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Pulmonary Effects of Welding Fumes: Review of Worker And Experimental Animal Studies

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Background *Approximately one million workers worldwide perform welding as part of their work duties. Electric arc welding processes produce metal fumes and gases which may be harmful to exposed workers.*

Methods *This review summarizes human and animals studies which have examined the effect of welding fume exposure on respiratory health. An extensive search of the scientific and occupational health literature was performed, acquiring published articles which examined the effects of welding on all aspects of worker and laboratory animal health. The databases accessed included PubMed, Ovid, NIOSHTIC, and TOXNET.*

Results *Pulmonary effects observed in full-time welders have included metal fume fever, airway irritation, lung function changes, susceptibility to pulmonary infection, and a possible increase in the incidence of lung cancer. Although limited in most cases, animal studies have tended to support the findings from epidemiologic studies.*

Conclusions *Despite the numerous studies on welding fumes, incomplete information still exists regarding the causality and possible underlying mechanisms associated with welding fume inhalation and pulmonary disease. The use of animal models and the ability to control the welding fume exposure in toxicology studies could be utilized in an attempt to develop a better understanding of how welding fumes affect pulmonary health.* Am. J. Ind. Med. 43:350–360, 2003. *Published 2003 Wiley-Liss, Inc.*†

KEY WORDS: welding fumes; lung toxicology; animal studies; human studies; literature review

WELDING PROPERTIES AND FUNCTIONS

Welding Uses and Processes

Electric arc welding joins most metals and alloys that have been made liquid by heat produced as electricity passes from one electrical conductor to another [Howden et al., 1988]. Extreme temperatures in the arc heat the base metal pieces to be joined and the filler metal of a consumable electrode wire. The majority of the formed welding fume comes from the electrode or wire rod which is volatilized during the process [Palmer and Eaton, 2001]. The base metal, electrode coatings, shielding gases, fluxes, and paint or surface coatings also may contribute to the formation of the welding aerosol. The vaporized metals react with air, producing metal oxides which condense and form respirable-sized fume which is likely to be deposited in the alveolar regions of the lungs. Electron microscopy analysis of welding fume has revealed that individual particles aggregate together during generation to form longer chains of primary particles [Clapp and Owen, 1977]. This agglomeration is enhanced by the high temperatures and turbulent conditions generated during the welding process. Studies on welding

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fume have observed the individual particles to fall in the ultrafine size range of 0.01–0.10 μm [Villaume et al., 1979]. Importantly, ultrafine-sized particles in general have been observed to induce greater pneumotoxic effects than larger-sized particles of the same composition [Ferin et al., 1992; Oberdorster et al., 1992].

The most common types of welding include shielded manual metal arc welding (MMAW), gas metal arc welding (GMAW), flux-cored arc welding (FCAW), gas tungsten arc welding (GTAW), and others such as submerged arc welding, plasma arc welding, and oxygas welding. Each method has its own metallurgical advantages and operational applications (see Table I for descriptions). The composition and the rate of generation of welding fumes are characteristic of the individual welding processes, and may be affected by the welding current, shielding gases, and even the technique and skill of the welder. The choice of a particular technology depends on many factors, including the thickness and type of base metal to be welded, the size and strength of the weld desired, the speed or volume of welding, the position of the material to be welded (i.e., vertical or horizontal), and cost [Martin et al., 1997].

Worker Exposure

A recent estimate indicated that more than 400,000 workers were employed as welders, cutters, solderers, and brazers in the U.S. in 1999 [Bureau of Labor, 1999]. However, it is believed that greater than one million workers worldwide perform welding intermittently as part of their work duties. Welders comprise a heterogenous worker population. They work in both outdoor and indoor settings in open as well as confined spaces, underwater, and above ground on construction sites. They utilize a number of different welding and cutting processes, each of which may present its own potential health and safety hazard. The current American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value-Time Weighted Average (TLV-TWA) is 5 mg/m^3 total fume concentration in the breathing zone of the welder or others in the area during welding of iron, mild steel, and aluminum [ACGIH, 2001].

