonitis (HP), or extrinsic allergic alveolitis, is an interstitial lung disease that involves an immunologic reaction to repeated inhalation of foreign antigens. Metal working fluid (MWF) is a known cause of HP associated with aerosol-related exposure to fungal or bacterial antigen present in the MWF [Bernstein et al., 1995; Kreiss and Cox-Ganser, 1997]. Occupational exposure to MWF is common with over 1.2 million workers in the United States involved in machine finishing, machine tooling, and other metal-working and metal-forming operations being potentially exposed [NIOSH, 1977].

Hypersensitivity pneumonitis was first reported among metal machining workers in 1995 [Bernstein et al., 1995]. In the following years, additional outbreaks were reported [Meredith and McDonald, 1994; Rose et al., 1996; Freeman et al., 1998; Zacharisen et al., 1998; Fox et al., 1999; Hodgson et al., 2001]. The last outbreak was reported in the published literature in 2001 [Weiss et al., 2002]. Whether these outbreaks reflect the recognition of a disease that is often under- or misdiagnosed or reflects some change in work practices has not been determined. Gaps in knowledge regarding risk factors, exposure-response relationships, intervention efficacy, and natural history of this disease as well as surveillance needed in order to define the extent of the problem in the industry have been previously summarized [NIOSH, 1998a].

Three outbreaks of HP with a definite diagnosis of HP was diagnosed among seven patients exposed to MWF in three different automobile part manufacturing plants in Michigan in 2003–2004 are reported. The clinical presentations, analysis of the work conditions, and a review of Michigan Occupational Safety and Health Administration (MIOSHA) investigations of the three plants are described. This report highlights the fact that HP due to MWF still exists as a problem and may be far more prevalent than is currently recognized. Awareness by clinicians, active surveillance, and continued research is needed to prevent further outbreaks.

METHOD

The cases were identified through the Occupational Disease surveillance system in the State of Michigan and referrals for evaluation to the Division of Occupational and Environmental Medicine at Michigan State University (MSU).

In 1988, the State of Michigan instituted a surveillance program for work-related diseases with financial assistance from the National Institute of Occupational Safety and Health (NIOSH). The surveillance program is a joint project of the MIOSHA in the Michigan Department of Labor and Economic Growth (MDLEG) and MSU [Rosenman et al., 1997]. The two major sources of Occupational Disease Reporting are reports from physicians and hospitals. Reports from hospitals were requested once each year. Hospital discharge summaries for individuals with a primary or secondary diagnosis of HP (ICD 495.0–.9) were obtained and the medical chart was reviewed to determine whether the healthcare provider had determined the etiology of HP. Reporting by both Michigan practitioners and hospitals is required under part 56 of Public Act 360 of 1978, which requires the reporting of all known or suspected occupational diseases.

An individual was considered to have work-related HP if he/she met the diagnostic criteria of HP as defined by Schuyler and Cormier [1997] (Table I).

In view of the limited utility of different diagnostic criteria of HP when used alone [Fink et al., 2005], we confirmed the diagnosis of definite HP with other currently used diagnostic criteria [Terho, 1986; Richerson et al., 1989; Lacasse et al., 2003].

The MIOSHA conducted an industrial hygiene investigation at the work places where the cases reported had

TABLE I. Diagnostic Criteria for Hypersensitivity Pneumonitis

Major criteria	Minor criteria
Symptoms compatible with HP	Bibasilar rales
Evidence of exposure to appropriate antigen	Decreased diffusion capacity
by history or detection in serum and/or BAL[a] antibody	Arterial hypoxemia, (rest/exercise)
Findings compatible with HP on chest radiograph or high resolution CT scan	
BAL lymphocytosis (if BAL performed)	
Pulmonary histologic changes compatible with HP	
Positive "natural challenge" (reproduction of symptoms and laboratory abnormalities after exposure to the suspected environment)	

Diagnosis is conformed if the patient fulfills four major criteria and two minor criteria and other diseases with similar symptoms are ruled out.

[a]Broncho-alveolar lavage.

Adapted from Schuyler and Cormier [1997] with permission of the publisher.

worked. Occupational Safety and Health Administration (OSHA) Injury and Illness logs, which employers with 11 or more employees are required to complete and maintain on all occupational injuries and illnesses that require more than first-aid, were reviewed to identify workers with potential respiratory problems. Maintenance procedures, unit operations, personal protective equipment, and engineering and work practice controls were reviewed. The industrial hygienist conducted air monitoring and reviewed the company's health and safety program. At the conclusion of the investigation, a report was prepared and when appropriate, citations issued for violations of MIOSHA standards.

The human subjects review board at MSU approved this activity.

