

Effects of Welding on Health, XIV



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Effects of Welding on Health, XIV

Prepared for the
AWS Safety and Health Committee

Research performed by
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Abstract

This literature review was prepared under contract to the American Welding Society for its Safety and Health Committee. The review deals with studies of the health effects of fumes, gases, radiation, and noise generated during various welding processes. Section 1 summarizes recent studies of occupational exposures, Section 2 contains information related to human health effects, and Section 3 discusses the effects of exposures in animals and cell cultures.



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Foreword

This literature review was prepared for the Safety and Health Committee of the American Welding Society to provide an assessment of current information concerning the effects of welding on health, as well as to aid in the formulation and design of research projects in this area, as part of an ongoing program sponsored by the committee. Previous work consists of the reports Effects of Welding on Health I through XIII each covering approximately 2 to 3 years. Conclusions based on this review and recommendations for further research are presented in the introductory portions of the report. The current report includes information published between January 2003 and December 2005. In addition, an appendix has been added with short summaries of articles on the effects of welding on human health published between 2006 and 2009.

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Glossary*

ACGIH	American Conference of Governmental Industrial Hygienists
BALF	Bronchoalveolar lavage fluid
CI	Confidence Interval
COPD	Chronic obstructive pulmonary disease
Cr(III)	Trivalent chromium
Cr(VI)	Hexavalent chromium
CT	Computed tomography
ELF-EMF	Extremely low frequency electromagnetic field
Dyspnea	Difficulty breathing; shortness of breath
FCAW	Flux cored arc welding
GMAW	Gas metal arc welding
GTAW	Gas tungsten arc welding
Ig	Immunoglobulin
IL	Interleukin (a class of proteins or cytokines important in regulation of the immune system/lymphocyte function)
Leukocyte	White blood cell
MAC	Maximum Allowable Concentration
mRNA	Messenger ribonucleic acid (template for protein synthesis; mRNA transmits genetic information from DNA to the cytoplasm where proteins are synthesized)
n	Number
nm	Nanometer
NIOSH	National Institute for Occupational Safety and Health
OA	Occupational asthma
OR*	Odds ratio
OSHA	Occupational Safety and Health Administration
PAH	Polycyclic aromatic hydrocarbons
PEL	Permissible Exposure Limit
PMN	Polymorphonuclear leukocyte
ROS	Reactive oxygen species
RR*	Relative risk
SMAW	Shielded metal arc welding
SMR*	Standardized mortality ratio
SOD	Superoxide dismutase
TLV	Threshold Limit Value
µm	Micrometer
µg	Microgram
UV	Ultraviolet

*Abbreviations for commonly used pulmonary function tests and for epidemiological terminology used in this document are found in Appendix A and B, respectively. The appendices describe the derivation of these terms and how they are used.

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Introduction

The health of workers in the welding environment is a major concern of the American Welding Society. To stay abreast of this subject, the health literature is periodically reviewed and published in the report *Effects of Welding on Health*. Thirteen volumes have been published to date; the first covered data published before 1978, while the remainder covered 2- to 3-year periods between 1978 and December 2002. The current report includes information published between January 2003 and December 2005. In addition, an appendix has been added with short summaries of articles on the effects of welding on human health published between 2006 and 2009. This volume should be read in conjunction with previous volumes for a comprehensive treatment of the literature on the *Effects of Welding on Health*. Included in Section 1 of this volume are studies of the characteristics of welding emissions that may have an impact on the control technologies necessary to protect the welder. In keeping with previous volumes, health reports and epidemiological studies of humans are discussed in Section 2 and organized according to the affected organ system. Research studies in animals and cell cultures are discussed in Section 3.

Many of the studies on the effects of welding on health published during the current report period focused on matters that have been explored in the older literature. The effects of welding on the respiratory tract continue to be examined and attention has been paid to the elevated incidence of pneumonia among active welders. Studies in animals suggest that SMAW of stainless steel may be responsible for this effect and that the soluble chromium component of SMAW fumes plays an important role in the suppression of the pulmonary defense responses against bacterial infection. The neurological effects of aluminum and manganese continue to receive attention. Much of the research has focused on whether exposure to manganese in welding fumes can cause Parkinson's disease or a Parkinson's disease-like syndrome (parkinsonism). Several large epidemiologic studies published during this report period addressed this question and most indicate that welders do not have an elevated risk for this condition.

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Executive Summary

Effects on the Respiratory Tract

Pulmonary Function. Decrements in pulmonary function that may be associated with inhalation of workplace pollutants can be evaluated using spirometric tests which measure the lung volume, the maximum amount of air that can be inhaled, and the flow rates that can be achieved after a maximal inhalation. Six studies examined the effects of welding exposures on pulmonary function (Ref. 34, 38, 77, 113, 147, 157). Significant decrements in pulmonary function among welders were observed in five of them. An increase in the respiratory symptoms cough, sputum production, wheezing, dyspnea (shortness of breath), and bronchitis was observed among welders in four of these studies (Ref. 34, 77, 147, 157), including the one in which no changes in pulmonary function were observed (Ref. 157).

In their study at four worksites in New Zealand, Fishwick et al. (Ref. 38) found that work-related respiratory symptoms reported by 27% of welders were significantly related to nickel exposures. Exposure to aluminum was significantly associated with a decline in FEV₁ of 5% or more after 15 minutes of work. Total fume exposure and cumulative welding experience of greater than 10 were non-significantly associated with the incidence of respiratory symptoms.

Occupational Asthma. Based on a review of published studies, the American Thoracic Society estimated that approximately 15% of asthma in the adult population is attributable to occupational exposures (Ref. 7). McDonald et al. (Ref. 106) analyzed all cases of work-related respiratory disease reported by thoracic and occupational health physicians to the National Heart and Lung Institute in London between 1992 and 2001. The study focused on diseases with a short latent period: occupational asthma (OA), allergic alveolitis, and illness caused by “inhalation accidents” (e.g., those resulting from inhalation of strong irritant gases). Occupational asthma accounted for 25% of these diseases. Reports from chest physicians identified welding as the causative agent for 3% of the cases of OA; other exposures to metals or metallic compounds accounted for an additional 4%.

It is compulsory for physicians in Finland to report all new cases of OA to the Finnish Register of Occupational Diseases. Piipari and Keskinen (Ref. 125) analyzed all of the cases of OA reported between 1988 and 1997 and found that 4% of them could be attributed to exposure to welding fumes.

In Norway, occupational diseases must be reported by physicians to the Labor Inspection Authority. Using the registry of these reports, Leira et al. (Ref. 89) investigated the incidence of OA during the period 1995–1999. Workers in the aluminum industry had the highest reported incidence of asthma. This was due, in part, to the recognition of OA as a disease among aluminum potroom workers in Norway and to the requirement for active screening of these workers, making it less likely that the disease would be underreported in this group than in the industrial population as a whole. Among the cases from outside the aluminum industry, male welders were the third most likely group to have been reported with OA. Since the majority of cases still had symptoms 2 to 6 years after their initial diagnosis, Leira et al. concluded that they were likely to have been reported at an advanced stage of the disease. They recommended that, since OA tends to become chronic and irreversible unless exposure is reduced when symptoms first develop, it is advisable to transfer workers with OA to an exposure-free workplace at an early stage of the disease.

El-Zein et al. (Ref. 30, 31) performed a prospective study of 286 apprentice welders in whom changes in pulmonary function and signs of asthma were followed during the course of their 15 months in welding school. Data concerning respiratory symptoms suggestive of asthma (e.g., cough, wheezing, and tightness in the chest) experienced by the apprentices were collected at the beginning and end of the study. Spirometric and methacholine provocation tests were completed with 194 of the apprentices before they commenced the apprenticeship and at the end of the 15-month study period. Significant changes were found in FEV₁ and FVC during that time. Persistent welding-related respiratory symptoms were found in 7.6% of the subjects. Based on symptoms and the response to methacholine provocation tests, six of these subjects were diagnosed with probable OA at the end of the study.

Hammond et al. (Ref. 59) compared rates of physician-diagnosed asthma among men who had worked in 1999 as car body welders, paint shop workers, or assembly workers in an automotive assembly plant. The welders were exposed to dusts, welding fumes, and pyrolysis products from coatings, fluxes, and oils while welding, brazing, and grinding of the car body in preparation for painting. The painters were exposed to vapors from solvents, primers, paints, reducers, and thinners, in addition to dust from sanding the various coats. The assembly workers had minimal exposure to vapors or metal fumes during their work installing engines, doors, tires, dashboards, seats, and other car parts. Physician-diagnosed asthma, chronic obstructive pulmonary disease (COPD), sinusitis, and allergy were more common among welders than among assembly workers, but this difference was significant only for diagnosis of COPD. The authors noted that 20% of the body welders and 16% of the painters reported symptoms of asthma. Health care providers had confirmed asthma in at least half of these cases. The expected incidence of asthma among these workers was only 3%.

