

Asthma, hypersensitivity pneumonitis and other respiratory diseases caused by metalworking fluids

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Purpose of review

To highlight advances in understanding the respiratory disease associated with metal machining, a common work process involving approximately 1.2 million workers in the USA.

Recent findings

Recent studies emphasize that work-related asthma and hypersensitivity pneumonitis continue to be caused by exposure to metalworking fluid. Identification of an individual patient indicates the need for follow-up investigations at the work site to prevent additional disease and/or identify additional effected individuals. Identification of the causal agent for hypersensitivity pneumonitis has centered on microbial contamination of metalworking fluids with a number of studies focusing on *Mycobacterium immunogenum*.

Summary

Both asthma and hypersensitivity pneumonitis occur among workers exposed to metalworking fluid. The incidence of these diseases among such workers is unknown. Outbreaks of these conditions continue to be identified among metal machinists. Whether these are true outbreaks associated with some breakdown in workplace controls or, rather the recognition of ongoing endemic disease that is typically misdiagnosed as pneumonia or common adult onset asthma, needs further evaluation. Further work to elucidate the specific causal agent(s) is necessary to affect effective workplace controls. Treating an identified individual case as an index case with a follow-up workplace investigation will only be possible if practicing physicians interact with public health authorities to report newly diagnosed cases.

Keywords

asthma, hypersensitivity pneumonitis, metalworking fluid, *Mycobacterium immunogenum*

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Introduction

Metalworking fluid (MWF) is used in the machining and shaping of metal parts. Table 1 summarizes the work processes and respiratory conditions that have been associated with MWF. Both obstructive disease – asthma and chronic bronchitis – and restrictive disease – hypersensitivity pneumonitis – occur from exposure to MWF. With increased automation and substitution with alternative materials, the throughput of metal parts being processed has increased in the last 30 years, and without simultaneous changes in engineering and ventilation controls had the potential to increase worker exposure, although to a smaller number of workers. For example, the increase in the use of water-based synthetic MWFs as an alternative to the straight oil MWFs is presumably an important factor for the repeated outbreaks of hypersen-

sitivity pneumonitis, which were first recognized in the mid-1990s [1,2].

Workers with exposure to MWF are generally in the manufacturing sector. Like other blue-collar workers, they generally have a higher prevalence of cigarette smoking than the general population. This increased prevalence of smoking in conjunction with workplace exposures will increase the likelihood of chronic bronchitis and irritant symptoms more so than if the group only smoked cigarettes or only had the workplace exposures. On the contrary, the trend over time of a decreasing prevalence of cigarette smoking in this population as in the general population may be a contributing factor in the increased recognition of hypersensitivity pneumonitis since the development of hypersensitivity pneumonitis is rare in cigarette smokers.

Table 1 Work processes, exposures, and respiratory conditions with exposure to metalworking fluids

Work process	Exposure	Respiratory conditions
Machining	MWFs	Asthma, bronchitis, hypersensitivity pneumonitis, irritative symptoms, laryngeal cancer, rhinitis
Forging/ stamping	Drawing compounds	Asthma, bronchitis, hypersensitivity pneumonitis, irritative symptoms, laryngeal cancer, rhinitis

MWF, metalworking fluid.

Work processes

The work processes that use MWF are metal machining, forging, and stamping. The current US OSHA standard is 5 mg/m³ despite recommendations in 1998 from the National Institute for Occupational Safety and Health and in 1999 from an OSHA Metal Working Standard Advisory Committee that the allowable level be reduced to 0.5 mg/m³. A 2007 study from Pennsylvania demonstrated readily available engineering and work processes to meet the lowered proposed standard [3•] and two 2008 surveys of industries in Finland and Sweden showed that companies in these countries were below the even lower air standard of 0.2 mg/m³ [4,5]. The American Conference of Governmental Industrial Hygienists has recommended a threshold limit value of 0.2 mg/m³.