RESULTS

Of the seven cases of HP, three were reported as part of the occupational disease reporting system while the other four were referrals to our MSU Occupational and Environmental Medicine clinic. Table II contains a brief description of the seven patients. All seven met the diagnostic criteria for definite HP.

A summary of three cases, one from each of the three plants follows:

Case Report 1 (Plant A)

A 52-year-old African American female with a past medical history of recurrent episodes of acute bronchitis with chest congestion and productive cough for the last 7 years reported worsening of her symptoms in June, 2003. The patient stated that her symptoms started when she began working in the area of her workplace where MWFs were used. In 06/2003, she had another episode of fever, chest congestion, and productive cough. This was associated with difficulty in breathing at rest and with exertion. The patient reported that nine other people who worked in the same area also had similar symptoms. She denied any other past occupational exposure, contact with sick individuals, allergies or contact with pets. She had smoked one pack of cigarettes a day for 5 years, but quit 25 years ago. She was evaluated at her work place with a chest X-ray, which was reported as abnormal, and she was told that she had possible HP to contaminated MWF. She was treated with prednisone, which was tapered off, and the patient returned to her usual work in August 2003 and was provided a respirator.

Her symptoms recurred in October 2003, at which time she underwent a more complete pulmonary evaluation. She was noted to have oxygen saturation of 90% at room air with bibasilar lung crackles. Chest X-ray revealed bilateral lung infiltrates in an interstitial pattern. She was initially treated with antibiotics for atypical pneumonia with no improvement. High resolution CT of the chest revealed diffuse bilateral ground glass opacities predominantly in the upper lobes. Pulmonary function tests (PFTs) were obtained with the following findings: forced vital capacity (FVC) of 1.52 L (50% of predicted), forced expiratory volume in 1 second (FEV_1) of 1.32 L (54% of predicted) with post bronchodilator improvement of 26% in both; FEV_1/FVC ratio was 85% (113% of predicted); diffusion capacity of carbon monoxide (D_LCO) was 9.66 ml/min/mmHg (42% of predicted). She stopped working and subsequently had near complete resolution of her symptoms. A repeat chest CT in January 2004 showed almost complete resolution of previously noted pulmonary infiltrates. At follow-up in July 2004, the patient had no symptoms, clear lungs on auscultation, and oxygen saturation of 99% at room air. Her repeat PFTs showed the following findings: FVC of 3.63 L and FEV_1 of 3.09 L (95% and 106% of the predicted value, respectively), FEV_1/FVC ratio was 85% (113% of predicted), and D_LCO was 21.24 ml/min/mmHg (91% of the predicted value). This patient met four major and two minor diagnostic criteria for HP.

Case Report 2 (Plant B)

A 55-year-old Hispanic male was in good health until 01/2004 when he had an episode of dry cough, which he thought, was a mild upper respiratory tract infection. His symptom progressed with increasing cough and difficulty in breathing on exertion. He saw a physician at his work place and was treated with a course of levofloxacin followed by clarithromycin. The patient's symptoms were progressive and he reported worsening on the days he worked. He felt fatigued and reported fevers in the range of 102 degree Fahrenheit. With these symptoms, he was admitted to the hospital in March 2004. He reported that his symptoms started at work where he was employed as a pipe fitter for the last 3 years. He believed that his symptoms started after two tanks of MWFs were cleaned with their fluid drained. He reported similar symptoms in several of his co-workers. He denied any history of allergies, smoking, and any previous occupational or residential exposure to molds.

His physical examination revealed bibasilar lung crackles. Chest X-ray revealed bilateral interstitial lung infiltrates. High resolution CT of the chest demonstrated diffuse alveolitis with minimal interstitial lung fibrosis. PFTs were obtained with the following findings: FVC of 2.92 L (63% of predicted); FEV_1 of 2.4 L (74% of predicted); FEV_1/FVC ratio of 84%; and a D_LCO of 11.1 ml/mmHg/min (45% of predicted). A subsequent lung biopsy was read as, "Lung parenchyma shows intra-alveolar collection of macrophages and other chronic inflammatory cells, some areas show intra-alveolar plugs of immature collagen; some poorly formed non-necrotic granulomas are present. These demonstrate a pattern of brochiolitis obliterans organizing pneumonia pattern with features suggestive of

TABLE II. Clinical Findings for Seven Individuals With Hypersensitivity Pneumonitis (HP)—Auto-Part Production Plants A, B, and C, Michigan, 2003–2004.