Hannu et al. (Ref. 61) described the progression of OA in two men who had performed SMAW on different formulations of high chromium steel at a plant that manufactured machines for the pulp and paper industry. The first man had been welding for the same employer for over 20 years when he started welding SMO steel (19.5% Cr, 17.5% Ni, 6% Mo). He experienced dry cough, severe dyspnea, and wheezing on the evening following his first exposure and for the next 2 days as he continued welding this type of steel. He was hospitalized after the third day and was placed on sick leave for 2 weeks, during which time his symptoms subsided. Welding challenge tests with both mild steel and a common stainless steel produced negative results but when he welded the SMO steel, he experienced a delayed asthmatic reaction with a 37% drop in FEV₁. Six months later, after ceasing work with SMO steel, he continued to experience dyspnea after work. Pulmonary function tests administered at that time showed that his ratio of PEF/FEV₁ was suggestive of asthma.

The second case was 17 years old when he began working as a welder in 1984. He was examined in 2001 after he began to experience shortness of breath following welding of Duplex steel (21%–24% Cr, 3.5%–6% Ni, 0.1%–3% Mo). Welding challenge tests with mild and stainless steel produced negative results, but a similar challenge with Duplex steel resulted in a delayed reaction, with a 31% drop in FEV₁. Concentrations of metals measured in the inhalable dust during the challenge tests showed that nickel, chromium, and aluminum were considerably higher in the fumes from welding the SMO steel, but were only slightly higher in the Duplex steel fumes, compared with those of stainless steel. Nevertheless, the authors concluded that welding of the high-chromium special steels was the likely cause of these two cases of OA.

Pneumoconiosis. Siderosis (arc welder's lung) is a form of pneumoconiosis in which inhaled iron oxide particles accumulate in the lungs and cause tissue changes that are visible as radio-opacities in chest X-rays. Although siderosis has been considered to be a benign condition, more serious effects such as fibrosis or decreased pulmonary function have been reported in association with pneumoconiosis after long-term exposure to welding fumes. Studies in rats by Yu et al. (Ref. 170) have shown that repeated inhalation of fumes generated by SMAW of stainless steel can cause pulmonary fibrosis which is irreversible after prolonged exposure to high doses. Statistically significant dose-dependent decreases were seen in tidal volume (a lung function parameter) of exposed rats (Ref. 150). The tidal volume returned to normal after a 60-day recovery period following the last fume exposure in all rats except in those exposed to the dose that caused irreversible fibrosis.

Six welders with pulmonary siderofibrosis were described in case reports published by Buerke et al., Doherty et al., and Yokoyama et al. (Ref. 17, 27, 167). All of these cases had extensive histories of welding, some with exposure to high levels of welding fumes in poorly ventilated workplaces. Deficits in pulmonary function were observed in the five welders who were subjected to spirometric tests (Ref. 17, 27).

Six cases of systemic iron overload, as evidenced by elevated serum ferritin concentrations, were described in welders with siderosis (Ref. 27, 44, 75, 167). Chronically elevated iron levels can lead to serious conditions including liver cirrhosis, diabetes, cardiac arrhythmias, and heart failure. As with hemochromatosis, a hereditary disease in which excess iron is absorbed from food and accumulates in body tissues, the standard treatment for iron overload is phlebotomy, in which blood is periodically withdrawn by venipuncture to lower systemic iron levels. Concentrations of serum ferritin normally range from 30 ng/mL to 300 ng/mL. In most of the case reports of iron overload in welders with siderofibrosis, ferritin levels ranged from 1000 ng/mL to 2300 ng/mL. Serum ferritin levels of 6352 ng/mL were observed in a welder described as having progressive massive fibrosis (Ref. 167). Treatment by phlebotomy was successful in reducing blood iron levels in those cases where it was applied (Ref. 27, 44).

Cancer

Lung Cancer. Two studies (Ref. 129, 166) found a significantly elevated risk for lung cancer among welders. Richiardi et al. (Ref. 129) conducted a case-control study of lung cancer related to occupational exposures in northern Italy in which 1132 incident lung cancer cases were matched by sex and age with 1553 randomly-selected controls from the same geographic area. Significantly increased risks for lung cancer were found among welders and flame cutters. Yiin et al. (Ref. 166) analyzed the incidence of lung cancer and leukemia deaths among 13,468 civilians who had worked for at least one day at the Portsmouth Naval Shipyard in Kittery, Maine, between 1952 and 1992 and who had been monitored for radiation exposure. The primary emphasis of the study was to determine the effects of cumulative radiation dose on the risk of death from each of the two types of cancers. Asbestos and welding fume exposure were analyzed as covariates, along with demographics and solvent exposure. Of the employees surveyed, 3861 had died by the end of 1996, including 411 who died from lung cancer. Workers with any welding fume exposure had a significantly greater risk for lung cancer than did those with no welding fume exposure. The association between welding and lung cancer was somewhat dampened by the finding that the relative risk did not increase with increased exposure to welding fume.

Cancer of the Eye. Ocular melanoma, the most common malignancy of the eye in adults, is an uncommon disease with a poor prognosis. In a review of the literature on the association between ocular melanoma and welding, Dixon and Dixon (Ref. 26) noted that ocular melanoma is probably due to exposure to UV radiation. They stated that several studies have demonstrated an association between welding and the risk for developing this disease. Lutz et al. (Ref. 96) examined potential occupational risks for ocular melanoma in a population-based case-control study in which the 292 incident cases were recruited from the populations of nine European countries. A significant excess risk for ocular melanoma was found in welders and sheet metal workers. Shah et al. (Ref. 140) examined risk factors for ocular cancer in a meta-analysis of five studies with a total of 1137 cases. Ever having welded was found to be a significant risk factor for ocular melanoma.

Vajdic et al. (Ref. 158) conducted a population-based epidemiologic study in Australia of the risk of ocular melanoma associated with exposure to artificial sources of UV radiation. The study population comprised 290 cases diagnosed between 1996 and 1998. There was a weak non-significant relationship between risk for ocular melanoma and ever having welded. There were stronger, but still non-significant associations between ocular melanoma and having more than 22 years welding experience or having used both arc welding and oxy-acetylene welding techniques. The risk for melanoma increased with the duration of the welding experience, but the trend was not significant overall. The authors stated that the weak associations between welding and ocular melanoma found in their study may have been due to the more regular use of protective eyewear by welders in Australia than in other countries where related studies had been conducted. They concluded that, taken altogether, their results were supportive of the positive associations between welding and ocular melanoma observed by other investigators.

Cancer at Other Sites. Pan et al. (Ref. 122) performed a case-control study of malignant brain cancer in eight Canadian provinces. A total of 1009 incident cases and 5039 controls were included. No associations were observed between the risk for brain cancer and welding.

Two studies examined associations between occupational exposures and bladder cancer. Gaertner et al. (Ref. 45) investigated occupational risk factors for bladder cancer in seven Canadian provinces. The 887 incident cases of bladder cancer in adults age 20 to 74 were matched with 2487 randomly selected population controls. Welders were found to have a non-significantly elevated risk for bladder cancer. Gordon et al. (Ref. 51) performed a case-control study in southern Israel of 150 men with histologically confirmed cases of bladder cancer and 150 matched controls. Occupational exposures significantly associated with bladder cancer were organic solvents, aromatic amines and/or paints, and polycyclic aromatic hydrocarbons. Occupations significantly associated with bladder cancer were metal working and welding.

Zeegers et al. (Ref. 174) conducted a prospective study of prostate cancer among 58,279 men in the Netherlands. Men who had ever welded had a moderate, but non-significantly increased risk for developing prostate cancer.

A case-control study of endocrine gland tumors conducted by Hakansson et al. (Ref. 57) showed a significantly increased risk for all endocrine tumors among the population that had ever welded. There was an apparent exposure-response association between hours per week spent arc welding with all tumors combined and with parathyroid gland tumors. The authors stated that, while confounding from welding fume exposures could not be dismissed, the most likely factor in the association of welding with endocrine gland tumors was the extremely low frequency electromagnetic field generated during welding.

Inflammation and Oxidative Stress

Some conditions known or suspected to be associated with welding exposures, including metal fume fever, pulmonary fibrosis, bronchitis, and asthma, have been attributed to oxidative stress and/or inflammatory processes in the lung. Oxidative stress occurs when the generation of reactive oxygen species (ROS: superoxide, hydroxyl radicals, and hydrogen peroxide) and nitrogen species (nitric oxide and peroxynitrite) outbalance the quantity of antioxidants (e.g., superoxide dismutase, glutathione peroxidase, and reduced glutathione) available to inactivate them. The production of oxidizing species is a central part of the mechanism by which macrophages and polymorphonuclear leukocytes (PMNs) destroy pathogens; but the production of ROS by phagocytes when responding to the presence of non-pathogenic particles such as those in welding fume may also damage host tissues.

Inflammatory processes in the lungs are the first observable response to inhaled welding fumes. Proinflammatory cytokines such as interleukin-6 (IL-6) and IL-8, are released from lung cells and are measurable in bronchoalveolar lavage fluid (BALF). These cytokines are chemotactic for macrophages and neutrophils. Cytokines released from cells such as macrophages and neutrophils can further enhance the inflammatory process in the lungs potentially leading to fibrosis and other pulmonary conditions. They can also cause systemic effects, such as metal fume fever, as they are released from the lungs into the blood stream.

