HEALTH EFFECTS FROM WELDING EXPOSURES:

2022 LITERATURE UPDATE

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List of Acronyms and Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
AGSW	Argon Gas Shielded Welding
AWF	Automatic Welding Filters
AWS	American Welding Society
BAL	Bronchoalveolar Lavage
CFD	Computational Fluid Dynamics
CI	Confidence Interval
CO	Carbon Monoxide
CO_2	Carbon Dioxide
CO_2SW	Carbon Dioxide Shielded Welding
Cr	Chromium
CrIII	Trivalent Chromium
CrIV	Hexavalent Chromium
DNA	Deoxyribonucleic Acid
EBC	Exhaled Breath Condensate
ECHA	European Chemical Agency
FCAW	Flux-core Arc Welding
Fe	Iron
FEF	Forced Expiratory Flow
FEV1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
GMAW	Gas Metal Arc Welding
GSH-PX	Glutathione peroxidase
HBM4EU	European Human Biomonitoring Initiative
HPRT	Hypoxanthine Phosphoribosyl transferase
HRV	Heat Rate Variability
ICNIRP	International Commission on Non-Ionizing Radiation Protection
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
ILO	International Labor Organization
IncRNA	noncoding RNA
IOL	Intraocular Lenses
IPM	inhalable particulate matter
MFF	Metal Fume Fever
Mn	Manganese
MRI	Magnetic Resonance Imaging
mRNA	Messenger RNA
MSD	Musculoskeletal Disease
MW	Manual Welding
Ni	Nickel
NOAEL	No Observed Adverse Effect Level

OBAA	Oxidative Burden – Ascorbate Assay
OEL	Occupational Exposure Limits
OGG1	8-oxoguanine DNA glycosylase
OPAA	Oxidative Potential – Ascorbate Assay
OR	Odds Ratio
P	Plasma
Pb	Lead
PCR	Polymerase Chain Reaction
PEF	Peak Expiratory Flow
PEFR	Peak Expiratory Flow Rate
PexA	The Particles in Exhaled Air Method
PIXE	Particle-induced X-ray Emission
PPE	Personal Protective Equipment
PR	Prevalence Ratio
RBC	Red Blood Cells
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
REBA	Rapid Entire Body Assessment
RMM	Risk Management Measures
RN	Red Nucleus
RNA	Ribonucleic Acid
RQ	Risk Quotient
RR	Relative Risk
SMAW	Shielded Metal Arc Welding
SRQ	Sum of the Risk Quotients
SWORD	Surveillance of Work Related Occupational Respiratory Diseases
U-Cr	Urinary Chromium
WF	Welding Fume
WHAT-ME	Workers Health in Apprenticeship Trades-Metal working and Electrical
WHO	World Health Organization
WRMD	Work-related Musculoskeletal Disorders
XRF	X-ray Fluorescence
γ-GCS	Glutamate–cysteine ligase
ZnO	Zinc Oxide

1.0 INTRODUCTION

On behalf of the American Welding Society (AWS), Epsilon Associates conducted a comprehensive literature search and summary of studies related to the health effects of welding. In this update, we included literature published in 2022 (including electronic publications or epubs) but excluded any articles that have been included in previous literature updates. This report describes the literature search methods, provides a summary of the results of our searches (*e.g.*, how many articles we identified), and explains how we identified relevant articles to include in the report (Section 2). We also present summaries of the exposure-related studies in Section 3, and of relevant health effects studies in Section 4.

2.0 METHODS

We searched the PubMed database for articles relevant to welding exposures and health effects as described below.

2.1 Search Strategy

1. To capture all the potentially relevant literature, the initial keyword searches included the word "welding" or "welders" or simply weld* (where the "*" is wild).
2. Searches were restricted to the year 2022 either electronically (epubs) or in print. Articles included in previous reviews were excluded from this review.
3. Where possible search terms were limited to searches of the titles and abstracts.
4. Searches were also limited to full text publications.
5. To further limit searches, we used the additional search word "health".

2.2 PubMed and NIOSHTIC-2 Searches

An initial search yielded 1,311 citations. We further refined the search to include "health", and this reduced the number of citations to 412. The 412 citations were uploaded to excel for further screening for relevance. We also searched the NIOSHTIC-2 database using the key words "welding" or "welder" in all fields for the year 2022.

2.3 Literature Review

We reviewed titles to assess the relevance to exposure and health effects from welding and identified duplicates for exclusion. We also excluded commentaries, conference abstracts, and any foreign studies that were deemed to be of little or no relevance. Some of the references were included in the 2021 review and thus not summarized in this report. The remaining citations were retained, and the article titles and abstracts were reviewed for relevance and sorted into the following categories:

- Particle characterization and exposure studies
- Epidemiology and controlled human exposure studies.
- Animal studies
- Mechanistic/cell/*in vitro* studies
- Reviews

The breakdown of the remaining references by category is listed in Table 2.1.