Patient description	Length of exposure[3] (in years)	Smoking status	Symptoms and physical findings		HRCT[5] findings		PFTs[6] (% predicted)		Biopsy	Diagnostic criteria of HP[8]
			Before	After[4]	Before	After	Before	After		
Plant A										
[a]1. Age (in years): 52, Sex: female, race[1]: AA, job title: not known	7	Ex, 5 pack year—25 years ago	Cough with sputum, dyspnea, fever, bibasilar crackles	None (4 months)	Ground glass opacification in interstitial pattern	Clear (2 months)	FVC: 50, FEV_1: 54, TLC: 93, D_LCO: 42	FVC: 106, FEV_1: 95, TLC: 111, D_LCO: 91 (2 months)	Not done	Four major, two minor
2. Age: 43, Sex: male, race: AA, job title: MO[2]	6	Never	Cough, dyspnea, scattered bilateral rales	None (1 month)	Bilateral ground glass infiltrates	Clear (1 month)	FVC: 85, FEV_1: 82, TLC: ND[7], D_LCO: 50	FVC: 96, FEV_1: 91, TLC: 102, D_LCO: 78 (5 months)	Not done	Four major, two minor
Plant B										
3. Age: 60, sex: male, race: H, job title: tank cleaner	14	Never	Cough, wheezing, dyspnea, crackles	Improved (2 months)	Ground glass opacification, small bilateral lung nodules	No change in lung nodules, otherwise clear (7 months)	FVC: 62, FEV_1: 65, TLC: 96, D_LCO: 51	FVC: 79, FEV_1: 83, TLC: 86, D_LCO: 63(7 months)	Consistent with HP	Four major, two minor
4. Age: 46, sex: male, race: C, job title: pipe fitter	4	Never	Cough, dyspnea, fever	Improved (2 months)	Diffuse bilateral ground glass opacification	Clear (2 months)	FVC: 72, FEV_1: 73, TLC: ND, D_LCO: ND	FVC: 99, FEV_1: 94, TLC: 95, D_LCO: 68 (3 months)	Consistent with HP	Four major, one minor
[a]5. Age: 55, sex: male, race: H, job title: pipe fitter	3	Never	Cough, dyspnea, fever scattered lung crackles	None (6 months)	Diffuse alveolitis	No residual alveolitis (2 months)	FVC: 63, FEV_1: 74, TLC: 82, D_LCO: 45	FVC: 87, FEV_1: 89, TLC: 86, D_LCO: 66 (4 months)	Difficult to interpret, clinical correlation may suggest HP.	Four major, two minor
6. Age: 40, sex: male, race: C, job title: MO	3	Never	Fever, cough, malaise, dyspnea, wheezing bilateral crackles	Improved (3 months)	Diffuse alveolitis and bronchiectasis	Clear (3 months)	FVC: 59, FEV_1: 66, TLC: ND, D_LCO: ND	FVC: 75, FEV_1: 82, TLC: ND, D_LCO: ND (3 months)	Not done	Four major, one minor
Plant C										
[a]7. Age: 35, sex: male, race: C, job title: MO	7	Never	Dyspnea, cough with sputum, fever, weight loss, bibasilar crackles	None (3 months)	Bilateral interstitial pattern ground glass opacification	Clear (4 months)	FVC: 62, FEV_1: 68, TLC: ND, D_LCO: 94	FVC: 79, FEV_1: 82, TLC: 94, D_LCO: 130 (4 months)	Consistent with HP	Four major, two minor

[a]Patients described in case scenarios. 1, Patient ethnicity: C, Caucasian; AA, African American; H, Hispanic. 2, Machine operator. 3, Years exposed to metal working fluids. 4, Condition after removal from the exposed are with number of months in parenthesis. 5, High resolution computed tomography scan of lungs. 6, Pulmonary function tests: FVC, forced vital capacity (normal $>$ 80% of predicted); FEV_1, forced expiratory volume at one second (normal $>$ 80% of predicted); TLC, total lung capacity (normal $>$ 80% of predicted); D_LCO, diffusion capacity of carbon monoxide (normal $>$ 80% of predicted). 7, Test not done. 8, Diagnostic criteria of HP.

hypersensitivity pneumonitis." The patient was started on treatment with oral steroids. His symptoms improved gradually and he was discharged on a steroid taper. The patient continued to be off work and his steroids were discontinued with resolution of his symptoms within 6 months. A subsequent CT scan revealed clearing of the earlier noted alveolitis while his PFTs 4 months after removal from exposure had the following findings: FVC of 3.77 L (87% of predicted); FEV_1 of 3.15 L (89% of predicted); normal FEV_1/FVC ratio; and a D_LCO of 16.4 ml/mmHg/min (66% of predicted). This patient met four major and two minor diagnostic criteria for HP.