Five studies found significant differences in concentrations of biomarkers of oxidative stress or inflammation in blood from welders and controls (Ref. 34, 60, 84, 91, 175). Kim et al. (Ref. 84) found that, C-reactive protein, a marker of inflammation, was significantly increased in blood 16 hours after welding exposures. A significant increase in neutrophil count and a significant decrease in fibrinogen were seen in blood following welding fume exposure in non-smoking welders. Further work from this laboratory (Ref. 160) showed that the genes whose expression was altered following welding fume exposure were clustered in biologic processes related to the inflammatory response, oxidative stress, intracellular signal transduction, and cell cycle. The greatest variations in gene expression were seen in the non-smoking welders. The effects of welding fume exposure on gene expression were transient, and most of the observed effects diminished within 19 hours post exposure (Ref. 159).

Two studies (Ref. 34, 147) examined whether decrements in pulmonary function in welders were associated with biomarkers of oxidative stress. In the first, Fidan et al. (Ref. 34) found that the respiratory symptoms cough, sputum, and chronic bronchitis were significantly more prevalent among the welders than controls while the pulmonary function measures FEV₁/FVC, FEF₂₅, FEF₇₅, and FEF₂₅₋₇₅ were significantly lower in the welders than in the controls. Indicators of oxidative stress, plasma thiobarbituric acid reactive substances (TBARS: an indicator of lipid peroxidation) and protein carbonyl levels were elevated while total protein thiols (SH) and reduced glutathione levels in erythrocytes were significantly decreased in welders, revealing a reduction of available anti-oxidants. No significant correlations were found between serum oxidant/antioxidant levels and any of the pulmonary function test results, but TBARS levels were significantly elevated and SH and reduced glutathione levels were significantly reduced in welders with chronic bronchitis, suggesting a role of oxidative stress in the pathogenesis of that condition.

In the second study, Stepniowski et al. (Ref. 147) found that lung function, as measured by the spirometric tests FEV₁, %FEV, MEF₅₀, and MEF₂₅₋₇₅, was significantly reduced among welders compared with controls. Low, but significant, correlations were found between catalase concentrations in blood and FEV, and between total antioxidant status and FVC.

Infections

Analyses of occupational mortality data in Great Britain have shown that welders have a greater than normal risk of dying from infectious pneumonia (Ref. 20). The elevated mortality occurs only during the period of employment as a welder. Palmer et al. (Ref. 121) conducted a hospital-based case-control study to determine if the elevated risk is restricted to pneumonias caused by specific microorganisms, if it is related to exposure to specific metals, or if the elevated risk is for developing a pulmonary infection as well as for dying from it. The risk for pneumonia was found to be significantly associated with occupational exposure to metal fume during the year prior to the onset of illness but not with exposures to metal fume that had occurred more than a year prior to onset of illness. Fumes from iron and steel were associated with increased susceptibility to infectious pneumonia, but involvement of other metal fumes could not be ruled out. In cases associated with exposure to ferrous metal fumes, the risk was significantly elevated for lobar and segmental pneumonia, but not for bronchopneumonia, and the elevated risk was not limited to fatalities. The investiga-

tors postulated that the elevated risk for pneumonia could be related to oxidative damage to lymphocytes or macrophages or, alternatively, that inhaled iron particles could act as a nutrient source promoting the growth of certain microorganisms.

Antonini et al. (Ref. 5) investigated the effects of fumes from GMAW of mild and stainless steel (GMAW-MS and GMAW-SS, respectively) and SMAW of stainless steel (SMAW-SS) on pulmonary defense responses to bacterial infection in rats. The soluble and insoluble fractions of SMAW-SS fume were tested separately. Fume samples were introduced into rat lungs by intratracheal instillation on day 0 followed by the bacterium *Listeria monocytogenes* on day 3. Animals were sacrificed on days 6, 8, or 10 and the numbers of *Listeria* colony forming units were determined. Only the intact SMAW-SS fumes were found to alter lung infectivity. Clearance of *Listeria* from the lungs was markedly delayed in rats pretreated with SMAW-SS fumes compared with rats pretreated with the GMAW fumes or either the soluble or the insoluble fractions of the SMAW fume. By day 10, 30% of the rats treated with SMAW-SS had died whereas all of the rats in the other treatment groups were still alive. Histological examination of the lung tissue showed severe pneumonitis on day 10 in rats treated with SMAW-SS fumes but not in those treated with the other fume samples.

Several assays were performed to examine possible mechanisms by which SMAW-SS fumes may reduce lung defenses. Bronchoalveolar lavage fluid taken from rats that had been instilled with SMAW-SS fumes had elevated lactate dehydrogenase (an indicator of loss of membrane integrity in cells that are injured or dead) and albumin (an indicator of damage to the integrity of the alveolar-capillary barrier), and significant increases in numbers of macrophages, PMNs, eosinophils, and lymphocytes compared with BALF from rats instilled with saline alone. This suggested that immune and inflammatory responses were enhanced in rats treated with SMAW-SS fumes. It was also found that the proinflammatory cytokines TNF- α , IL-6, and IL-10 were elevated in BALF from rats treated with SMAW-SS fumes and *Listeria*. Reactive oxygen species and nitric oxide and its oxidation products (NOx: nitrate and nitrite) were markedly elevated in macrophages and BALF before and after infection in rats treated with SMAW-SS. Further tests showed that both the soluble and insoluble components of SMAW-SS fumes contribute to the inflammatory response elicited by the intact fume (Ref. 153) and that the soluble chromium component of SMAW fumes plays an important role in the suppression of the pulmonary defense responses against bacterial infection (Ref. 4).

Effects on the Nervous System

Aluminum. Giorgianni et al. (Ref. 48) administered neuropsychological tests to 50 aluminum welders. The welders scored significantly less well than controls on tests of memory and abstract reasoning and slightly less well on tests of attention. The investigators concluded that occupational exposure to aluminum welding fumes can affect cognitive function. In contrast to these findings, tests of a group of 98 aluminum welders by Buchta et al. (Ref. 16, 83) revealed no significant differences between welders and controls in motor-performance, short-term memory, or switching attention. Simple reaction time performance differed significantly between welders and controls. Since the differences between the two groups did not change during tests repeated three times over a 4-year period, the investigators concluded that the differences may have been due to random a priori differences between the groups and were most likely not associated with welding exposures.

Manganese: Subclinical Effects. Halatek et al. (Ref. 58) conducted a study of 59 welders from a Polish shipyard to assess whether neurophysiological tests could be used to detect early effects of exposure to low concentrations of manganese. Subjective neurological symptoms, including increased emotional irritability, headache, and sleepiness, were reported by half of the welders. Abnormalities found in electroencephalographs (EEG) of 32% of the welders and in visual evoked potentials (VEP) from 22% of the welders correlated both with current exposure to airborne manganese in excess of 0.3 mg/m³ (the Polish TLV) and with a cumulative exposure index based on years of exposure and airborne manganese levels. The authors concluded that neurological tests, VEP, and EEG may be used to detect early effects of exposure to low levels of manganese.

He and Niu (Ref. 66, 118) assessed subclinical neurophysiological changes in 68 welders who worked in a factory in China and who had histories of chronic exposure to low levels of manganese. Mean exposures of 138.4 $\mu\text{g}/\text{m}^3$ manganese, 12.6 $\mu\text{g}/\text{m}^3$ cadmium, and 3.8 $\mu\text{g}/\text{m}^3$ nickel were measured in air samples collected at breathing height on the factory floor. Welders and controls were subjected to a battery of examinations and neurobehavioral tests. Changes were seen in EEGs and in brain electrical activity mapping of the welders. They also had lower test scores on more of the

neurobehavioral tests than did controls. Scores on the Profile of Mood States indicated a depressed emotional status in the welders. The investigators concluded that these changes were due to chronic exposures to low levels of manganese.

Bowler et al. compared neuropsychological function, emotional status, and visual function of 76 welders with that of 42 controls (Ref. 11). Welders had lower scores than controls in tests of motor function, verbal learning, working memory, cognitive flexibility, and visuomotor processing speed, while they scored as well as controls in tests of verbal skills, verbal retention, and auditory span. Tests of emotional status indicated that the welders had elevated levels of mood disturbance. The investigators noted that the welders worked in the chemical industry where they may have been exposed to solvents with neurotoxic effects which could have confounded the results of this study. Another confounding factor was that the welders selected for the study were involved with civil and workers' compensation litigation related to impairments incurred during their employment as welders. In their critique of this study, Lees-Haley et al. (Ref. 88) stated that this work was "fatally flawed by participant selection bias." Another difficulty pointed out by Lees-Haley et al. was that the welder population had a lower educational background than did controls which could have caused them to fare less well on some of the tests of cognitive skills.

Manganese: Clinical Effects. Chronic exposures to excessive levels of manganese can result in neurological damage, causing an array of symptoms (referred to as manganism or parkinsonism) that resemble those of idiopathic Parkinson's disease. Manganism and idiopathic Parkinson's disease are difficult to differentiate, especially in later stages. It has been reported that exposure to welding (Ref. 127) or to manganese in welding fumes can cause Parkinson's disease, but the evidence for this is limited and much research continues to be conducted towards resolving this issue.

Manganism and Parkinson's disease are both caused by degeneration of cells in the basal ganglia, a control center of the brain involved in the production of smooth, coordinated movements. Manganese accumulates selectively in the globus pallidus of the basal ganglia, where it can produce hyperintense signals in T1-weighted magnetic resonance images (MRI) of the brain. Manganese-related changes in MRI scans tend to disappear following withdrawal from the manganese source as manganese is cleared from the brain tissue, even though permanent neurological damage may have occurred.