The concentration of the fume in the welder's vicinity is dependent on the volume of the space in which the welding is performed and the efficiency of fume removal by

TABLE I. Welding Processes and Applications*

Process	Synonyms	Applications
Shielded manual metal arc welding (MMAW)	Stick welding	-welds all ferrous metals -welding in all positions -inexpensive -can be performed by unskilled welders
Gas metal arc welding (GMAW)	Metal inert gas welding (MIG)	-top quality welds of all metals & alloys in industry -little post-weld cleaning (no slag) -welding in all positions -high speed, economical
Flux-cored arc welding (FCAW)	—	-smooth, sound welds -deep penetration -high quality deposited weld
Submerged arc welding (SAW)	—	-high welding speed -high metal deposition rates -deep penetration -smooth weld appearance -easily removed slag covering -wide range of material thickness weldable
Gas tungsten arc welding (GTAW)	Tungsten inert gas welding (TIG)	-top quality welds of all metals & alloys in industry -little post-weld cleaning (no slag) -welding in all positions -no weld splatter -requires highly skilled operator -well-suited for thin plates, fine work, and using difficult materials such as aluminum and magnesium

*Adapted from Hobart Institute of Welding Technology, 1977.

ventilation [Beckett, 1996a]. The rate at which fumes are formed is a function of the particular process, current level, and composition of the wire/flux used [Villaume et al., 1979]. Larger current levels give higher fume rates. The presence of a flux generally leads to higher fume rates for a given current. Traditionally, the control of fumes and gases in the workplace has been by enclosure and local exhaust ventilation; respiratory protective equipment also may be necessary in certain circumstances, particularly in confined spaces [Hewitt, 2001]. In the absence of good ventilation, general contamination of the welding area can occur rapidly.

Clean air for indoor welding operations is provided by ventilation systems, which typically consist of local exhaust systems and general ventilation supply and exhaust systems [American Welding Society, 2001]. The most efficient method of contamination control in the occupied zone of an indoor welding area, particularly in the breathing zone of the welder, is local exhaust which captures the contaminants at or near their source. Control of fume in the welding area can reduce plant maintenance costs because welding fumes are abrasive. A cleaner workplace also may lead to an increase in employee productivity. Lyttle [1999] demonstrated that decreased fume formation increased worker productivity, and that proper selection and utilization of welding consumables led to an improved worker environment, reduced welding costs, and ultimately provided greater protection for the welder.

Hazardous Components of Welding

The adverse health effects of welding comes from chemical, physical, and radiation hazards. Common chemical hazards include metal particulates and gases. Physical hazards include electrical energy, heat, noise, and vibration. Electromagnetic radiation occurs at visible, ultraviolet, and infrared wavelengths. However, the fume and noxious gases formed during the welding process are considered to be the most harmful exposure in comparison with the other byproducts of welding.

Fume

The fume refers to the solid metal suspended in air which forms when vaporized metal condenses into very small particulates [Howden et al., 1988]. The vaporized metal becomes oxidized when it comes in contact with oxygen in air, so that the major components of the fume are oxides of metals used in the manufacture of the consumable electrode wire. Most welding materials are alloy mixtures of metals characterized by different steels. Fumes formed during welding using stainless steel (SS) electrodes are designed to resist corrosion by the addition of ~18% chromium and 8–11% nickel. Fumes generated during mild steel (MS) welding are mostly iron (>80%) with little or no chromium or nickel present. The common fume components and their uses and potential hazards are listed in Table II.

Gases

Significant levels of different toxic gases (i.e., carbon monoxide, ozone, nitrogen oxides) may be formed during common arc welding processes [Howden et al., 1988]. In GMAW, shielding gases are supplied to reduce the oxidation that may occur during the welding process, thereby protecting the resultant weld. The molten metal formed during the reaction is shielded from oxygen and nitrogen in the air by

TABLE II. Hazardous Welding Fume Constituents

Fume	Uses	Potential hazard concern
Aluminum	Alloy and filler metal	Conducive to ozone production
Barium	Fluxing agent	Eye, nose, and throat irritant
Cadmium	Plating and brazing alloy	Respiratory irritant, metal fume fever
Chromium	Stainless steel alloy	Lung carcinogen
Copper	Alloy and coating material	Respiratory irritant, metal fume fever
Fluorine	Fluxing agent	Respiratory irritant
Iron	Most common fume component when welding steel	Siderosis
Lead	Brass, bronze, and steel alloy	Nervous system and kidney effects
Magnesium	Light metal alloy	Respiratory irritant, metal fume fever
Manganese	Steel alloy	Nervous system effects, respiratory irritant
Molybdenum	Steel alloy	
Nickel	Stainless steel alloy	Lung carcinogen
Silicon	Fluxing agent	
Tin	Bronze and solder alloy	Metal fume fever
Titanium	Fluxing agent	
Zinc	Galvanized steel, paint coatings	Metal fume fever