Case Report 3 (Plant C)

A 35-year-old Caucasian male was evaluated in February 2004 by one of the authors for his complaint of progressive shortness of breath that began in October 2003. He complained of dyspnea both at rest and with exertion. He denied symptoms consistent with orthopnea or paroxysmal nocturnal dyspnea. He had a chronic cough that was intermittently productive. He felt fatigued and had an unintentional weight loss of 9 pounds in 3 months. He denied any fever or chills. The patient had undergone uvulopalatopharyngoplasty for sleep apnea in 04/2003 with complete resolution on a subsequent sleep study. He reported childhood allergies that resolved after allergy shots. He denied any history of smoking, recent travel, contact with pets, working at a farm, or any kind of residential exposure to molds. He has been working in an auto-parts manufacturing facility for the previous 9 years and as a machine operator for the last 7 years where he was exposed to MWF. He had noted that his symptoms were worse during the days he worked and slightly improved on the weekends.

The patient had previously undergone evaluation of his symptoms with a pulmonologist in 11/2003. Then, he was noted to have oxygen saturation of 95% at room air. Physical examination had revealed bibasilar crackles. Chest X-ray had shown bilateral interstitial lung infiltrates. High resolution computed tomography (HRCT) scan in 12/2003 showed ground glass opacification diffusely throughout the lung fields suggestive of acute reactive or atypical infectious pneumonitis (Fig. 1). He was initially treated for atypical pneumonia with two courses of antibiotics, doxycycline and levofloxacin, with no improvement. PFTs were obtained with the following findings: FVC of 3.47 L (62% of predicted), FEV_1 of 3.18 L (68% of predicted) with a normal FEV_1/FVC ratio and normal D_LCO. The patient subsequently underwent a lung biopsy in 01/2004 that showed ''chronic bronchioloitis with peri-bronchial interstitial inflammation with poorly formed granulomas,'' consistent with a diagnosis of HP (Figs. 2 and 3). Biopsy was negative for stains of fungus, acid-fast bacillus, and WBCs. Subsequently, he was initiated on treatment with oral steroids and he was removed from his work place. He reported near resolution of his symptoms. Repeat HRCT scan in 03/2004 showed complete resolution of the diffuse ground glass opacity seen earlier. The patient's steroids were tapered and he returned to work in 04/2004 at the same facility, 20 yards away from his previous work area, in an area where no MWFs were used. He wore a cartridge respirator. The patient did not report any recurrent symptoms. PFTs obtained in 03/2005 showed a FVC of 4.39 L (79% of predicted), FEV_1 Of 3.5 L (82% of predicted) with a normal FEV_1/FVC ratio, and normal D_LCO. This patient met four major and two minor diagnostic criteria for HP.

Table III summarizes the findings of the OSHA investigations which were conducted as a follow-up of the

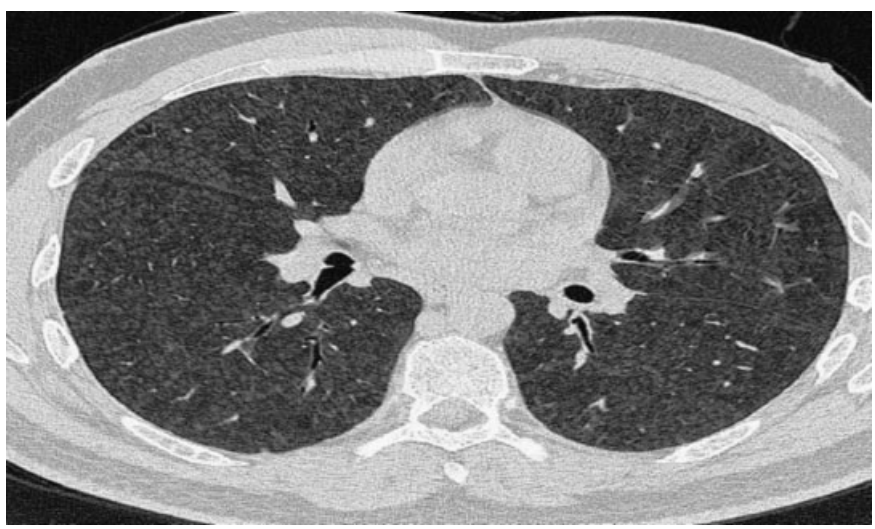

FIGURE 1. High resolution computed tomography (HRCT) of the chest revealing patchy areas of ground glass attenuations scattered in both lungs (Case 7).

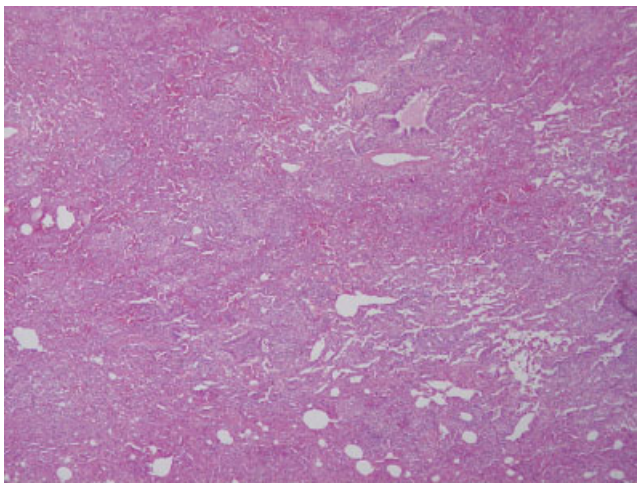

FIGURE 2. Low resolution view of lung tissue demonstrating diffuse interstitial (peri-bronchial) inflammation with loosely formed granulomas (Case 7—H & E stain).

above cases. Table IV lists the ingredients of MWFs and biocides associated with the outbreaks of HP in Michigan, 2003–2004.