Racette et al. (Ref. 128) compared the prevalence of parkinsonism in a large sample of welders from Alabama with that in a general population, age-adjusted sample of male residents from Copiah County, Mississippi. The welders from Alabama had been referred to the investigators for medical-legal evaluation for Parkinson disease. The prevalence of parkinsonism among residents of Copiah County had previously been determined in a study by Schoenberg et al. (Ref. 138). Racette et al. found that parkinsonism occurred more frequently among the Alabama welders than among the comparison population from Copiah County. Analysis of age of onset of parkinsonism supported Racette's earlier findings that Parkinson's disease occurred at an earlier age among welders than among controls (Ref. 127).

Reports that Parkinson's disease occurs at a younger age among welders or that welders have an increased incidence of parkinsonism have not been supported by recent epidemiologic studies (Ref. 40, 41, 50, 145). Using a population of 2072 patients being treated for Parkinson's disease or parkinsonism in movement disorder clinics located in New York, Atlanta, and San Jose, Goldman et al. (Ref. 50) investigated occupational associations with these conditions. The study focused on occupations (teaching, healthcare, farming, and welding) that had been associated with an increased risk of Parkinson's disease in previous studies. Three welders, all of whom had typical Parkinson's disease, were identified among the clinical patients. The frequency of Parkinson's disease or parkinsonism in welders was not significantly elevated compared with the control population. In addition, the mean age at which Parkinson's disease was first diagnosed in the welders did not differ significantly from that of the entire clinical population.

Stampfer (Ref. 145) examined mortality data in the U.S. National Center for Health Statistics (NCHS) National Cause of Death data base for evidence linking occupation as a welder with mortality from neurodegenerative diseases. The analysis included 4,252,490 men who died between 1985 and 1999. During the study period, Parkinson's disease accounted for 49,174 deaths and was listed as a contributing or underlying cause of death among 1.0% of the men with any welding-related exposure and 1.2% of the men in the reference population. Welders were slightly, but significantly less likely to have Parkinson's disease as the contributing or underlying cause of death. In addition, the risk of death from motor neuron disease, other diseases of the basal ganglia, and other extrapyramidal disorders did not differ significantly between welders and the reference population. Stampfer concluded that "the present study... suggests that employment as a welder is not associated with an increase in mortality from Parkinson's disease or other neurodegenerative conditions."

Fryzek et al. (Ref. 41) conducted a retrospective cohort study of the rates of hospitalization for Parkinson's disease and other neurodegenerative disorders among 27,839 Danish metal-manufacturing workers. This study included 9817 men

who were employed in departments engaged in mild or stainless steel welding, of whom 6163 were welders. The number of hospitalizations for Parkinson's disease among the welders or men working in welding departments did not differ from that expected for the entire cohort nor did the mean age of onset of Parkinson's disease differ between the welders and the other workers. The incidence of Parkinson's disease was not associated with the duration of the welding experience. The investigators concluded that the rates of Parkinson's disease and other neurological conditions among welders were consistent with those of the general population of Denmark.

Fored et al. (Ref. 40) examined the incidence of basal ganglia and movement disorders in Swedish welders and flame cutters by comparing the health and employment records of 49,488 male welders with those of 489,572 male workers who had no history of exposure to welding or flame cutting at work. Parkinson's disease and other neurological disorders occurred at a slightly lower rate among welders than in the comparison population. There was no difference in mean age of first occurrence of Parkinson's disease between the welders and flame cutters and the comparison cohort.

Marsh and Gula (Ref. 101) conducted a case-control study among the 12,595 workers who had ever been employed between 1976 and 2004 at three Caterpillar heavy equipment plants in Illinois and were eligible to make medical insurance claims between 1998 and 2004. Cases of neurological disorders were identified from company medical claims and comprised the 70 persons who had filed claims for either idiopathic Parkinson's disease or secondary parkinsonism and the 153 persons who had filed claims for other progressive diseases of the basal ganglia and essential and other specific forms of tremor. Controls were drawn from members of the study population who were not identified as cases. No statistically significant associations between ever having welded in any Caterpillar plant and any of the neurological disorders studied were found.

Manganese: Bioavailability. In his analysis of the evidence for an association between manganese exposure in welding fumes and Parkinson's disease or parkinsonism, McMillan (Ref. 107) noted that the physicochemical properties of manganese emanating from different processes differ which could affect its bioavailability. Manganese in welding fumes is often present as complex oxides in ultrafine particles which are sometimes surrounded by a shell composed of silicon oxide. McMillan reasoned that manganese in that form may be less bioavailable than manganese in dusts or particles released from other processes such as mining. Particles in dusts released during mining are in much simpler forms and have been clearly related to manganism.

Yu et al. (Ref. 169) investigated the distribution of manganese in the rat brain following exposure by inhalation to fume generated by SMAW of stainless steel. The rats were exposed for 2 hours per day for up to 60 days to welding fume concentrations of 63.6 mg/m³ or 107.1 mg/m³ containing 1.6 mg/m³ manganese and 3.5 mg/m³ manganese, respectively. Groups of animals were sacrificed periodically and manganese concentrations were determined in samples of blood, brain, lung, and liver. Manganese concentrations in the lung and liver increased with the dose and with the duration of exposure. Statistically significant increases in manganese levels in the cerebellum were seen at all time points at both doses after 15 days of exposure but only slight increases were seen in the substantia nigra, basal ganglia (including the caudate, nucleus, putamen, and globus pallidus), temporal cortex, and frontal cortex after 60 days of exposure. Yu et al. compared their results with those obtained by St-Pierre et al. (Ref. 148) who exposed rats by inhalation to manganese dusts for 15 weeks. In that study, there was a high accumulation of manganese in the striatum and globus pallidus of the basal ganglia and a lower accumulation in the cerebellum. These findings suggest that the pharmacokinetics involved in absorption of manganese from welding fumes differ from those involved in absorption of manganese from neat manganese dusts.

Effects on Reproduction

Wong et al. (Ref. 162) examined the effects of lifestyle, occupation, and medical history on sperm count in a case-control study of 73 sub-fertile and 92 fertile Caucasian males. The sub-fertile males had significantly lower sperm counts and sperm motility and a significantly higher percent of abnormal spermatozoa than did the fertile males. Antibiotic use, a history of mumps, and occupational exposure to pesticides were significantly related to subnormal sperm counts. The risk for subnormal sperm counts was non-significantly elevated in men with occupational exposures to welding fumes.

Danadevi et al. (Ref. 24) compared the quality of semen collected from 57 welders who worked at a plant in South India and 57 controls. The percent of subjects with normal sperm morphology, normal sperm counts, and rapid linear sperm motility were significantly lower among the welders than among controls. Nickel and chromium concentrations in blood were positively correlated with the percentage of tail defects in semen from welders. Blood concentrations of chromium,

but not nickel, were significantly correlated with decrements in sperm count, sperm vitality, and rapid linear progressive motility. The investigators concluded that exposure to welding fumes containing nickel and chromium is associated with abnormal semen parameters.

Oxidative damage to DNA in sperm may be measured by the level of 7-hydro-8-oxo-2'-deoxyguanosine (8-oxodG) in sperm DNA. Working with 225 Danish couples who were planning to conceive their first child, Loft et al. (Ref. 92) investigated whether these DNA modifications affect sperm function. Semen samples were collected monthly for up to 6 months following the cessation of the use of contraception. There was a significant inverse relationship between the level of 8-oxodG in sperm DNA and the occurrence of pregnancy during this time. The level of 8-oxodG did not differ significantly in sperm from the 80 men who performed daily welding and the 145 men who did not.

Hjollund et al. (Ref. 67) investigated whether paternal stainless steel welding affects the incidence of spontaneous abortion among women who had become pregnant by in vitro fertilization. Rates of spontaneous abortion were compared among 319 couples in which the male partners were welders and 2925 couples in which the males had no known exposures to welding fumes. Spontaneous abortion of pregnancies before 28 weeks of gestation occurred in 18% of the couples with paternal exposure to stainless steel welding, in 25% of those with paternal exposure to mild steel welding, and in 28% of those with no paternal welding exposure. These differences were not statistically significant and it was concluded that welding does not affect the rate of spontaneous abortion in pregnancies that are initiated by in vitro fertilization.

Technical Summary

The Exposure

Fume Composition

Yoon et al. (Ref. 168) examined the effects of welding current on fume generation rates (FGR) and on the production of total chromium and hexavalent chromium [Cr(VI)] during CO₂-shielded flux cored arc welding (FCAW) of stainless steel in a fume collection chamber. The FGR, total chromium, and Cr(VI) produced during FCAW increased with the welding current.

Sampling Strategies for Ultrafine Particles

Brouwer et al. (Ref. 15) compared three methods—a condensation particle counter, a scanning mobility particle sizer, and an electrical low pressure impactor—for measuring number concentrations and size distributions of ultrafine particles generated during welding. The investigators found that each of the measurement methods has its drawbacks, but that in combination they can be useful in providing insight into the characteristics of fine particles in the workplace.