flowing an inert gas mixture (i.e., argon, helium, or carbon dioxide) directly over the weld. The shielding gas can intensify ultraviolet radiation leading to the photochemical formation of pneumotoxic gases, such as nitrogen oxides and ozone. Carbon dioxide present in the shielding gas may be reduced and converted to the more stable, but highly toxic, carbon monoxide. In FCAW or shielded MMAW, fluxes are incorporated into the consumable electrode and used in place of shielding gases. The molten fluxes help carry away impurities from the weld in a liquid stream. The fluxes may be an additional source of inhalation exposure for welders.

PULMONARY EFFECTS

Lung Function

Many investigators have examined the effects of welding fume inhalation on the lung function of welders. Ambiguous results have been observed because some studies have been conducted in laboratories, others in controlled work environments, and some during actual workplace conditions. Moreover, the severity of exposure to welding fumes varies due to differences in welding processes and materials, duration of exposure, and ventilation of the exposure area. In addition, other factors may confound the results of pulmonary function tests in welders, such as tobacco smoking [Stern, 1981]. A definitive association between welding and occupational asthma has yet to be determined. As with lung function, the development of asthma after exposure to welding fumes is difficult to determine because of differences in worker populations and the types of welding exposure. Some studies have indicated that exposure to welding fumes may be a possible cause of asthma [Wang et al., 1994; Simonsson et al., 1995; Beach et al., 1996].

Sferlazza and Beckett [1991] concluded after a review of the literature that most studies suggest that there are little to no measurable effects due to welding exposure alone on lung function. It is likely that a number of susceptible welders who work in heavily exposed areas may account for the differences in lung function observed between welders and control populations. It has been documented that shipyard welders, who are exposed to higher fume conditions because of work in confined, poorly ventilated areas, had greater decrements in lung function than welders who worked in well-ventilated places [Oxhoj et al., 1979; Akbar-Khanzadeh, 1980, 1993]. In a comparison of workers in the same plant, Mur et al. [1985] demonstrated that welders who worked in confined spaces had reduced lung function as compared with those who worked in well-ventilated areas.

It has been suggested that transient effects on pulmonary function can occur at the time of exposure in the workplace, which then return to normal during unexposed non-working periods [Sferlazza and Beckett, 1991]. Akbar-Khanzadeh [1993] performed pulmonary function tests before and after a working shift and observed significant decreases from morning to afternoon in all three tests measured in both welders and controls. However, the reduction was approximately four times greater among welders. Sobaszek and coworkers [2000] assessed the respiratory effects of both SS and MS welders and non-welding controls at the start and end of a work shift. It was demonstrated that SS welders had more significant across-shift reductions in lung function after 20 years of welding as compared with MS welders with similar exposure histories. In addition, the across-shift decreases in lung decrements were related to MMAW welding processes as opposed to GMAW processes. Donoghue and colleagues [1994] examined the peak expiratory flow (PEF) of non-smoking welders and non-welders over a 12-hr period from the start of work at the beginning of a work week. A mean change in PEF was observed at 15 min among welders which was significantly different from that of the non-welders, and the group mean for the maximum fall in PEF at any time during the 12-hr period was significantly greater for the welders.

In a comprehensive study examining the respiratory symptoms of welders over a 3-year period, Beckett and colleagues [1996b] observed a slight but significant reduction in maximal mid-expiratory flow at the time of welding when compared with measurements on non-welding days. The aggregate number of respiratory symptoms was reported to be low, whereas the total number of symptoms increased during the work day and decreased on non-work days. During the first year, 35% of the welders reported an excess in cough, phlegm production, wheezing, and chest tightness during the work week which improved on weekends. These symptoms were significantly more frequent among welders as compared with controls throughout the study, but the complaints subsided as welding exposure diminished during the course of the 3-year period. The authors concluded that welding was associated with reversible, work-related respiratory symptoms, and small, transient across-shift reductions in lung function. However, no increase in airway reactivity was observed among welders over the 3-year examination period, indicating that exposure to welding fumes is unlikely to cause significant chronic effects on lung function. Unfortunately, studies using laboratory animals to assess the effects of inhaled welding fumes on pulmonary function are lacking.