Plant A

A Michigan Occupational Safety and Health Administration investigation was initiated at the plant in August 2003 in response to an employee complaint alleging illness caused by MWF. A report of the findings and recommendations was submitted in February 2004.

Plant A made braking systems. The plant had a unionized work force of 1,350. Five employees from Department 455, including Cases 1 and 2, and three from adjacent departments were recorded as having a work-related

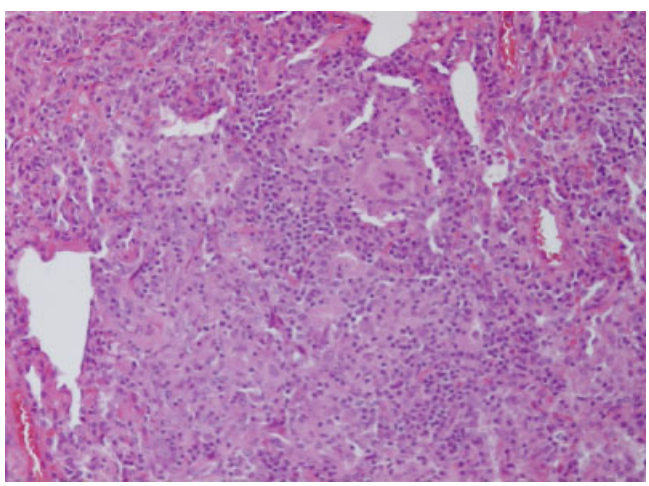

FIGURE 3. High resolution view demonstrating poorly formed granulomas (Case 7—H & E stain).

respiratory illness during the summer of 2003. Review of the "Injury and Illness" log showed the diagnosis of HP, bronchitis, and restrictive lung disease for these people. Seventy employees were considered exposed to MWF. Six of the eight employees returned to work with some using R-95 dust mask respirators.

Most of the employees who reported sick with respiratory complaints were machine operators. Employee interviews indicated that their illness started when the MWF used in Department 455 was changed. A new semi-synthetic MWF, Multan EA20, was introduced to machine brake parts in Department 455 in September 2002. Multan EA20 contained primarily severely hydrotreated heavy naphthenic petroleum distillates as well as amines. Prior to this, the company was using a synthetic MWF, Multan 8305, which primarily contained amines, supplied by the same company. Department 455 was supplied by a 44,000 gallon reservoir where the MWF was mixed with water and stored in a 6–9% concentration. The MWF also contained an isothiazolone group biocide, Kathon 886 MW, a fungicide and rust prevention chemicals. The MWFs underwent routine sampling and analysis for pH, concentration, and general biological activity. After the employee illness was reported, additional testing was initiated in the MWF reservoirs of five departments (including Department 455) in July 2003 for acid fast bacteria (AFB) and viable mycobacteria. High concentrations of *Mycobacteria immunogenum* and AFB were reported from the five systems with the highest concentration being reported from Department 455. Repeat sampling at different times consistently showed that AFB and mycobacteria level were highest in Department 455. The company started treating the MWFs with a different biocide, Kathon CC, which contains copper. After several treatments, studies indicated no detectable viable mycobacteria. Several of the systems still had high levels of non-viable AFB. During a shut-down of the plant for scheduled vacation, the management employed a contractor to remove the non-viable mycobacteria and other contamination and installed a new permanent high-speed centrifuge and filter system. This reportedly changed air quality noticeably as reported by the employees working in the Department 455. Management also drafted a MWF management plan to guide future MWF maintenance.