Thoriated Electrodes

Gafvert et al. (Ref. 46) measured breathing zone concentrations outside the welder's helmet during full-time welding of steel and aluminum with thoriated electrodes in five workshops in Sweden. Welding with alternating current produced higher levels of thorium radioactivity in the breathing zone than did welding with direct current. Estimates of annual exposure to radioactivity from thorium calculated from the welding and grinding sampling data were well below the Nuclear Regulatory Commission exposure limits.

Saito et al. (Ref. 136) measured ²³²Th exposure during welding and grinding with thoriated electrodes in a welding shop in Japan. Breathing zone samples were collected during gas tungsten arc welding (GTAW) of aluminum, GTAW of stainless steel, and during sharpening of the electrode tips on a grinding wheel. The estimated annual radiation dose derived from these data was well below the Japanese annual limit of 160 Bq.

Ultraviolet Light

Garcia-Guinea et al. (Ref. 47) examined the composition of 14 different consumable coated electrodes and found the coatings to consist of quartz, calcite, sodium and the potassium-rich feldspars, muscovite and rutile. Thermoluminescence measurements conducted on these materials showed that, with the exception of rutile, they all produced strong emission peaks in the UV-A range (320 nm–400 nm) and the UV-B range (280 nm–320 nm).

Incidental Exposures

Gjolstad et al. (Ref. 49) examined exposure of refrigerator repair workers to HF, HCl, phosgene, and volatile organic compounds during welding. HCl was detected during welding when difluorochloromethane was the refrigerant and HF

was detected during welding of refrigerant systems containing difluorochloromethane, tetrafluoroethane, or R404A (a mix of 1,1,1,2-tetrafluoroethane, pentafluoroethane, and 1,1,1-trifluoroethane).

Workplace Exposures

With the goal of characterizing the aerosol formed by natural mixing of welding fumes with the air in a typical industrial setting, Stephenson et al. (Ref. 146) sampled particle emissions during SMAW of carbon steel in a metal shed. In samples collected 3 m downwind of the welding, the number concentration of particles in the range of 0.05 μm to 0.5 μm increased by almost 100-fold, while the concentration of larger particles did not differ from background levels.

Matczak and Przybylska-Stanislawski (Ref. 104) measured concentrations of metals and fluorides in samples collected in the breathing zone of welders using ten types of welding wires during FCAW. Welding with certain types of flux cored wires resulted in breathing zone concentrations of total dust and manganese well in excess of regulatory limits.

Ventilation

Using a robotic welding apparatus, Iwasaki et al. (Ref. 76) tested the effectiveness of a push-pull ventilation system to control exposures to fumes produced by CO_2 -shielded gas metal arc welding (GMAW). The investigators stated that the two important design criteria for a push-pull ventilation system—(1) the production of stable air velocity and direction in the vicinity of the weld, to prevent formation of blow holes and (2) the effective removal of welding fume from the occupied area—were both achieved when the ventilating air flow velocity was maintained between 0.3 m/s and 0.8 m/s.

Harris et al. (Ref. 63) evaluated the effectiveness of general dilution ventilation by means of exhaust fans in controlling a welder's exposure to manganese during SMAW in a confined space. With an exhaust rate of 2000 cubic feet per minute (CFM), manganese concentrations in breathing zone samples collected from the welder were less than the ACGIH TLV of 0.2 mg/m^3 for manganese. However, the TLV was exceeded in area sample locations that served as surrogates for welders' helpers, indicating that the exhaust flow rate of 2000 CFM recommended by OSHA for confined spaces may be insufficient to protect bystanders from excess manganese exposure.

Zaidi et al. (Ref. 173) examined the effectiveness of two local exhaust ventilation systems developed in rural India for use during welding. The systems were shown to reduce breathing zone concentrations of manganese from 22 $\mu\text{g}/\text{m}^3$ (portable unit) or 70 $\mu\text{g}/\text{m}^3$ (mobile unit) to 8 $\mu\text{g}/\text{m}^3$.

Accidents and Injuries

In a cross-sectional survey in Pakistan, Shaikh (Ref. 142) found that 61 of 208 welders sustained injuries during a period of 6 months. The most common types of injuries were burns on the limbs or trunk, and foreign bodies in the eye.

Effects of Welding on Human Health

Respiratory Tract

Pulmonary Function. Meo (Ref. 111, 113) administered pulmonary function tests to 50 male arc welders who worked in small shops with minimal ventilation in Pakistan. The welders had statistically significant reductions in maximal voluntary ventilation (MVV), forced expiratory volume (FEV_1), FEV_1 /forced vital capacity (FVC), and peak expiratory flow. Fishwick et al. (Ref. 38) measured breathing zone exposures and pulmonary function in welders at four work sites in New Zealand. A significant positive correlation between respiratory symptoms and exposure to nickel was found. Pulmonary function tests showed a 5% decline in FEV_1 in 23% of the welders after the first 15 minutes of work which was significantly correlated with aluminum exposures, but not with total fume exposure. Jafari and Assari (Ref. 77) examined lung function and respiratory symptoms in a group of 63 welders from workshops in Hamadan, Iran. Significant decrements in vital capacity, FVC, FEV_1 , and forced expiratory flow (FEF_{25-75}) were found when smoking welders were

compared with smoking controls and when non-smoking welders were compared with non-smoking controls. The incidence of chronic bronchitis was significantly higher among the welders than among controls. Tunc et al. (Ref. 157) found significantly higher incidences of cough, sputum, dyspnea, and bronchitis in welders than in controls but spirometric tests showed no differences in lung function between the two groups.

Fidan et al. (Ref. 34) found deficits in lung function and a significant increase in the prevalence of cough, sputum, and chronic bronchitis among welders in Afyon, Turkey. Chronic bronchitis was significantly correlated with a reduction in protein thiol and glutathione levels in erythrocytes and elevated thiobarbituric acid reactive substances in plasma. Stepniewski et al. (Ref. 147) examined pulmonary function and antioxidant enzymes in blood from 94 welders and 115 age-matched controls. Lung function was significantly reduced among the welders compared with the controls but the values for total antioxidant status, superoxide dismutase, and catalase activity measured in blood samples were not significantly different. Signs of chronic obstructive pulmonary disease (COPD) were more frequent in the welders than in the controls. In a case-control study designed to ascertain the risk of COPD associated with different occupations, Mastrangelo et al. (Ref. 102, 103) found that welders have a significantly greater risk for COPD which increases slightly, but significantly, with duration of exposure and age.

Occupational Asthma. McDonald et al. (Ref. 106) examined the incidence of asthma among cases of work-related respiratory disease reported by thoracic and occupational health physicians to the National Heart and Lung Institute in London between 1992 and 2001. Welding was identified as the causative agent for 3% of all cases of occupational asthma (OA). Piipari and Keskinen (Ref. 125) analyzed all cases of OA reported to the Finnish Register of Occupational Diseases during the period 1988–1997 and found that 4% of OA could be attributed to welding fumes. In Norway, occupational diseases must be reported by physicians to the Labor Inspection Authority. Using the registry of these reports, Leira et al. (Ref. 89) found that, among the cases of OA reported between 1995 and 1999 from outside the aluminum industry, male welders were the third most likely occupational group to have been reported with this condition.

El-Zein et al. (Ref. 32) examined data concerning respiratory symptoms associated with asthma and metal fume fever collected from 351 welders during a survey of industrial workers in Canada. The occurrence of two respiratory symptoms suggestive of OA was significantly related to the incidence of probable metal fume fever. El-Zein et al. (Ref. 30, 31) later performed a prospective study of apprentice welders in whom changes in pulmonary function, signs of asthma, and symptoms of metal fume fever were followed during the course of their 15 months of exposure in welding school. Significant changes were found in their performance on the lung function tests FEV₁ and FVC at the end of the 15-month study period and welding-related respiratory symptoms were found in 7.6% of the subjects; six of these subjects were diagnosed with probable OA at the end of the study.

Hammond et al. (Ref. 59) examined the incidence of respiratory symptoms among men who worked in an automotive assembly plant. Welders reported having been diagnosed with COPD significantly more frequently than did the other workers and about 10% of the welders had been diagnosed with asthma. Hoppin et al. (Ref. 71) examined the incidence of wheezing among 20,898 farmers in Iowa and North Carolina. They found that welding, which was engaged in by 57% of the farmers with reported wheeze, was associated with a significantly increased risk for wheezing.

Hannu et al. (Ref. 61) described the progression of OA in two men who had performed SMAW on different formulations of high chromium steel in the same workplace.

Pneumoconiosis. In 2002, Buerke et al. (Ref. 18) described 15 welders who had pneumoconiosis and clinical respiratory symptoms. Spirometric tests of three of the welders showed deficits in pulmonary function and examination of biopsied lung tissue revealed patchy interstitial fibrosis (Ref. 17). Particulate material with an elemental composition typical of welding fumes was found in activated alveolar macrophages and in lung tissue close to areas of fibrosis.

Doherty et al. (Ref. 27) described the cases of three welders who had both siderosis and elevated serum ferritin levels. Spirometric tests showed deficits in pulmonary function in these men, and examination of biopsied lung tissue revealed patchy interstitial fibrosis. Fukuda et al. (Ref. 44) described a case of pneumoconiosis and iron overload in a 26-year-old man who had worked as an arc welder without benefit of respiratory protection for 2 years. The numerous iron-laden alveolar and interstitial macrophages observed in lung biopsy specimens and his serum ferritin levels were markedly reduced following repeated treatments by phlebotomy. Other cases of welders with siderosis and iron overload were reported by Ishida et al. (Ref. 75) and by Yokoyama (Ref. 167).