Lung Cancer

The potential association between welding and the development of lung cancer has been extensively studied. After a review of 23 epidemiological studies examining the incidence of cancer in welders, the International Agency for Research on Cancer (IARC) concluded that welding fumes were "possibly carcinogenic" to humans [IARC, 1990]. This finding was based on limited evidence in humans and inadequate evidence in animals.

The interpretation of an excess lung cancer risk in welders is often difficult because of uncertain exposure assessment and inadequate information on smoking habits and exposure to other work-related carcinogens, such as silica and asbestos [Hansen et al., 1996]. In a nine nation historical cohort study which pooled data from 21 case-control and 27 cohort studies of 11,092 welders in Europe, Simonato and colleagues [1991] observed a significantly greater mortality rate from lung cancer among welders, but asbestos exposure was implicated as a confounding factor. Some studies have not accounted for the duration of the welding experience. Beaumont and Weiss [1981] suggested that the increased lung cancer risk observed in welders was not apparent until at least 20–30 years after the first exposure to welding fumes.

It has been hypothesized that MS welding, which accounts for ~90% of all welding, poses little risk for the development of lung cancer [Stern, 1983]. Some investigators believe the risk is confined to SS welding in which chromium and nickel (known human carcinogens) have been measured in significant quantities in welding fumes [Becker et al., 1985; Peto, 1985; Sjogren et al., 1987]. Sjogren and colleagues [1994] performed a meta-analysis of data from five studies of lung cancer among SS welders, controlling for both smoking habits and asbestos exposure. Although a significant increase in the relative risk for lung cancer was observed among SS welders, the risk was significantly less than that observed with other occupations in the chromate industry. In a review of early studies, Langard [1994] concluded that there was no definitive evidence to implicate nickel or chromium as the prime causative agents in the measured lung cancer mortality excess observed in welders.

Other investigators have indicated that MS welders may have an increased risk for developing lung cancer. Moulin and colleagues [1993] studied 2,721 welders from five French factories and reported a significant increase in lung cancer mortality among welders exposed to MS fumes for 20 or more years. In addition, Danielsen and colleagues [1993] found that the lung cancer incidence among MS welders in a Norwegian shipyard was significantly higher than the general population, even after controlling for asbestos and smoking exposure. However, Steenland and colleagues [1991] observed no trend of increased risk of cancer among MS welders with increased duration of welding exposure in a historical cohort study of 4,459 MS welders in the U.S.

In more recent studies, Hansen et al. [1996] evaluated the cancer risk in 10,059 metal workers in Denmark and observed no statistically significant incidence of lung cancer among all welders. In addition, no correlation between the length of employment as a welder and risk for lung cancer was established. Moulin [1997] performed a meta-analysis of 36 independent studies on the relative risks for lung cancer development among different groups of welders. In all welding categories and in all types of studies, a significant elevated risk for lung cancer was observed as compared with the respective control group populations. The relative risk of lung cancer for all welders was estimated to be 1.38 and was no different when comparing MS and SS welders. In a historical follow-up study of 1,213 arc welders exposed to chromium and nickel in Germany, Becker [1999] indicated that cancer mortality remained significantly increased as compared with the control group and the general population by 35%. However, an elevated cancer risk was not associated with the presence of chromium and nickel in welding fumes. Danielsen and colleagues [2000] examined the incidence of lung cancer among shipyard workers and observed no association between exposure to welding fumes and lung cancer.

Few in vivo animal studies exist which have examined the development of cancer after exposure to welding fumes. Migai and Norkin [1965] administered a suspension of 50 mg of a SS welding fume to rats by intratracheal instillation. The fume contained significant amounts of manganese, chromium, and fluoride. Groups of ten rats were sacrificed at both 9 months and 1.5 years after exposure. None of the animals exposed to the SS welding fumes exhibited any evidence of lung tumor formation. Reuzel and colleagues [1985] examined the potential bronchocarcinogenic effects of MMAW-SS and GMAW-SS fumes in hamsters after intratracheal instillation of 0.5 or 2.0 mg of the fumes once weekly for 340 days. The animals from the high dose treatment had increased lung weight and evidence of interstitial pneumonia and emphysema. Histopathological analysis revealed two malignant lung tumors in the MMAW-SS group, whereas none were detected in the GMAW-SS group.