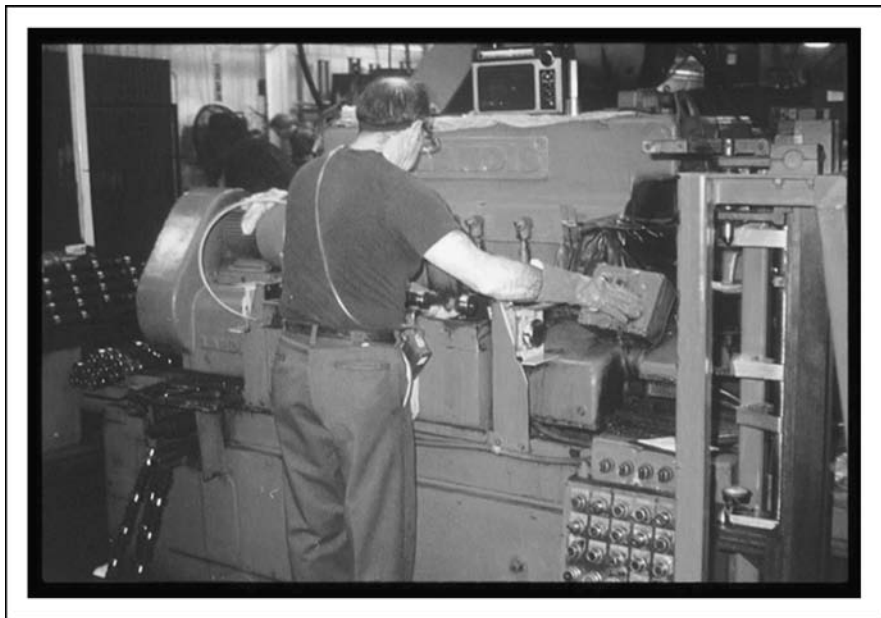
Metal machining

Although plastic has been substituted for many metal parts, machining of metal parts remains a common activity. An estimated 1.2 million workers in the USA do machining

with MWF (NIOSH Metalworking Fluids website, <http://www.cdc.gov/niosh/topics/metalworking/>). Metal pieces need to be cut, drilled, shaped, and smoothed. In order to facilitate this machining, MWFs are used. Alternative names include metal removal fluids, cutting oils, lubricants, machining fluids, and coolants. A patient is most likely to refer to them as coolants, although their primary properties are actually to remove metal particles, protect or treat the surface of the metal being machined, and prolong the life of the machining equipment. Figure 1 shows a machining operation with MWF being used.

There are four types of MWFs: straight (mineral oil, natural, neat), emulsified, semisynthetic, and synthetic fluids. Straight fluid as the name implies is 100% petroleum oil and generally is what was used prior to the 1970s. Water-based oils are now more commonly used; emulsified oil is an emulsion of mineral oil and water; semisynthetic fluids, which contain smaller amounts of mineral oil than the emulsified oils; and synthetic oils, which contain no mineral oils. The three types of nonstraight MWFs are water-based products and corrosion inhibitors as well as dyes and biocides to inhibit microbiological growth are added to these fluids. Typically, these fluids are collected in sumps around the machining operations and repeatedly reused in the machining process after the metal particles are filtered out. Specific personnel are designated to check the pH, assess the biological content, and put in additives in response to the sampling results. These fluids are not sterile and with repeated use multiple organisms grow in the fluids and in biofilms on pipes, and containers. These biofilms, which are an accumulation of microorgan-

Figure 1 Worker machining metal part in an auto part manufacturer



isms (bacteria, fungi, and/or protozoa, with associated bacteriophages and other viruses), embedded in a polysaccharide matrix and adherent to the surfaces of pipes and containers, make it very difficult to eliminate particular microorganisms.

Forging/stamping

Similar to machining, MWFs, called drawing compounds, are used when cold rolled steel is stamped out into metal parts (stamping) or compressive force is used on heated metal to form metal parts to conform to the shape of dies (forging). Both processes use drawing compounds, as forging generally involves heated metal, pyrolysis, and volatilization of the drawing compound is likely to increase the potential for exposure.

Specific respiratory conditions

Recent investigations have been focused on hypersensitivity pneumonitis occurring with MWF exposure, although the incidence of asthma from exposure to MWF is at least equal if not greater than that of hypersensitivity pneumonitis [6^{••}].

Work-related asthma

In two population-based surveillance systems, MWF is the second most common cause of work-related asthma [7,8]. In a 2008 study from the West Midlands of England, MWF was the cause of 11% of the reported work-related asthma with the most frequent cause of work-related asthma being the isocyanates at 21% [7]. These results are similar to those from a 2007 study from Michigan where MWF was the cause of 11% and the isocyanates of 14% of the work-related asthma cases [8]. These results are in contrast to a 2007 study from Finland that found that although occupational skin disease was increased in machinists, respiratory disease was not [9]. These low rates of respiratory diseases in Finland may be secondary to the more stringent workplace controls discussed in the section on work processes [4].

Although microbiological contamination of nonstraight MWFs has been associated with outbreaks of hypersensitivity pneumonitis and there are concurrent cases of work-related asthma during these outbreaks [6^{••}], the causal agents for work-related asthma that have been documented with specific antigen bronchoprovocation antigen testing have all been chemicals. There have been no recent studies that have provided data to support or refute the role of microbiological contamination of MWF rather than a chemical constituent as being the cause for work-related asthma.