Fireman et al. (Ref. 37) described the case of a 43-year-old welder who suffered from dyspnea. A high resolution computed tomography scan revealed small, well-defined micronodules throughout his lungs and multiple granulomas were

identified in a lung biopsy specimen. Scanning electron microscopy combined with energy dispersive X-ray spectroscopy revealed abundant particles of aluminum compounds in sputum and biopsy samples. The welder's condition was diagnosed as sarcoid-like granulomatous-induced aluminum disease. The case of a 23-year-old welder who was admitted with chest pain to a hospital in Turkey was described by Fidan et al. (Ref. 33). Chest X-rays revealed complete collapse of a lung which was caused by a large pneumothorax.

Respiratory Tract Infections. Exposure to ferrous welding fumes increases the susceptibility of welders to pneumonia. A case-control study conducted by Palmer et al. (Ref. 121) showed that the elevated risk is not restricted to pneumonias caused by specific microorganisms. They found that the risk for pneumonia is significantly associated with occupational exposure to metal fume during the year prior to the onset of illness and the risk is significantly elevated for lobar and segmental pneumonia, but not for bronchopneumonia.

Recent reports of pulmonary mycoplasma infections in welders have appeared in the Japanese literature. Matsushima described cases of pulmonary *Mycobacterium kansasii* infection in three welders who worked on the same line in a factory in Japan (Ref. 105). Fujita et al. described five cases of men with respiratory infection associated with siderosis (Ref. 42).

Cancer

Lung Cancer. In a case-control study of lung cancer related to occupational exposures in two areas of northern Italy, Richiardi et al. (Ref. 129) found significantly increased risks for lung cancer among workers identified by the International Standard Classification of Occupations codes as welders and flame cutters and as gas and electric welders. Finkelstein and Verma (Ref. 35) examined causes for mortality in a cohort of 25,285 members of a union of the plumbing and pipe fitting industry in Canada. Lung cancer mortality was significantly higher than expected among those employed for 20 or more years as plumbers, pipefitters, or sprinkler fitters. Yiin et al. (Ref. 166) analyzed the incidence of lung cancer and leukemia deaths among 13,468 civilians who had worked for at least one day between 1952 and 1992 at the Portsmouth Naval Shipyard in Kittery, Maine. Workers with any welding fume exposure had a significantly greater risk for lung cancer than did those with no exposure to welding fume. The relative risk did not increase with increased exposure to welding fume.

Mesothelioma. Nesti et al. (Ref. 117) analyzed data from the Italian National Mesothelioma Registry and found that welders were among those with the highest incidence of mesothelioma in the metallurgy and steel industries. Fujiwara et al. (Ref. 43) described the case of a welder who had been exposed throughout his 28-year career to asbestos dust generated when he sharpened slate pencils used to draw lines for arc cutting of steel plates. At the age of 53, he was diagnosed with pericardial mesothelioma, an extremely rare cancerous disease of the tissue layers surrounding the heart.

Cancer of the Eye. Lutz et al. (Ref. 96) examined occupational risks for ocular melanoma in a population-based case-control study. A significant excess risk for ocular melanoma was found in welders and sheet metal workers. In a meta-analysis of studies of risk factors for ocular cancer, Shah et al. (Ref. 140) found welding to be a significant risk factor for ocular melanoma. In a population-based epidemiologic study of the risk of ocular melanoma associated with exposure to artificial sources of UV radiation, Vajdic et al. (Ref. 158) found only non-significant relationships between risk for ocular melanoma and welding. They stated that the weak associations found in their study may have been due to the regular use of protective eyewear by welders in their study population and concluded that, taken altogether, their results were supportive of the positive associations between welding and ocular melanoma observed by other investigators.

Cancer at Other Sites. Gordon et al. (Ref. 51) performed a case-control study of 150 men with histologically-confirmed cases of bladder cancer and 150 matched controls in southern Israel. Occupations significantly associated with bladder cancer were metal working and welding. In a study of occupational risk factors for bladder cancer performed in seven Canadian provinces by Gaertner et al. (Ref. 45), welders did not have a significantly elevated risk for bladder cancer.

A case-control study of 140 cases of endocrine gland tumors by Hakansson et al. (Ref. 57) revealed a significantly increased risk for endocrine tumors among the population that had ever welded.

A prospective study of prostate cancer among 58,279 men in the Netherlands by Zeegers et al. (Ref. 174) showed that men who had ever welded did not have a significantly increased risk for developing prostate cancer. In a case-control study of malignant brain cancer in eight Canadian provinces, Pan et al. (Ref. 122) found no significant associations between brain cancer and welding.

Metal Fume Fever

Taniguchi et al. (Ref. 152) described the case of a 57-year-old welder who developed high fever and difficulty breathing after exposure to zinc oxide fumes while welding without a protective mask. He was diagnosed as having chemical pneumonia. Hassaballa et al. (Ref. 64, 65) described the case of a 25-year-old male welder who developed metal fume fever after working without wearing a respirator in a poorly ventilated area where galvanized steel was being cut. While on the job, he developed a cough and difficulty breathing. He later developed a rapid heart beat and abnormally rapid breathing; examination revealed pericarditis, pleuritis, and pneumonitis.

Effects on the Eye and Vision

Eye Injuries. Lombardi et al. (Ref. 93) used Workers' Compensation claims filed during the year 2000 with a U.S.-based insurance provider to examine the incidence of eye injury among welders. Eye injury accounted for 5% of the compensation claims made by all workers but represented 25% of the claims filed by welders. Foreign body injuries and UV-associated eye burns represented 71.7% and 19.7%, respectively, of the eye injuries sustained by the welders.

Cornea. Aziz and Rahman (Ref. 6) examined the incidence of corneal foreign bodies among people who sought medical attention at an emergency eye clinic in Bangladesh in 2002. Of the 200 persons for whom background data had been recorded, 20 corneal foreign bodies were sustained while welding and 31 occurred while grinding. Yen et al. (Ref. 165) assessed the causes of photokeratitis (arc eye) among the 106 patients who reported with this condition to the emergency room at a hospital in Taiwan over a period of 1 year. Only 4 of the 87 patients who had received their exposures from welding arcs were professional welders and none were wearing eye protection at the time of their accident.

Magovern et al. (Ref. 99) attributed spheroidal degeneration of the cornea in a 79-year-old man to his welding experience while serving in the Navy during World War II when he put in long days repairing PT boats and landing craft. At that time, he experienced photokeratitis 3 to 4 times a week. Magovern concluded that a degenerative effect was initiated during this relatively short period of intense UV exposure.

Doughty and Oblak (Ref. 28) examined 51 welders and 51 controls to determine whether high levels of UV radiation can damage the corneal epithelium. While the incidence of pingueculae in welders was twice that in controls, no evidence of an association between welding and damage to the corneal endothelium was found.

Retina. In a case control study conducted with workers from a large metal manufacturing facility in Austria, Maier et al. (Ref. 100) found no significant differences in function or morphology of the retina between welders and controls and no signs of phototoxic damage to the retina in welders.

Effects on the Ear

A case of a welder who had tympanic membrane injury was described by Simmons and Eibling (Ref. 143). A spark entered his ear while he was welding on an overhead gas line. He experienced a sharp, burning pain at the time of the incident and then developed intermittent episodes of purulent discharge from the injured external ear.

Effects on Connective Tissue—Scleroderma

Magnant et al. (Ref. 97) performed a prospective study of the association between occupational risk factors and severity markers of systemic sclerosis (SSc). Of the 39 SSc patients who had received occupational exposures to any of the materials under study, 20 were exposed to solvents, 3 were exposed to silica and welding fumes, 4 to a combination of solvents, silica, and welding fumes, and 7 to a combination of epoxy resins, solvents, silica, and welding fumes. These occupational exposures tended to be associated with diffuse SSc, the more severe form of the disorder. Magnant and Diot (Ref. 98) later concluded that while silica and solvents appear to play a causal role in the development of the disease, the available data did not justify conclusions about a role of epoxy resins or welding fumes in the development of SSc.

Effects on the Nervous System

Nervous System Diseases. Using death certificate data from 22 states, Park et al. (Ref. 123) conducted a case-control study of potential associations between mortality from neurodegenerative diseases and occupational exposures to solvents, pesticides, oxidative stressors, electromagnetic fields (EMF), and welding. Of the four diseases analyzed (Alzheimer's disease, Parkinson's disease, motor neuron disease, and pre-senile dementia), only Parkinson's disease was associated with welding, and this was true only for the 20 deaths from Parkinson's disease that occurred before the age of 65.

Hakansson et al. (Ref. 56) examined the association between occupational exposure to extremely low frequency electromagnetic fields (ELF-EMF) and mortality from amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, and multiple sclerosis. No significant associations were found between ELF-EMF exposure and the risk for Parkinson's disease or multiple sclerosis. The relative risks were significantly elevated for Alzheimer's disease and for ALS. It cannot be discerned from the data provided if ELF-EMF from welding contributed to the increased risk for either of these nervous system disorders.