In vitro genotoxicity studies have indicated that SS welding fumes were toxic to mammalian cells and mutagenic using a Salmonella assay, whereas MS welding fumes had little mutagenic activity [Hedenstedt et al., 1977; Maxild et al., 1978]. Shielded MMAW-SS fumes were shown to have a toxic and transforming effect on baby hamster kidney (BHK) cells which was shown to be associated with the presence of Cr^{+6} [Hansen and Stern, 1985]. Baker and colleagues [1986] demonstrated that both the soluble and insoluble fractions of a MMAW-SS fume induced sister chromatid exchange in proportion to the Cr^{+6} content, but that exposure to other fume constituents such as Cr^{+3}, fluorides, nickel, and manganese had little effect. However, Stern and Hansen [1985] showed that the toxicity of GMAW-SS fumes to Syrian hamster embryo (SHE) cells was greater than expected on the basis of Cr^{+6} content. The increased transformation potential was determined to be due in part to the nickel content of the SS fumes.

DNA modifications can influence the initiation and promotion of cancer [Costa et al., 1993a]. Inappropriate covalent DNA-protein cross-links may disrupt gene expression and chromatin structure, leading to deletions of DNA sequences during replication [Costa et al., 1993b]. In an

examination of 39 electric arc welders and 18 controls matched for age, sex, and smoking habits, Popp and colleagues [1991] observed an elevation in DNA-protein cross-links in the lymphocytes of welders as compared to controls. A significant correlation was found between the frequency of sister chromatin exchange and the concentration of chromium in the urine in the welders. In a related study, Costa and colleagues [1993b] found the percentage of DNA-protein cross-links to be significantly higher among welders than among controls. They concluded that an excess of DNA-protein cross-links in cells may be more common in welders than the general population, thus predisposing them to the development of altered genotoxic events, such as cancer. More recently, Quievryn et al. [2001] indicated that Cr^{+3}-DNA adducts are the major form of DNA damage resulting from metabolism of Cr^{+6}-containing welding fumes by cysteine (a major intracellular reducing agent).

Pneumoconiosis/Fibrosis

The appearance of numerous opacities on chest radiographs of asymptomatic welders was reported early after the introduction of arc welding [Doig and McLaughlin, 1936, 1948; Enzer and Sander, 1938]. Upon examination at autopsy, multiple deposits of iron oxide were observed without the presence of fibrosis. This condition became known as siderosis and has been classified as a benign form of pneumoconiosis [Liss, 1996]. Most of the deposited iron oxide particles are present in alveolar macrophages without thickening of the alveolar septa or the presence of alveolitis [Morgan, 1989]. In addition, pulmonary function in welders with siderosis has been reported to be within normal limits and not significantly different from matched, non-welding controls [Kleinfeld et al., 1969]. Attfield and Ross [1978] found a 7% prevalence of pneumoconiosis without any cases of progressive massive fibrosis in a survey of 661 British electric arc welders.

There are reports of welders who have experienced X-ray abnormalities and extensive fibrosis [Liss, 1996]. These have often resulted from non-welding inhalation exposures of mixed-dusts (i.e., silica, asbestos, and coal dust) encountered in the welder's working area [Morgan, 1962; Guidotti et al., 1978]. However, high fume exposure levels and improper ventilation in the welder's working area also may lead to debilitating chronic lung disease. Rosler and Woitowitz [1996] described the case of a welder with interstitial lung fibrosis that was attributed to the pulmonary accumulation of high levels of iron oxide. The welder had worked for 27 years in confined spaces with inadequate ventilation. By 10 years, he had developed siderosis with no respiratory symptoms. After 27 years, his condition was diagnosed as a restrictive ventillatory disorder with reduced diffusion capacity. Histology of biopsied lungs revealed iron deposits in close proximity to fibrotic areas, leading the investigators to conclude that the siderosis had progressed into interstitial fibrosis. His condition was attributed to exposure to high levels of welding fumes in confined spaces.

In addition, Funahashi and colleagues [1988] measured the elemental composition of biopsied lung tissue from 10 symptomatic welders. They observed the presence of iron deposits in areas of fibrotic alveolar septa. Silicon levels in the tissue of the welders were no different from controls, ruling out the likelihood of exposure to silica dust. The authors concluded that it was possible for welders to develop interstitial pulmonary fibrosis. In a related study, Buerke and colleagues [2002] examined the lungs of 15 welders who had been exposed to high levels of welding fumes over long periods of time (mean duration of exposure for 28 years) while working in poorly-ventilated work areas. Lung function studies indicated a pattern of restrictive or combined restrictive-obstructive disease, low diffusion capacity, and reduced blood oxygen tension at exercise. Patchy areas of interstitial fibrosis were observed with accumulations of particular matter which were typical for welding fume exposure. Elemental analysis of deposited particles in the lungs by energy dispersive X-ray analysis demonstrated increased iron load and a close topographical relationship between tissue-embedded welding fumes and areas of fibrosis.