Table 2.1 Breakdown of Abstracts Reviewed by Study Category

Study Category	Totals from all databases
Particle characterization and exposure	17
Epidemiology and controlled human exposure	30
Animal	2
Mechanistic/cell/*in vitro*	6
Reviews	9
Overall Total	**64**

3.0 EXPOSURE STUDIES

We identified 17 exposure-related studies or studies related to regulation or health and safety in welding occupational groups published in 2022 (*i.e*., particle characterization and exposure). Some studies were published online in 2022 (*i.e*., 2022 was the "epub date") and these were included in our summary. Articles that were not relevant or were included in prior AWS updates were excluded. A brief summary of the exposure abstracts is provided below for all the relevant studies.

Bocca (2023, epub 2022) measured levels of metal oxide nanoparticles (Cr_2O_3, Mn_3O_4 and NiO) in 18 stainless steel welders and 15 unexposed controls that worked in two Italian engineering companies. The authors collected samples of exhaled breath condensate (EBC) and urine pre-shift (1^{st} day) and post-shift (5^{th} working day), as well as plasma and inhalable particulate matter (IPM) post-shift (5^{th} working day). All samples were analyzed using Inductively Coupled Mass Spectrometry (ICP-MS). The authors reported median IPM concentrations and particle sizes of Cr_2O_3, Mn_3O_4, NiO of 871,574 particles/m^3 and 70 nm, 713,481 particles/m^3 and 92 nm, and 369,324 particles/m^3 and 55 nm, respectively. In EBC samples, post-shift concentrations of Cr_2O_3 were significantly higher than pre-shift concentrations (64,645 particles/mL and 55 nm vs. 5,836 particles/mL and 58 nm). Detectable levels of NiO in EBC and plasma were found only in post-shift samples (22,000 particles/mL; 65 nm and 8248 particles/mL; 37 nm, respectively). Metal-oxide concentrations were not detected in the urine samples. Overall, the authors concluded that biological and air samples of metal-oxides were a good approach for assessing exposure risks and implementing management practices to reduce exposures.

Čargonja et al. (2023, epub 2022) collected hair and nail samples from metal workers to evaluate long-term exposures to metals. Samples were analyzed using Inductively Coupled Mass Spectrometry (ICP-MS) for 12 different elements. In addition, workplace concentrations of 12 elements in particulate matter were determined using X-ray fluorescence (XRF) and particle-induced X-ray emission (PIXE) methods. The authors reported significantly higher concentrations of metals in welders compared to unexposed controls, especially of titanium, manganese, iron, and cobalt.

Galarneau (2022) developed and validated an exposure matrix that was used to estimate exposures to total dust, manganese, nickel, chromium, and aluminum for welders in the Workers Health in Apprenticeship Trades-Metal working and Electrical (WHAT-ME) cohort. The aim of the study was to assess associations between pregnancy and birth outcomes and welding exposures. The authors conducted a systematic review of the literature to identify data on welding dust and/or metals exposures. The data were extracted and used to derive exposure estimates based on the welding process, base metals used, and different welding scenarios. To validate the exposure models, the most common welding scenarios were replicated, and personal measurements of welding dust and metals were obtained in a controlled laboratory setting. The laboratory-derived estimates were compared to estimates derived from the literature. The authors reported that the literature search resulted in 92 publications and over 700 summary statistics representing 4620 samples of personal total dust, 4762 manganese, 4679 of nickel, 3972 of chromium, and 676 of aluminum. The highest exposures to total dust were from flux-core arc welding (FCAW). For individual metals, mild steel produced the highest manganese exposures, while high alloyed steel from gas metal arc welding yielded the highest nickel exposures. The highest chromium exposures were from stainless steel using manual metal arc welding. Lastly, FCAW welding on aluminum yielded the highest aluminum exposures. A total of 21 scenarios were tested in the laboratory (about 90% of the scenarios in the WHAT-ME study). The results showed strong and statistically significant Spearman rank correlations between measured and estimated exposures for total dust rho 0.93 ($P < 0.001$) and manganese 0.87 ($P < 0.001$). Weaker but statistically significant or close to significant correlations were observed for nickel 0.54 ($P < 0.024$) and chromium (0.43, $P = 0.055$). For aluminum the correlation was poor and not statistically significant (0.29, $P = 0.210$). The authors concluded that the study provided a comprehensive and validated exposure matrix that could be used to estimate welding exposures over a wide range of welding processes, base metals, and welding scenarios.

