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Metal Fume Fever: A Review of the Literature and Cases Reported to the Louisiana Poison Control Center

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Metal fume fever (MFF) is an important occupational-related illness resulting from inhalation of volatile metal oxides, especially zinc, that are produced during welding or cutting of metal materials. Onset of MFF is rapid, occurring within a few hours after inhalation of the fumes. Symptoms include fever, chills, cough, dyspnea, headache, myalgia, and malaise. Symptoms are self-limiting and typically resolve within 24 hours with a subsequent short-lived tolerance to zinc oxide fumes that disappears after one to two days of avoidance. In this report, we present an overview of MFF's history, pathogenesis, clinical presentation, regulatory guidelines, and prevention recommendations. This review is followed by a description of MFF cases reported by the Louisiana Poison Control Center to the Louisiana Office of Public Health's Section of Environmental Epidemiology and Toxicology during a two-year period.

INTRODUCTION

Exposure

Metal fume fever (MFF) is an occupational disease caused by the inhalation of metal oxides, primarily zinc oxide. It was first described in the mid-1800s among brass foundry workers and in the early 1900s in welders of galvanized steel.[1] Over the years, it has been known by a variety of names, including Monday fever, brass founders' ague, smelter chills, welder's ague, and zinc shakes.[2]

The main sources of exposure are breathing fumes from welding, heating, or cutting galvanized metal. Galvanized metal is steel in some form that has received a thin coating of zinc oxide. Zinc is used to protect the steel from elements that normally lead to oxidation, corrosion, and the eventual weakening of the steel. Due to the increased use of galvanized steel in many industries (eg, construction, shipping, mining), workers engaged in tasks that involve the heating or welding of galvanized materials are at risk of exposure to zinc oxide fumes. Zinc is also used in the manufacture of brass and various other alloys. Although exposure to zinc oxide is the most common metal associated with MFF, other metals like copper, magnesium, manganese, nickel, titanium, chromium, boron, and arsenic are also reported to produce the syndrome.[1]

MFF occurs most commonly in welders. It is estimated that 1,500 to 2,500 cases of MFF occur annually in the United States.[2] In 2006, there were approximately 700 metal fume exposures reported to US Poison Control Centers. Approximately one third of these cases sought medical treatment.[3]

Symptoms

The symptoms of MFF are generally nonspecific flu-like complaints including fever, chills, nausea, fatigue, muscle ache, and joint pain. The onset of MFF symptoms is rapid, occurring three to 10 hours after inhaling the metal. The initial symptoms may include a sweet metallic taste associated with throat irritation, dyspnea and thirst followed by chills, a low-grade fever, myalgia, arthralgias, malaise, fatigue, and a nonproductive cough.[4,5] These symptoms may be accompanied by excessive sweating and shaking chills.[1] Occasionally nausea, vomiting, and headache are present.[4] The symptoms are self-limiting and resolve within 24 to 48 hours, with subsequent short-lived tolerance to zinc oxide fumes that disappears within one to two days after avoidance of exposure.[1,5,6,7] It often takes four days to recover fully.

Diagnosis

Since MFF resembles influenza or acute lung injury, it is often misdiagnosed. There is no specific diagnostic test available for MFF, so a work history is essential for an accurate diagnosis. A sweet or metallic taste may be reported along with a dry throat.[8] Serum, urine, plasma, and skin zinc levels may be elevated as well.[9] Patients may also exhibit increased white blood cell counts (leukocytosis). The routine diagnostic tests, such as chest X-ray, pulmonary function tests, and arterial blood gas usually show normal results.[7,9,10] In severe cases, transient X-ray infiltrates, decrease in lung volume, and diffusing capacity of lung for carbon monoxide have been observed.[6] A detailed work history can identify work activities such as welding, heating or cutting galvanized metal that indicate exposure to metal oxide fumes. Diagnosis is primarily based on an exposure history and the timing of the onset of symptoms following exposure to metal fumes.

Long-Term Effects

There is little information in the literature regarding the long-term effects or complications of zinc oxide fume exposures.[5,8,11] It has been hypothesized, but not proven, that MFF may lead to later occurrences of occupational asthma.[8] However, it remains unclear if the symptoms associated with MFF resolve without damage to the lung or if repeat episodes of MFF may lead to pulmonary impairment. One study examining the respiratory effects of welders over a three-year period concluded that welding was associated with reversible respiratory symptoms and small across shift reductions in lung function. Due to no increase in airway reactivity, the authors concluded that exposure to welding fumes is unlikely to result in significant chronic effects on lung function.[2]

It has been reported that chronic exposure to extremely high concentrations of zinc oxide fumes or dust for more than six months may lead to the development of dermatitis, boils, conjunctivitis, and gastrointestional disturbances.[12] In some of these reports, however, exposures to other chemicals were likely.