A number of in vivo animal studies have been performed in an attempt to determine the mechanisms by which welding fumes may cause lung injury and inflammation. In agreement with the most human worker studies, animal studies have shown that short-term exposure to low levels of welding fume produces little histopathological change in the lungs. Hewitt and Hicks [1973] exposed rats to a MS welding fume for 4 hr and observed substantial lung deposition of iron with only minimal histopathological changes. Using a welding fume generating system, Yu and colleagues [2000] exposed rats to 62 mg/m^3 of SS fumes for 4 hr and observed no significant histopathological changes in any region of the respiratory tract at any time point after exposure.

It has been demonstrated with in vivo animal studies that welding fumes generated from different processes and electrodes produce different pulmonary responses. White and colleagues [1981] intratracheally instilled rats with different welding fumes at doses which ranged from 0.5–5.0 mg/animal and measured the toxic effects in the lungs. It was determined that a single treatment with MMAW-SS fumes had a greater acute toxic effect in the lungs 7 days post-instillation as compared to MS fumes. Coate [1985] exposed rats to a single inhalation of welding fumes using seven different types of electrodes at a concentration of 0.6 mg/l for 6 hr. Fume generated during MMAW-SS welding caused the greatest amount of inflammatory cell infiltration and lung injury and was considered the most toxic fume that was evaluated. Two GMAW fumes using different MS electrodes induced only slight histopathological changes and were considered non-toxic.

In other intratracheal instillation studies, Antonini and colleagues [1996, 1997] observed that GMAW-SS and MMAW-SS fumes (2 mg/rat) were more pneumotoxic and were retained in the lungs longer when compared to MS fumes. Two pro-inflammatory cytokines, tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), were significantly elevated in the bronchoalveolar lavage fluid recovered from the lungs of rats one day after the instillation of the GMAW-SS and MMAW-SS fumes.

Animal studies also have been useful in attempting to determine which component of welding fume may be the causative agent of the potential toxic responses observed. White and colleagues [1982] treated rats with a single intratracheal instillation of the soluble or insoluble fraction of SS welding fumes or potassium dichromate ($K_2Cr_2O_7$) containing concentrations of Cr^{+6} comparable to the levels present in welding fumes. Most of the toxicity observed was related to the content of soluble Cr^{+6}. In addition, an in vitro study by Antonini and colleagues [1999] has demonstrated that the soluble metals present in welding fumes may be responsible for the cytotoxic effects observed in previous animal studies. Antonini et al. [1998] intratracheally instilled freshly generated SS welding fumes or fumes which had been aged for 1 and 7 days. The freshly generated SS fumes induced greater lung inflammation and injury than aged fumes, suggesting that this was due to a higher concentration of reactive oxygen species present on fume surfaces.

Welding fumes also have been shown to produce fibrosis in laboratory animals. Hicks and colleagues [1984] examined the histopathological changes of rat lungs after a single intratracheal instillation of very high doses (10 or 50 mg/rat) of MMAW-MS or GMAW-SS welding fumes. Diffuse areas of fume deposits were observed in the alveolar and alveolar ductal regions. Massive nodular aggregates were present in the lungs after treatment with either of the fumes. Evidence of fibrosis was observed in the nodules of the MMAW-MS-treated lungs. Yu and colleagues [2001] established a lung fibrosis model by exposing rats to SS welding fumes at concentrations of 57–67 mg/m^3 (low dose) or 105–118 mg/m^3 (high dose) for 2 hr/day in an inhalation chamber for 90 days. Histopathological examination of the lungs from the low dose group did not reveal any progressive fibrotic changes, whereas the lungs from the high dose group exhibited early signs of fibrosis at day 15. Interstitial fibrosis appeared at day 60 and became prominent by day 90. These two studies indicate that excessively high concentrations of either MS or SS welding fumes can lead to the formation of interstitial pulmonary fibrosis.