Personal air monitoring data, conducted by the management, were reviewed. They revealed air levels to MWF well below the MIOSHA permissible exposure limit (PEL) for mineral oil mist and total particulates. Eight-hour time weighted average (TWA) breathing zone samples of two employees showed the presence of particulates with an average exposure concentration range of 0.48–0.56 mg/m^3 with a mean of 0.52 mg/m^3. Eight-hour TWA of one employee showed 0.051 parts per million of formaldehyde. Three other employees had TWA that ranged from 0.012 to 0.083 mg/m^3, mean of 0.044 mg/m^3 and median of

TABLE III. Review of MIOSHA Inspections of Auto-Part Production Plants A, B, and C, Michigan, 2003–2004

	Plant A	Plant B	Plant C
Plant type	Auto parts (braking systems)	Auto parts (driveline components)	Auto parts (various types)
Number of employees	1,350	1,135	340
Number of workers with respiratory illness	8	4	1
Type of MWF used	Semi-synthetic	Semi-synthetic	Semi-synthetic
Type of Ventilation system	General and local exhaust	Centralized exhaust system	Natural and local exhaust
Air monitoring data results[a]	Below PEL	Not obtained	Below PEL
Air monitoring conducted	No	No	Yes
MWF bio-sampling results[a]	*Mycobacteria immunogenum*	Mycobacteria	No bacteria or fungi detected.

[a]Reviewed from company records.

TABLE IV. Ingredients of MWFs and Biocides Associated With Outbreaks of Hypersensitivity Pneumonitis, Michigan 2003–2004

	Plant A	Plant B	Plant C
MWF #1	Multan EA20	Same as Plant A	CMX 501H
Ingredients	• Severely Hydrotreated Heavy naphthenic petroleum Distillates • Amine Salt • Amine Soap • Triethanolamine • Hexylene glycol • Sodium petroleum sulfonate • Ethanol, 2-(2-aminoethoxy)- • Amines • Triazene • Poly (oxy-1,2-ethanediyl), α-9-octa decenyl-w-hydroxy-, (z)-, phosphate		• Severely Hydrotreated Naphthenic petroleum Distillates • Monoethanolamine • Petroleum sulfonic acid, sodium salt • Monoisopropanolamine • Alkoxylated linear, alcohols
MWF #2	Multan 8305	—	Cimperial 1010
Ingredients	• 2-Amino-2-methyl-1-propanol • 2-(2-Aminoethoxy) ethanol		• Severely hydrotreated Naphthenic petroleum Distillates • Petroleum sulfonic acid, sodium salt • Nonylphenol ethoxylate • Sodium alkylbenzene sulfonate • Triethanolamine • Aminomethylpropanol
Biocide #1	Kathon 886 MW	Same as plant A	—
Ingredients	• 5-Chloro-2-methly-4-isothiazolin-3-one • 2-Methyl-4-isothiazolin-3-one • Magnesium nitrate • Magnesium Chloride • Water		
Biocide #2	Kathon CC	Busan 30B	—
Ingredients	• Kathon 886 MW stabilized with copper	• 2-(thiocyanomethylthio) benzothiazole • Ethylene glycol	

0.038 mg/m^3 for ethonalamine and diethanolamine. Review of the ventilation system designs noted that general and local exhaust ventilation (LEV) were being used in Department 455 and adjacent departments.

The final MIOSHA report recommended: maintenance of all air filters, ventilation control, and MWF spray enclosure systems as designed so as to minimize MWF exposure; monitor MWF for mycobacteria and treat as needed to prevent contamination; and a medical program to monitor employee health to identify any work-related respiratory illness.

Plant B

A Michigan Occupational Safety and Health Administration investigation was initiated at the plant in May 2004 in response to a referral from our clinic after we had evaluated Index Case 3 and confirmed the diagnosis of work-related HP. A report of the finding and recommendations was submitted in August 2004.

Plant B was an automotive supplier of driveline components and utilized machining, grinding, assembly, and heat-treating operations. The plant was unionized with a work force of 1,135 employees. The plant was a 750,000 square feet building on 100 acres of land with 40% of floor area involved in operations requiring MWF. The four employees (Index Cases 3, 4, 5, 6) had been diagnosed with HP. No other respiratory complaints were reported and a review of the ''Injury and Illness'' log from 2003 did not reveal any other employees recorded with a respiratory condition. Investigation was limited to departments 59/60, 61/62, and 64 from which the four cases of HP were reported. Two of the index cases were pipe fitters in Department 61/62, one was a machine operator in Department 61/62, and one was responsible for turn-around operations that involved tank cleaning. A total of 90 employees working in these departments were covered by the investigation.

Each of the departments was equipped with a central 50,000 gallon MWF coolant system containing Multan EA20, a semi-synthetic MWF as the primary MWF along with several additives including a biocide, fungicide, and other rust prevention chemicals. This MWF was recently introduced by the management in 2003 after routine cleaning of the reservoir. On report of the employee illness noted in 01/2004, management started its own investigation for potential problems and obtained biomass and MWF microbial samples from various departments. Elevated levels of mycobacteria were noted in the MWF reservoirs. Management requested the MWF manufacturer and a private consulting group to evaluate its MWF management practices. The MWF reservoir in Department 62 underwent multiple biocidal and fungicidal treatments, with Kathon 886MW biocide and Busan 30 B fungicide, respectively, as part of a ''priority cleaning plan.'' Repeat sampling after each treatment showed that elevated levels of mycobacteria had persisted. Also, mycobacteria growth was noted in one of the systems within 2 months after complete system cleaning and fluid change out. Management's investigation concluded that they needed to replace Multan EA20 with a suitable MWF; until a suitable replacement was found, each of the MWF systems needed to be treated appropriately with anti-microbial agents; and they needed to conduct frequent evaluation of the work environment with regards to employee health and safety. The report of the MIOSHA investigation agreed to the steps being taken by the management for managing MWF-related practices.