Underlying Mechanism

The exact pathogenesis of MFF, though unknown and poorly understood, is thought to involve a cytokine-mediated immune response.[2] Increased levels of TNF-α, IL-6, and IL-8 have been found in the lungs of exposed individuals, and cumulative data suggest these increased levels likely result from direct stimulation of the resident pulmonary macrophages by the metal fume.[2] TNF-α is thought to play a pivotal role in the onset of MFF as it is elevated in the initial stages, whereas IL-6 and IL-8 are likely involved at later stages.[3] Exposure to zinc oxide fumes also causes an exposure-dependent neutrophilic infiltration into the airway.[2] This infiltration may further contribute to the pathogenesis of MFF through a mechanism involving oxidative damage.[13]

The mechanism underlying the short-lived tolerance associated with MFF is also poorly understood. One hypothesis suggests increased expression of metallothioniens following metal fume exposure protects against metal toxicity through sequestration mechanisms and scavenging of free radical species.[14] Metallothioniens are proteins that bind strongly to metals, and induction of metallothionein genes following metal exposure is a common cellular response in most animal and human tissues.[15]

Treatment and Prevention

Treatment of mild MFF consists of bed rest and symptomatic therapy (eg, analgesics, oxygen therapy, and antipyretics) as indicated. Corticosteroids have not been shown to be of any benefit.[5,9] Prevention of MFF in workers

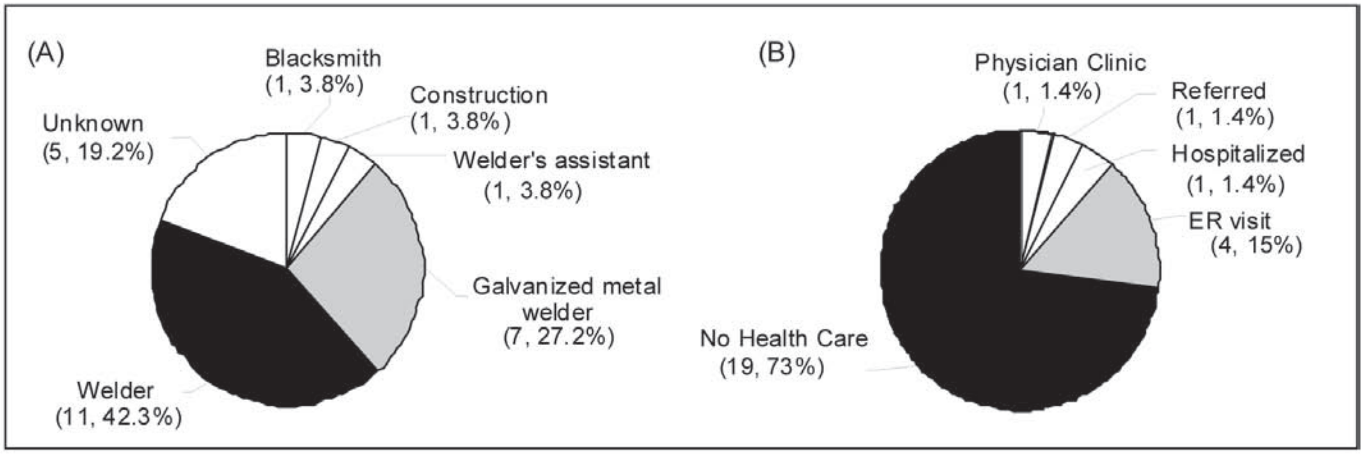

Figure 1. The distribution of cases of metal fume fever reported to Louisiana Poison Control Center by occupation (A) and healthcare management (B) are shown. The number of reported cases and the percent of the total are given.

who are at risk (such as welders) involves avoidance of direct contact with potentially toxic fumes, improved engineering controls (exhaust ventilation systems), personal protective equipment (respirators), and education of workers regarding the features of the syndrome itself.