Infection/Immunity

In a recent report, Wergeland and Iversen [2001] indicated that the Norwegian Labor Inspection Authority have warned all Norwegian physicians about the possible lethal risk of an association of pneumonia with the inhalation of metal fumes. The warning advises physicians who diagnose pneumonia to consider the occupational exposure of the patient. It was suggested that pneumonia after exposure to fumes from welding, cutting, or grinding may require hospitalization and that the inhalation of metal fumes may seriously aggravate the prognosis of pneumonia. It has been reported that the frequency and severity of both acute upper and lower respiratory tract infections are increased among welders [Howden et al., 1988].

Doig and Challen [1964] found that the excesses in mortality caused by exposure to welding fumes were due to pneumonia. Interestingly, the increased risk of pneumonia was not due to age, but was constant throughout the welder's active working life. Silberschmid [1985] described a case of a welder who had been working without proper local ventilation and thus was exposed to high concentrations of fume. He developed sudden work-related pulmonary disease with symptoms of exertional dyspnea, bronchial hyperreactivity, and recurrent episodes of pneumonia that persisted for 7 years. Coggon and colleagues [1994] analyzed three sets of occupational mortality data for England and Wales that spanned the years 1959–1990 and found a significant increase in mortality from pneumonia among welders. Importantly, retired welders did not demonstrate an increase in pneumonia deaths, leading the authors to rule out non-occupational confounding factors.

It is possible that welding fumes may increase the susceptibility to infection in welders. However, limited data exists which examines the immunosuppressive effects of welding fume inhalation. Boshnakova and co-workers [1989] performed both immunoglobulin measurements and intradermal challenges on 74 healthy shipyard welders between the ages of 20–53 years of age. They concluded that a significantly higher proportion of welders had evidence of decrements in cell-mediated immunity. Tuschl and colleagues [1997] reported that many welders had experienced recurrent respiratory infections due to a reduction in natural killer cell activity, an important host defense mechanism against infection. The authors concluded that the reduced cytotoxic activity of immune cells from welders may be responsible for the reported increases in respiratory infections.

Animal studies investigating the effects of welding fumes on the immune system are lacking. Antonini and co-workers [2001] intratracheally instilled rats (2 mg/rat) with a highly soluble MMAW-SS fume or one of two relatively insoluble GMAW-SS and GMAW-MS fumes before pulmonary inoculation with the bacterial pathogen, *Listeria monocytogenes*. Pre-treatment with the MMAW-SS fume significantly impaired the clearance of the bacteria from the lungs, severely damaged the lungs, and increased animal morbidity. This reduction in bacterial clearance induced by the MMAW-SS fume was attributed to a suppression in lung

defense mechanisms, specifically, an alteration in bacterial killing by lung defense systems. In addition, Yamamoto and colleagues [2001] demonstrated that inhalation of fluoride (a common component in welding electrode fluxes) suppressed lung antibacterial defense mechanisms in mice. Pulmonary bactericidal activity of *Staphylococcus aureus* was decreased in a concentration-dependent manner after exposure to either 5 or 10 mg/m^3 of fluoride for 14 days for 4 hr/day. These studies indicate that soluble metals and fluxing agents present in welding fumes may suppress antibacterial defenses of the lungs, thus increasing the susceptibility of welders to lung infection.

Metal Fume Fever

The most frequent acute respiratory complaint of welders is metal fume fever. It has been estimated that 1,500–2,500 cases of metal fume fever occur annually in the U.S. [Blanc et al., 1993] This is a self-limited but uncomfortable condition which closely resembles influenza. The condition is very common among welders and goes by many names including "Monday morning syndrome," "foundry fever," "smelter shakes," and "welder's ague" [Martin et al., 1997]. Metal fume fever is characterized by an acute onset of 4–8 hr and often simulates a flu-like illness [Liss, 1996]. The symptoms include thirst, dry cough, a metallic taste in the mouth, chills, dyspnea, malaise, muscle aches, headaches, nausea, and fever. The illness usually resolves in 24–48 hr after onset and is often caused by the inhalation of freshly formed zinc oxide fumes during the joining or cutting of galvanized zinc-coated steel [Sferlazza and Beckett, 1991]. Metal fume fever also has been caused by the inhalation of other metal oxides often present in welding fumes, such as copper, magnesium, tin, or cadmium. An interesting feature of metal fume fever is the development of short-term tolerance in which workers are asymptomatic with repeated exposure, and episodes of metal fume fever often occur on Mondays after a weekend break from exposure [Martin et al., 1997].