The ventilation systems were reviewed in all the departments. Each department, which was originally equipped with a centralized ventilation exhaust system, was undergoing a ventilation upgrade at the time of investigation. This upgrade consisted of equipping the machine operations and MWF system with HEPA filter-equipped LEV system which would re-circulate the filtered air back into the plant. Air monitoring data were not reviewed and no air monitoring was performed as part of the MIOSHA investigation.

Plant C

A MIOSHA investigation was initiated at the plant in May 2004 in response to a referral from the occupational disease surveillance system where an employee (Index Case 7) of the company was diagnosed with HP. A report of the findings and recommendations was submitted in July 2004.

Plant C manufactured disc converter clutches, steering and suspension components, and differentials. The facility covered an area of 300,000 square feet with a unionized work force of 340 employees. The plant used water-based MWF in the Transfer area, VCC area, and Gears area. Index Case 7 was working on K-lines of the Gears area when he was diagnosed with HP. The Gears area had 20 employees per shift for a total of 62 employees most of whom worked as machinists. No other respiratory complaints were reported and a review of the ''Injury and Illness'' log from 2003 did not reveal any other employees recorded with a respiratory condition. Investigation was limited to these departments of the plant where MWF was used. Two hundred and thirty-five employees were covered by the inspection.

Each of the department had a different reservoir with 3,000–5,000 gallons of MWF for each of the assembly lines. A semi-synthetic MWF, CMX501H, was used in the gears area. Air monitoring for oil mist, previously performed by the company, was reviewed and the results were well below the MIOSHA PEL. Personal air monitoring for oil mist was conducted on two employees each in the Gears area. The mean and range of average exposure to MWF was 0.12 mg/m^3 and 0.10 mg/m^3 to 0.14 mg/m^3, respectively. Air monitoring data for the VCC area that was using a different

MWF, Cimperial 1010, were also reviewed. Personal air monitoring was conducted for two employees with no violations seen in this area. The range of average exposure to triethanolamine was 0.005 mg/m^3 to less than 0.02 mg/m^3. The company was routinely managing their MWF with weekly sampling of MWF for mold, bacteria, oil concentration, and pH. The company was using a centrifuge to coalesce and filter the fluids. Different biocides were used to treat the MWF reservoirs.

The ventilation system was reviewed and the company was found to be using natural ventilation and LEV with a Torrit system to collect oil mist. Most of the machines were fully enclosed and were only being opened for switching parts. Two employees were interviewed who did not complain of any respiratory illness and mentioned that air quality has improved significantly since the company had introduced LEV.

Recommendations to management at the end of the investigation were: continued air monitoring to monitor concentrations of MWF; and regular and routine monitoring for mycobacteria.

DISCUSSION

Seven patients who developed work-related HP secondary to MWF exposure at three auto-parts manufacturing facilities over a period of 9 months starting in the summer of 2003 to early 2004 are described. All of the affected employees had worked in a machining environment for many years before they developed HP. No cases of HP before this time period have been recognized from these three facilities. One additional case of HP was reported from plant B in the fall of 2005.