For the safety and protection of workers, the Occupational Safety and Health Administration (OSHA) has set a legal limit of five milligrams of zinc oxide fume per cubic meter of air (mg/m^3) averaged over an 8-hour work shift. The National Institute for Occupational Safety and Health (NIOSH) recommends 5 mg/m^3 averaged over a work shift up to 10-hours per day, 40-hours per week, with a short-term exposure limit of 10mg/m^3 averaged over a 15-minute period. The American Conference of Governmental Industrial Hygienists set the time weighted average of 2 mg/m^3 for an 8-hour workday and 40-hour workweek.[16]

Surveillance Data

To evaluate the occurrence of MFF among Louisiana workers, an evaluation of calls made to the Louisiana Poison Control Center (PCC) reporting MFF was conducted. Cases are defined as a PCC call regarding an individual who developed MFF following a workplace exposure. The study reviewed reports from a 2-year period: March 2004 to March 2006. When available, supplemental information about the cases was obtained from medical records.

Variables analyzed included demographics, source of call, occupation/industry, healthcare utilization, and health effects. Industry and occupation were coded using the *2000 Census of Occupation and Industry Codes*. Industry and occupation are not routinely coded by poison centers. Capturing this information was accomplished through a variety of methods: searching for the worksite telephone number; reviewing medical records for payor or insurance information; and gleaning information from the PCC case-report narrative. Microsoft Access was used for data management, and Microsoft Excel was used for data analysis. Descriptive statistics were computed to determine the frequency and percentage of cases by each variable.

During the 2-year period, 26 cases of MFF were reported to the Louisiana Poison Control Center. All of the cases involved males ranging in age from 20 to 65 years (mean = 37.2; SD = 12.6). Fifty percent of the cases (n=13) were reported to the PCC by someone other than the patient, such as a relative or co-worker. Cases were predominantly located in the southern part of the state (n=20, 77%). The most commonly reported occupation was welder (Figure 1A). Thirteen cases (50%) involved individuals working with galvanized metal or pipes. Information on respirator use was not specifically collected by the PCC specialist, although four cases indicated that they had not worn a respirator. Several cases stated they were working in a confined space. For example, one patient reported that he was assisting with a pipe-cutting task while inside the pipe that was being cut.

Seventy-three percent of the cases did not seek any medical treatment other than the PCC consultation (Figure 1B). Of the six cases who sought medical care, one was hospitalized, four were treated in an emergency room, and one was treated at a physician's office. One case was referred for medical treatment by the PCC, but it was unknown if treatment was received. Cases reported 17 different symptoms; number of reported symptoms ranged from one to seven (mean = 2.6; SD=1.5). The most commonly reported symptoms are shown in Figure 2 and include fever/hypothermia, pain, body aches, and nausea/vomiting.

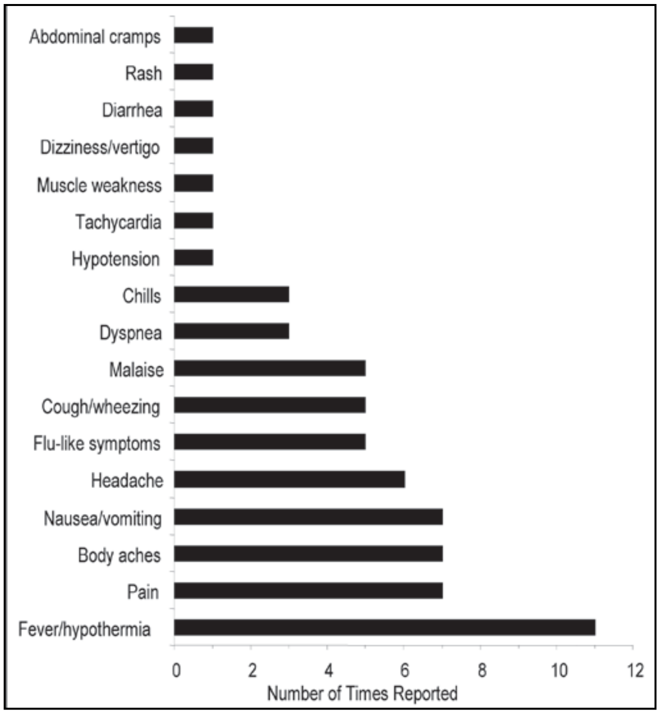

Figure 2. Frequency of symptoms reported to the Louisiana Poison Control Center by patients with metal fume fever.

CONCLUSION

MFF is the most frequently described occupational systemic illness in welders. Unfortunately, its diagnosis is easily overlooked due to the non-specific flu-like symptoms. Symptoms linked to a detailed occupational history are critical for accurate diagnosis and disease management. Preventing MFF in at-risk workers involves avoiding direct contact with metal fumes through engineering controls (exhaust ventilation systems), use of personal protective equipment (respirators), and education about safe work practices when cutting, welding, and heating steel and other metals. Increasing worker and physician awareness of MFF may help reduce its occurrence.

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