Weisskopf et al. (Ref. 161) conducted a prospective study of the association between occupational exposures and ALS mortality among more than 1 million participants in the Cancer Prevention Study II of the American Cancer Society. Only two welders died from ALS and welding was not associated with the risk for this disease.

Effects of Aluminum. Giorgianni et al. (Ref. 48) administered neuropsychological tests to a group of 50 asymptomatic aluminum welders. The welders scored significantly less well than controls on tests of memory and abstract reasoning and slightly less well on tests of attention. In contrast to these findings, Buchta et al. (Ref. 16, 83) examined 98 aluminum welders who worked at a car manufacturing plant for neurotoxic effects that could be associated with exposure to aluminum fumes. No significant differences were found between welders and controls in tests of motor-performance, short-term memory, or switching attention. Simple reaction time performance differed significantly between the two groups, but since these differences did not change when the tests were performed three times over a 4-year period, the investigators concluded that the differences may have been due to random *a priori* differences between the groups and were most likely not associated with welding exposures.

Manganese: Subclinical Effects. Halatek et al. (Ref. 58) conducted a neurological study of 59 welders who were exposed to concentrations of manganese in air that ranged from 0.003 mg/m³ to 3.37 mg/m³ in a Polish shipyard. Subjective neurological symptoms, including increased emotional irritability, headache, and sleepiness, were reported by half of the welders. Abnormalities were found in electroencephalograms (EEG) of 32% of the welders and in visual evoked potentials from 22% of the welders. Abnormal results in these tests were strongly correlated with current exposure to airborne manganese in excess of 0.3 mg/m³ and with a cumulative exposure index based on years of exposure and airborne manganese concentration. He and Niu (Ref. 66) assessed subclinical neurophysiologic changes in 68 welders who had histories of chronic exposure to low levels of manganese. Changes were seen in EEGs of the welders and in brain electricity activity mapping analyses. In other tests administered by Niu et al. (Ref. 118), welders had lower test scores on more of the neurobehavioral tests than did controls and the Profile of Mood States scores indicated a depressed emotional status.

Bowler et al. compared neuropsychological function of 76 welders with that of 42 controls (Ref. 11). Welders had lower scores than controls in tests of motor function, verbal learning, working memory, cognitive flexibility, and visuomotor processing speed while they scored as well as controls in tests of verbal skills, verbal retention, and auditory span. Tests of emotional status indicated that the welders had elevated levels of mood disturbance.

Manganese: Clinical Effects. Koller et al. (Ref. 87) conducted a double-blind study of the efficacy and safety of levodopa (L-dopa) treatment in 13 welders who had been diagnosed with manganese-induced parkinsonism. They found that L-dopa is not effective in welders with parkinsonism and concluded that L-dopa responsiveness may be useful for distinguishing between Parkinson's disease and manganese-induced parkinsonism.

Josephs et al. (Ref. 80) reviewed the medical records of eight welders who were referred to the Mayo Clinic with neurological problems and diagnosed with neurotoxicity associated with a history of welding. The characteristic manganese-associated increased T1 signal in the basal ganglia was seen in magnetic resonance images of the brains of all eight patients. Racette et al. (Ref. 128) examined the prevalence of parkinsonism in 1423 welders from Alabama who were referred to them by attorneys for medical-legal evaluation of Parkinson's disease. The investigators found that parkinsonism occurred more frequently and at an earlier age among the Alabama welders than among a comparison population of male residents from Copiah County, Mississippi.

Using a population of 2072 patients drawn from three movement disorder clinics, Goldman et al. (Ref. 50) investigated occupational associations with Parkinson's disease or parkinsonism. Three welders, all of whom had typical Parkinson's disease, were identified among the clinical patients. The frequency of Parkinson's disease or parkinsonism in welders was not significantly elevated compared with the control population. Fryzek et al. (Ref. 41) conducted a retrospective cohort study of the rates of hospitalization for Parkinson's disease and other neurodegenerative disorders among 27,839 male Danish metal-manufacturing workers. The rates of Parkinson's disease and other neurological conditions among welders were consistent with those of the general population of Denmark. No association was found between the incidence of Parkinson's disease with age or with the duration of the welding experience.

Using the U.S. National Center for Health Statistics (NCHS) National Cause of Death databases, Stampfer (Ref. 145) examined the relationship between occupation as a welder and mortality from neurodegenerative diseases. The study population included 4,252,490 men who died between 1985 and 1999; 107,773 had been welders. Welders were slightly, but significantly, less likely to have Parkinson's disease as the contributing or underlying cause of death. In addition, welders were not found to have increased odds of dying from Parkinson's disease at a younger age than men with other occupations.

Marsh and Gula (Ref. 101) conducted a case-control study among the 12,595 workers who had ever been employed between 1976 and 2004 at any one of three Caterpillar heavy equipment plants in Illinois. Cases of neurological disorders were identified from company medical claims and comprised the 70 persons who had filed claims for either idiopathic Parkinson's disease or secondary parkinsonism and the 153 persons who had filed claims for other progressive diseases of the basal ganglia and essential and other specific forms of tremor. There were no significant associations between ever having welded in a Caterpillar plant and any of the neurological disorders studied.

In a study conducted in Sweden, Forel et al. (Ref. 40) examined the incidence of basal ganglia and movement disorders in welders and flame cutters. The health and employment records of 49,488 male welders were compared with those of 489,572 male workers who had no history of exposure to welding or flame cutting at work. Neurological disorders including Parkinson's disease occurred at a slightly lower rate among the welders than in the comparison population. There was no difference in mean age at first occurrence of Parkinson's disease between the welders and flame cutters and the comparison cohort.

Sadek et al. described the case of a 33-year-old man who developed signs of manganism after being employed as a welder for 3 years (Ref. 135). He had worked in the shipbuilding industry where he had welded a manganese steel alloy in confined spaces and had rarely used respiratory protection.

Manganese: Bioavailability. In his analysis of the evidence for an association between manganese exposure in welding fumes and Parkinson's disease or parkinsonism, McMillan (Ref. 107) noted that manganese emanating from different processes may differ in its physicochemical structure which could affect its bioavailability. McMillan (Ref. 107), Roth and Garrick (Ref. 134) and others have argued that, since iron and manganese compete for the same transfer systems across the blood-brain barrier, iron from welding fumes might actually reduce the passage of manganese into the brain.

Inflammation and Oxidative Stress

Kim et al. (Ref. 84) compared markers of inflammation, including C-reactive protein, fibrinogen, and numbers of neutrophils, in blood from 24 welders and 13 non-exposed controls. C-reactive protein levels were significantly increased 16 hours after welding exposures. A significant increase in neutrophil count and a significant decrease in fibrinogen were seen in blood following welding fume exposure in non-smoking welders. In further work from this laboratory, Wang et al. (Ref. 160) showed that the genes whose expression was altered following welding fume exposure were clustered in biologic processes related to the inflammatory response, oxidative stress, intracellular signal transduction, cell cycle, and programmed cell death. The greatest variations in gene expression were seen in the non-smoking welders. Wang et al. (Ref. 159) later showed that the effects of welding fume exposure on gene expression were transient, and most of the observed effects diminished within 19 hours post exposure.

Han et al. (Ref. 60) conducted a study to identify potential biomarkers of oxidative stress in the serum of 197 welders. Significant differences in total antioxidant status, total protein, aconitase, glutathione peroxidase, and isoprostane were found between welders and controls. Li et al. (Ref. 91) found that erythrocytic superoxide dismutase (SOD) activity and serum malondialdehyde levels were 24% lower and 78% higher, respectively, in welders than in controls, suggesting that

occupational exposure to welding aerosols induces oxidative stress. Zhu et al. (Ref. 175) found that average concentrations of SOD, catalase, glutathione peroxidase, and the antioxidants vitamins C and E in plasma were significantly decreased and concentrations of lipoperoxides in red blood cells were significantly increased in welders compared with controls.

Borska et al. (Ref. 8) compared humoral constituents of the immune system and indicators of inflammation in peripheral blood from 20 men who worked as welders and grinders of stainless steel with those of controls who lived in the same geographical area. The number of phagocytic cells was significantly greater in blood from welders and grinders than from controls. Concentrations of all but 5 of 17 proteins, many of which are associated with the immune system or inflammation, differed significantly in the blood from the exposed subjects and the controls.

Hoffer et al. (Ref. 69) examined whether the release of superoxide anions from stimulated polymorphonuclear leukocytes (PMNs) obtained from healthy donors was affected by pre-incubation with serum from welders or from unexposed individuals. No difference was seen when serum from all welders was compared with that from all controls or when serum from smoking welders was compared with smoking controls. However, significantly less superoxide was generated following treatment with serum from non-smoking welders under age 40 than with serum from non-smoking controls in the same age group.

Oxidative DNA Damage

Kim et al. (Ref. 85) monitored particulate exposures and 8-hydroxy-2'-deoxyguanosine (8-OHdG: an indicator of oxidative DNA damage and repair) concentrations in urine from boiler makers for 5 days during an overhaul of oil-fired boilers. The urinary concentration of 8-OHdG increased during the work shift and was significantly related to workplace concentrations of particles with aerodynamic diameters less than 2.5 μm and to the content of V, Mn, Ni, and Pb in fumes.

Effects on the Cardiovascular System

Gurevitz et al. (Ref. 54) developed a simple, low risk screening protocol to assess interactions between EMF produced by industrial equipment and the implantable cardioverter defibrillator (ICD) to determine whether it is safe for patients with ICDs to return to the workplace.