To our knowledge, this is the first outbreak of HP reported from MWF exposure since 2001. Previous reports about HP have recommended the need of active surveillance and public health reporting of this disease for a better understanding of the disease process. Is HP due to MWF, a disease that occurs sporadically or is it continuously occurring but is misdiagnosed and/or underreported? A plausible explanation for the apparent sporadic occurrence of HP cases is that other outbreaks occur but patients are commonly misdiagnosed as having an atypical pneumonia, which has a similar clinical and radiographic presentation. Most of these patients are started on antibiotics as was seen in our cases and most of them are taken off work during the period they are acutely ill. During this time, the patient is not exposed to the inciting agent, the disease process abates, and the patient's symptoms improve. Meanwhile, changes at the patient's work place, such as addition of biocide, cleaning of tanks, or introduction of improved ventilation systems may occur. If and when the patient goes back to the same job, the patient is no longer exposed to the inciting agent and the incorrect diagnosis of atypical pneumonia remains. Physicians need to be more aware of HP as a differential diagnosis of interstitial pneumonia particularly in patients with certain jobs (e.g., machinists). In other situations, the physician may make a correct diagnosis but the case is not reported and therefore not recorded in surveillance systems or eventually written up in the medical literature. Despite recommendations from Federal safety agencies [NIOSH, 1998a,b], most facilities that use MWF are not performing periodic medical screening of workers exposed to MWF. When workers from these facilities become ill, they seek medical care from their personal physicians who often do not ask about nor consider the patient's occupational history and the patient's symptoms are attributed to a respiratory tract infection. The diagnosis of HP is much less likely to be missed if the possibility of an occupational or environmental cause is routinely considered in the differential diagnosis of all patients with a respiratory problem. The outbreaks reported in this article was recognized after a number of patients were sent to the same physicians and some of these physicians reported the cases to the State's occupational disease surveillance system. The fact that these cases occurred in small communities where the number of physicians available was less than in a larger urban setting contributed to the fortuitous recognition of this outbreak. Additionally, even though the Michigan surveillance system is incomplete; most states do not have as active a surveillance system for occupational diseases as the one in Michigan. The surveillance system in Michigan publishes a quarterly newsletter for physicians, has display booths at State medical meetings and provides a medical speaker for continuing medical education venues around the State [Rosenman et al., 1997].

A second explanation is that HP cases are truly sporadic and that a change at the facilities allowed the growth of certain organisms that cause HP. In two of the three plants from where six of the seven cases were reported, a new MWF was introduced. Co-incidentally, the new MWF introduced at the two plants was the same MWF. Was this the change that led to HP in at least two of these outbreaks? High levels of mycobacteria were found in the MWF sumps at these two facilities. Mycobacteria have been previously suspected to be the probable agent causing MWF-related HP [Muilenburg et al., 1993; Zacharisen et al., 1998; Shelton et al., 1999; Wallace et al., 2002], although occult microbiologic contamination of MWF with *Mycobaterium immunogenum* with no associated cases of HP has also been reported [Khan et al., 2005]. Despite changes in ventilation, the use of additional biocides and purging and cleaning of the systems, a single additional case of HP has recently been recognized from one of these facilities. No changes in MWF or work practices were known to have occurred prior to the development of HP at the third plant. The recognition of the case from the third facility is better explained by awareness in the physician community after the occurrence of the first two outbreaks.

In the cases described above, only two out of the seven patients returned to work. The other cases did not return to work because of concern about recurrence of their symptoms. The two patients who returned to work have not had recurrence of their symptoms. One has been working approximately 20 feet from where MWFs are used while the other works in an adjoining building around different MWFs. An issue that has been contested is whether cases of HP related to MWF should return to there workplace. Allowing a worker to return to the same workplace is risky given the uncertainty of what occurred in the plant that precipitated the disease and whether the corrective changes implemented corrected the problem(s). Despite this uncertainty some have suggested that people with HP may return to work after resolution of symptoms and normalization of pulmonary function and radiography if close medical monitoring, including frequent PFTs that includes measurement of diffusion capacity, is provided to check for recurrence of the disease. Providing close medical follow-up for returning HP patients is difficult in the typical facility using MWFs since most of these employers are not providing an ongoing medical surveillance program.

Occupational Safety and Health Administration investigations at all three sites found aerosol and oil mist exposures well below the current MIOSHA and OSHA PEL. Still, HP occurred in individuals who worked at these three sites. OSHA requirements either do not address the important elements needed to prevent HP, such as containing the microbial growth in MWFs or the PELs are too high to prevent the disease. The usefulness of a typical MIOSHA investigation to follow-up these cases in the workplace depends on the experience and expertise of the investigating industrial hygienist and is limited by the high costs of the investigations, particularly environmental and microbial sampling. The results of the investigations conducted were of insufficient scope to explain the cause of the outbreaks in the three facilities or why they ended.

The question remains: How to prevent HP secondary to MWFs? This is difficult to ascertain in view of the unclear etiology and sporadic recognition of this disease. Suggestions for preventing the disease have been compiled by OSHA in the Best Practices Manual [OSHA, 1999]. Several attempts with improvement of air quality and treatment of MWFs have been undertaken to prevent HP as discussed above. Experience with these efforts is limited and benefits of these remain to be seen. As mentioned above, we have recently been made aware of at least one new definite case of HP at one of the investigated plants that had implemented changes in ventilation and management of MWFs.

In summary, this report reinforces the need for continued surveillance for detecting MWF-related HP by users of MWFs in view of the limited consideration in the differential diagnosis of this condition by clinicians in the community and a clinical presentation similar to other common conditions. Employees, employers, and physicians in communities where MWFs are used should be educated and made aware of the possibility of this condition. Better enumeration of the number of individuals who develop HP and thorough workplace follow-up of the cases of HP would help to better understand the specific factors related to the development and prevention of this condition.

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