Case reports of work-related asthma documented by specific antigen bronchoprovocation testing have been reported with both used and unused emulsified MWF [10,11]. Tall oil, a derivative of pine rosin, was deter-

mined to be the causal agent in one of the studies [10]. A common component of the water-based MWFs, an ethanolamine compound, has also been shown by specific antigen bronchoprovocation testing to cause work-related asthma [12]. Studies of cross-shift changes in FEV₁ have reported the largest response among workers exposed to the semisynthetic and synthetic MWFs [13,14]. Similarly, a higher frequency of symptoms and prevalence of work-related asthma was associated with the semisynthetic and synthetic MWFs [15].

The diagnosis of work-related asthma from MWFs is similar to the diagnosis of work-related asthma from other chemicals. A new consensus statement from the American College of Chest Physicians is an excellent resource for both diagnosing and managing work-related asthma [16^{••}]. Healthcare providers need to inquire about a patient's employment at the time of onset of their asthma. A temporal association of symptoms during the day or at night after work with improvement on weekends and vacations is a sensitive but nonspecific finding. Unfortunately, however, this sensitive screening for work-related asthma is often overlooked. It has been consistently reported that physicians fail to document and presumably fail to ask about their patient's work and whether their patient's symptoms are associated with work. Collecting pulmonary function testing in conjunction with the patient's work allows the clinician to perform a natural challenge test, given the general unavailability of a laboratory which will perform specific antigen bronchoprovocation testing. With chronic exposure the patient may lose the temporal pattern and even with prolonged removal from work may continue to be symptomatic [16^{••}]. Early diagnosis and removal from exposure is the best predictor of which patients will either have complete remission of their asthma or be less likely to have progression of their disease defined as having more symptoms, requiring more medication, or developing lower FEV₁s. No skin tests nor IgE and IgG antibody testing is available from commercial laboratories for the MWFs or their components. The absence of a positive methacholine challenge in a patient currently exposed to MWFs is highly suggestive that the patient does not have asthma but an alternative diagnosis such as irritative symptoms or vocal cord dysfunction [16^{••}].

Hypersensitivity pneumonitis

Hypersensitivity pneumonitis from exposure to MWF was first reported in the mid-1990s in a facility in Michigan that manufactured auto parts [1]. A dozen or more outbreaks have subsequently been reported in the literature with most studies from auto or auto parts manufacturing facilities [2,6^{••},17–22]. The initial outbreak involved six patients. Antibodies to pseudomonas were identified in the cases of this initial study. The most recent outbreak was reported in 2007 from an auto engine

manufacturing facility in England [6^{••}]. In this latest outbreak, 19 individuals met the case definition for hypersensitivity pneumonitis and 74 for work-related asthma. Eight met the criteria for both conditions. Seven also met the case definition for 'Humidifier fever', which was defined as recurrent flu-like symptoms worse on the first day back to work after a break but no pulmonary function or radiographic changes. In this latest outbreak, workers had antibodies to actinobacter, or ochrobactrum that had been cultured from the used MWF. No cultures or antibodies were found for mycobacterium species, although in other recent outbreaks, *Mycobacterium immunogenum* has been the most common suspected microbiologic causal agent that has been identified [2,19,22–25]. Both live and heat-killed and lysed *Mycobacterium* cause hypersensitivity pneumonitis in mice [26,27]. The use of the biocide triazine as an additive in MWF has been associated with mycobacterial contamination [28]. However, the picture is not straightforward because as with the most recent outbreak from England [6^{••}] there have been other outbreaks when *M. immunogenum* has not been found [2,17] and *M. immunogenum* has been found in MWF in facilities without cases of hypersensitivity pneumonitis [29]. *M. immunogenum* is difficult to culture and identify from MWF and three publications from 2008 identify more sensitive methods involving PCR or fluorescence microscopy [30,31[•],32]. These more sensitive methods were not used in the two studies reported above that did not detect *M. immunogenum* [6^{••},17].

Patients with hypersensitivity pneumonitis have symptoms of cough, dyspnea and fever, ground glass opacification on their HRCT, and restrictive changes on spirometry and plethysmography and decreased diffusing capacity. Patients suffering from hypersensitivity pneumonitis are usually nonsmokers. An in-vivo study in mice and an in-vitro study in a mouse cell line have shown that nicotine inhibited alveolar macrophages and the inflammatory response [33]. The other factor known to influence the development of hypersensitivity pneumonitis is pregnancy. The most common cause of microchimerism, which is the persistence of foreign cells in an individual, is pregnancy with the persistence of fetal cells. Microchimeric cells have been associated with autoimmune diseases. A study in 2007 of 175 women, who had all been previously pregnant, found that the 103 women with hypersensitivity pneumonitis from exposure to pigeons had an increase in the presence of male fetal cells in their lungs versus 43 healthy control women and 30 women with idiopathic fibrosis, even though the idiopathic pulmonary fibrosis (IPF) women had delivered more sons [34]. Although this study did not involve MWF, it is potentially relevant to women who work as machinists.