Metal fume fever is a poorly understood condition. Bronchoalveolar lavage has been performed in subjects with metal fume fever with consistent findings of marked increases in lung polymorphonuclear leukocytes at 20–24 hr after exposure [Vogelmeier et al., 1987; Blanc et al., 1991]. Blanc and colleagues [1993] hypothesized that pro-inflammatory cytokines (TNF-α, IL-1, IL-6, and IL-8) may be involved with the development and progression of metal fume fever. They observed that the expression of the different cytokines appeared at different times post-exposure. TNF-α levels were elevated only at 3 hr, whereas IL-8 levels peaked at 8 hr, and IL-6 values steadily increased with time after exposure and reached a maximum concentration at 22 hr. It was concluded that TNF-α is a key mediator after exposure to zinc oxide fumes, playing an important role in the initial stage of metal fume fever, whereas IL-6 and IL-8 are likely involved at later stages.

TABLE III. Summary of Welding Fume Effects on the Pulmonary System

Effects	Worker studies	Animal studies
Lung function	-small, transient effects on lung function and respiratory symptoms	-in vivo animal studies lacking
	-uncertain association in the development of asthma	
Lung cancer	-listed as "possibly carcinogenic" due to presence of chromium and nickel in SS fumes by IARC	-in vitro cell studies indicate SS fumes are mutagenic
	-not definitely shown to induce cancer	-in vivo whole animal carcinogenicity studies limited
	-confounding effects of smoking and asbestos exposure	
Pneumoconiosis/fibrosis	-siderosis: significant lung accumulation of iron; benign pneumoconiosis without evidence of progressive fibrosis	-fumes generated from MMAW processes using SS electrodes are more pneumotoxic; likely due to presence of soluble metals and production of macrophage-derived inflammatory cytokines
	-reports of interstitial fibrosis; possibly due to improper ventilation or exceedingly high fume exposures	-exposure to exceedingly high levels of either MS or SS welding fumes can cause interstitial pulmonary fibrosis
Infection/immunity	-increase in frequency, duration, and severity of upper and lower respiratory tract infections	-in vivo animal studies limited
	-increased mortality due to pneumonia	-soluble metals and fluxing agents present in shielded MMAW fumes suppress macrophage function and other lung defense mechanisms
	-evidence of immunosuppression in welders	
Metal fume fever	-most frequent acute respiratory complaint	-no in vivo animal studies specifically evaluating the effect of welding fumes on metal fume fever available
	-self-limiting, short duration	-lung responses to zinc oxide in animals similar to humans
	-caused by oxides of zinc, copper, magnesium, or cadmium	
	-pro-inflammatory cytokines may be involved	

Gordon and colleagues [1992] exposed guinea pigs, rats, and rabbits for up to 3 hr to 2.5 or 5 mg/m^3 of the ultrafine zinc oxide fumes. They observed acute pulmonary inflammation in the guinea pigs and rats, but not rabbits. The inflammatory response was shown to be directly related to the quantity of inhaled zinc oxide retained in the lungs. The fraction of inhaled pulmonary dose was 20% for the guinea pigs, 12% for rats, and 5% for rabbits. To our knowledge, no animal studies have been performed which have specifically evaluated the effect of specific welding fumes on the development of metal fume fever.

CONCLUSIONS

The conclusions regarding the effects of welding fume inhalation on respiratory health are summarized in Table III. Inhalation exposure to welding fumes is unique. Welding fumes are a complex mixture of potentially toxic fume and noxious gases. With the development of increasingly sophisticated welding technologies which may alter the properties of the freshly-formed fumes, it has been suggested that new hazards will likely be introduced into the workplace [Martin et al., 1997; Hewitt, 2001]. Epidemiology indicates that large numbers of welders may be at increased risk for respiratory illness.

Many questions remain unanswered concerning the effects of welding fume exposure on respiratory health (e.g., are welding fumes carcinogenic?). Incomplete information exists regarding the causality and possible underlying mechanisms associated with welding fume inhalation and pulmonary disease. Moreover, carcinogenicity and long-term toxicology studies of welding fumes in animals are limited in number. The use of animal models and the ability to control the welding fume exposure in toxicology studies could be utilized in an attempt to develop a better understanding of how welding fumes affect pulmonary health. Extending our understanding of possible adverse health effects of exposure to welding fumes by utilizing both epidemiological and animal toxicology studies could be essential for risk assessment and the development of prevention strategies that would impact a large population of workers.

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