Effects on the Kidneys

Nogue et al. (Ref. 119) described a case of a welder with renal disease that was attributed to cadmium exposure. He was diagnosed with IgA mesangial glomerulonephritis, a condition in which circulating immunocomplexes containing the antibody IgA deposit in the glomerular mesangium of the kidney. Trevisan and Gardin (Ref. 156) described the case of a welder who was treated for a disorder in which proximal tubular function is impaired. He had been exposed to high levels of cadmium and his blood and urinary cadmium levels were greatly elevated. He developed kidney stones, which were attributed to chronic exposure to high concentrations of cadmium.

Effects on Reproduction

Wong et al. (Ref. 162) examined the effects of lifestyle, occupation, and medical history on sperm count in a case control study of 92 fertile and 73 sub-fertile men. The risk for oligozoospermia was non-significantly elevated in men with occupational exposures to welding. Danadevi et al. (Ref. 24) compared the quality of semen collected from 57 welders and 57 controls. The percent of subjects with normal sperm morphology, normal sperm counts, and rapid linear sperm motility was significantly lower among the welders than among controls. Nickel and chromium concentrations in blood were positively correlated with defects in semen.

Damage to DNA in sperm caused by oxidative stress may be measured by the level of 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) in sperm DNA. A study by Loft et al. (Ref. 92) showed that oxidative damage to sperm DNA may adversely affect fertility but that the level of 8-oxodG does not differ significantly in sperm from men who performed

daily welding and those who did not. A study by Hjollund et al. (Ref. 67) showed that welding does not affect the rate of spontaneous abortion in pregnancies initiated by *in vitro* fertilization.

General Health

Rongo et al. (Ref. 133) surveyed 101 welders in Tanzania for information about occupational exposures and occupation-related health problems. Only 50 of the welders reported using face shields, and only ten used goggles or protective eye-wear. The most common health complaints were skin burn, eye problems, headache, chest or throat pain, backache, hearing problems, and nasal and skin irritation.

Biological Monitoring

Chromium and Nickel. Stridsklev et al. (Ref. 149) examined the relationship between levels of chromium and nickel in air and in biological fluids from seven men engaged in FCAW of stainless steel. While the concentrations of nickel in air were not significantly associated with those in urine or blood, significant associations were found between the concentrations of Cr(VI) measured in air and those of total chromium in plasma and urine leading to the conclusion that post-shift urinary chromium concentrations may be useful for monitoring the uptake of chromium by welders.

Colli et al. (Ref. 21) evaluated the kinetics of urinary nickel excretion by three welders employed in SMAW of stainless steel. Mean urinary half-lives were calculated to be 59.5 hours during the work shift and 95.5 hours after the work shift and during the weekend, suggesting that nickel accumulates in two compartments in the body, with different elimination rates. The investigators concluded that measurement of nickel in a 24-hour urine sample collected throughout the entire work shift and during the 16 hours following exposure would yield the best information about exposures.

Polycyclic Aromatic Hydrocarbons. Mukherjee et al. (Ref. 115) measured concentrations of 1-hydroxypyrene (1-OHP: a biomarker for exposure to polycyclic aromatic hydrocarbons), Pb, V, Cr, Mn, Cu, and Ni in urine samples collected from boilermakers for five consecutive workdays. The concentration of 1-OHP was not significantly associated with the concentration of any of the metals at any time during the work week indicating that 1-OHP is not an appropriate surrogate marker for exposure to the metals studied.

Manganese. Wongwit et al. (Ref. 163) measured manganese concentrations in stool specimens and toenail clippings to determine if less invasive biological samples could be used in place of blood to monitor occupational exposures to manganese. The correlation of manganese concentrations among the three biological samples was found to be poor. It was concluded that blood remains the best medium for biomonitoring of manganese concentrations in occupationally-exposed individuals.

Lu et al. (Ref. 94) examined the relationship between exposure to manganese and serum concentrations of manganese in welders. Both iron and manganese tended to increase in serum with years of welding experience but the correlation was significant only for iron. The authors concluded that serum manganese may be useful as a biomarker for assessing recent, but not historic, exposures to airborne manganese. Based on arguments that manganese exposure modulates iron metabolism and the storage of iron in the body, Lu et al. investigated the relationship between serum concentrations of manganese, iron, and proteins involved in iron binding and transport. Levels of ferritin, but not of transferrin or transferrin receptor, increased significantly with years of welding experience. Serum concentrations of iron, ferritin and transferrin, but not transferrin receptor, were inversely associated with those of manganese.

Lead. Yang et al. (Ref. 164) described three welders found to have elevated blood lead levels (BLLs) during a survey taken in 1992 at a shipyard in Taiwan. When his BLL was found to be 54.1 µg/dL, the first welder was transferred to an office job. His BLL dropped to 31.6 µg/dL in 6 months and he returned to welding. Improvements in ventilation and regulations concerning use of personal protection devices were made at that time, and his BLL gradually decreased to 30 µg/dL by 2001. The other two welders, whose BLLs were about 50 µg/dL in 1992, were not removed from the job. They continued to weld in the same area and it took more than 4 years for their BLLs to decrease to less than 40 µg/dL after the ventilation was improved.

Genotoxicity

Danadevi et al. (Ref. 23) found that DNA damage, as measured by the comet assay in peripheral blood lymphocytes and by the frequency of micronuclei in buccal cavity epithelial cells, was significantly higher in welders than in controls.

Iarmarcovai et al. (Ref. 72) compared the levels of DNA damage in welders and controls using the comet and micronucleus assays in peripheral lymphocytes. The micronucleus assay showed a significant increase in the number of micronuclei in welders compared with controls indicating that welders had a higher frequency of chromosomal damage. The comet assay revealed significant differences between welders and controls at the end, but not at the beginning of the workweek, suggesting that DNA lesions induced by welding exposures are reversible.

Medeiros et al. (Ref. 110) compared the number of DNA-protein cross-links and the frequency of micronuclei in peripheral blood lymphocytes from tannery workers exposed to Cr(III), stainless steel welders exposed to both Cr(III) and Cr(VI), and non-exposed controls. The levels of DNA-protein cross-links were 2.5 times higher in welders than in tannery workers and were significantly higher in both exposed groups than in controls. The number of micronuclei was significantly elevated in lymphocytes from tannery workers, but not in welders.

Investigations in Animals and Cell Culture

Infectivity and Inflammation

Antonini et al. (Ref. 5) found that fumes from SMAW of stainless steel (SMAW-SS), but not from GMAW of mild steel (GMAW-MS) or stainless steel (GMAW-SS), enhanced infectivity by *Listeria monocytogenes* in rat lungs. Fume samples were introduced into rat lungs by intratracheal instillation followed, 3 days later, by instillation of *Listeria monocytogenes*. Treatment with SMAW-SS fume reduced pulmonary clearance of the bacterium and reduced survival of the rats. Lactate dehydrogenase, albumin, and numbers of macrophages, PMNs, eosinophils, and lymphocytes were elevated in bronchoalveolar lavage fluid (BALF) after treatment with SMAW-SS fume.

Taylor et al. (Ref. 153) compared the inflammatory response in rats exposed by intratracheal instillation to fumes from GMAW-MS, GMAW-SS, and SMAW-SS, and to the water soluble and insoluble components of SMAW-SS fume. All of the samples caused pulmonary inflammation but this effect was greater and lasted longer with the SMAW-SS fume. Both the soluble and insoluble fractions contributed to the inflammatory response elicited by SMAW-SS fume. Subsequent studies from this laboratory (Ref. 4) showed that soluble chromium was the component of SMAW fume most likely to be responsible for suppression of the lung defenses against *Listeria* infection. These investigators (Ref. 2) also reported that the SMAW-SS fume caused DNA strand breaks when incubated with DNA and hydrogen peroxide in a cell-free assay.

McNeilly et al. (Ref. 108) examined the effects of three different stainless steel welding fumes and their soluble and insoluble fractions on the production of the pro-inflammatory cytokine IL-8, and on the activation of the nuclear translocation factors NF- κ B and AP-1 by cultured human type II alveolar epithelial cells. IL-8 was significantly elevated following treatment with the soluble fraction of fumes produced with nickel-based and cobalt consumable electrodes. All fume samples and their soluble fractions depressed levels of the intracellular antioxidant glutathione within 2 hours after treatment. In a subsequent study, McNeilly et al. (Ref. 109) found that neutrophils were significantly elevated in BALF from rats treated with the whole fume or with the soluble fume fraction from the stainless steel welding electrodes; macrophages were significantly elevated in rats treated with the whole fume but not with the soluble fume fraction.

Pascal and Tessier (Ref. 124) treated cultured human lung epithelial cells with nickel, manganese, or potassium dichromate. At manganese or Cr(VI) concentrations between 0.2 μ M to 200 μ M, levels of IL-6 and IL-8 in the culture medium were up to 4.4 times greater than that found in controls. Levels of TNF- α were unchanged.

Fibrosis

Sung et al. (Ref. 150) measured pulmonary function and examined cells recovered in BALF from rats exposed by inhalation for up to 60 days to high and low doses of SMAW-SS fumes. The number of alveolar macrophages, PMNs, and