Respiratory symptoms and radiograph changes will clear and pulmonary function changes will markedly improve

over a period of months if the patient is removed from exposure soon after the onset of symptoms. If the patient is not removed from exposure, then fibrosis and increased respiratory symptoms are increasingly likely to occur as the exposure continues and the symptoms and radiographic changes are less likely to clear after removal from exposure.

The sporadic nature of these outbreaks has remained perplexing. Are there truly outbreaks associated with overgrowth of certain microbiological species or are there endemic, ongoing cases that are misdiagnosed as atypical pneumonia. Individual case reports including one in 2008 as well as outbreaks involving multiple cases also appear in the medical literature [35,36[•]]. If during the time the patient is off work, changes are made to the worksite such as cleaning tanks, replacing all the MWF with new unused MWF, or addition of a biocide so that when the patient returns to work the causal biological agent is not present, or present in a much lower concentration; the fact that the patient was misdiagnosed with atypical pneumonia may never be recognized. Typically, when an outbreak is identified, changes in the use of the MWF as described above are instituted as well as improvements in ventilation controls. The actual workplace changes that cause the outbreak to end have not been identified since multiple interventions are typically instituted at the same time.

Increased automation of machining with faster machines causing more aerosolization and increased use of water-based MWFs is the presumed reason that hypersensitivity pneumonitis was not recognized in association with this work process until the 1990s. Microbial growth does not occur in straight oil and hypersensitivity pneumonitis has not been reported in machining operations in which only straight oils are used. The current US OSHA standard for oil mist of 5 mg/m³ is not sufficiently protective to prevent hypersensitivity pneumonitis when emulsified or semisynthetic MWFs are used or relevant to microbiological contamination.

Irritative symptoms/chronic bronchitis

Exposure to water-based MWF is associated with respiratory symptoms, bronchitis, rhinitis, and doctor visits for respiratory symptoms [15,35,36[•],37–40].

Cancer

There are studies reporting a cancer risk from exposure to natural (straight) MWFs (mineral oils), with the best evidence of an association between MWFs and cancer being for laryngeal cancer and the nonrespiratory cancers of bladder, pancreas, rectum, scrotum, and skin [37].

Other respiratory conditions

Historically, there have been case reports of lipoid pneumonia among individuals working around straight MWF. Current exposures to the straight oils are usually too well

controlled and the synthetic oils do not contain petroleum products to cause this condition. Another condition of historical interest is Pontiac fever, an influenza-like condition that was reported in an engine-manufacturing plant using water-based MWF. Patients had antibodies to a species of legionella but no evidence of pneumonia [37]. Although theoretically possible, there are no studies that indicate an increased risk of pneumonia among individuals who work with MWF contaminated with microbiological agents. Endotoxin, which is produced by the Gram-negative bacteria commonly found in MWF, has been associated with flu-like symptoms without radiographic or pulmonary function changes. This is the presumed cause for the 'Humidifier fever' cases described in the recent outbreak in England [6**].

Conclusion

Exposure to the common MWF currently used in industry causes both work-related asthma and hypersensitivity pneumonitis. Recent work has concentrated on the presumed relationship between the microbiological contamination of MWF with *M. immunogenum* as the cause of hypersensitivity pneumonitis. The best documentation for the cause of work-related asthma and MWF is for the chemical constituents rather than a microbial contamination. However, when outbreaks of hypersensitivity pneumonitis occur, there has been a simultaneous recognition of work-related asthma, which suggests the same microbiologic agent is responsible for both diseases at least during outbreaks.

Clinicians need to consider whether their adult patients with asthma or suspected community-acquired pneumonia who may really have hypersensitivity pneumonitis have exposure to MWF. The recognition of the association of asthma and/or hypersensitivity pneumonitis with MWF is very important in treating a patient since removal from exposure is the most effective treatment modality. Additionally, this recognition of an association in an individual patient has significant public health importance. Follow-up at the work site by public health authorities of this patient is important to both identify and prevent additional cases as well as to further elucidate the specific causal agent(s) and work processes that cause these conditions.

References and recommended reading

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- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 178).

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