Galarneau et al. (2022a) assessed whether there were differences in exposures among men and women working in the same trade. Men and women that participated in the Workers Health in Apprenticeship Trades-Metal working and Electrical (WHAT-ME) study were recruited and followed for up to 5 years. A questionnaire was administered at the time of recruitment and every 6 months thereafter. The authors collected details regarding the welding work and collected urine samples that were analyzed using Inductively Coupled Mass Spectrometry (ICP-MS). Welding exposures were estimated from the welding process and materials used. The concentrations of 12 metals in 794 (434 welders and 360 electrical workers) samples were assessed. Urinary concentrations of aluminum and chromium were higher in welders compared to electrical workers. Female welders were found to have lower airborne exposures to chromium and nickel than male welders, but higher urinary levels of aluminum, chromium, and manganese. Using regression, the authors assessed the correlation between urinary metal concentrations and estimated exposures. There was a significant correlation for aluminum and chromium, but a weaker correlation for manganese and nickel. The authors noted that the higher metal concentrations in urine for female welders was a concern because of potential impacts on pregnancy outcomes.

Kuppusamy Vellingiri et al. (2022) evaluated exposures to welding fumes from gas metal arc welding stainless-steel using 3-mm, 5- mm and 6-mm thick stainless steel pieces, filler wire (ER316 L) and four shielding gas compositions. The authors tested two welding hood configurations, one with a square duct and another with a conical duct. Air samples were collected using glass fiber filters. The authors reported that the conical fume hood configuration was more effective at controlling welding fume exposures compared to the square duct. Higher fume formation was also observed with the addition of CO_2 to the shielding gas mixture. The authors also reported that socio-demographic characteristics of the workers (e.g., age, marital status, education, work experience) were associated with awareness of occupational hazards and use of personal protective equipment (PPE). The authors concluded that workers be better educated regarding occupational hazards and use of PPE.

Leese et al. (2023, epub 2022) evaluated the use of exhaled breath condensate (EBC) as a viable medium for determining hexavalent chromium (CrVI) or trivalent chromium (CrIII) exposures in workers, including stainless steel welders, in France, Finland, Italy and the Netherlands. EBC samples were collected pre- and post-work week from 177 exposed workers and 98 controls (no exposure). Samples were analyzed using inductively coupled plasma mass spectrometry (ICP-MS). The authors reported the highest CrVI exposures in chrome platers. In welders, a significant increase in EBC concentrations for both CrVI and CrIII was observed between pre- and post-work week samples. The authors concluded that EBC was a suitable and noninvasive method for detecting low inhalation exposures to chromium.

Lehnert et al. (2022) reported on findings from the InterWeld pilot study. The aim of the study was to determine the conditions under which occupational exposure limits (OEL) could be achieved in gas metal arc welding (GMAW) with a solid wire. Expert welders conducted forty tests under different exhaust ventilation conditions and with the use of welding torches with integrated fume extraction. Personal samples were obtained to measure exposures to respirable welding fume and manganese (Mn), hexavalent chromium, and nickel. Inductively coupled plasma mass spectrometry (ICP-MS) was used to analyze metal concentrations. Welding of 10 mm sheets produced higher concentrations of welding fumes and metals (two to five-times higher) than 2 and 3-mm sheets. The use of ventilation or torches with fume extraction reduced exposures to welding fume and Mn by 70-90%. Despite exposure reductions with proper ventilation or extraction combined with low-emitting processes, the authors noted that compliance with OELs is not always achieved and that further technical advancements are needed to further reduce exposures and achieve health protection in the workplace.

Li et al. (2022) evaluated different welding operations, including argon gas shielded welding (AGSW, JS80 welding wire), manual welding (MW, ZS60A welding rod) and carbon dioxide shielded welding (CO_2SW, 907A flux cored wire) in a laboratory setting, measuring concentrations of welding fumes, metals and the welding arc generated. The authors reported concentrations of welding fumes of 6.80 mg/m^3, 6.17 mg/m^3, and 3.13 mg/m^3 for the AGSW, MW, and CO_2SW processes, respectively. With regards to the welding arc, the effective irradiance from high to low was MW, CO_2SW, and AGSW (1,010.7, 740.9, 589.5 μW/cm^2, respectively). AGSW generated the highest long-wave ultraviolet light (1,500 μW/cm^2). The authors also reported that the highest manganese content was found in the JS80 welding wire (128493.2 mg/kg), the highest titanium concentration was found in the 907A flux cored wire (24355.5mg/kg), and the highest copper concentration was in the ZS60A electrode (24422.12 mg/kg). The authors concluded that each welding process presented their own unique health hazards and that protective measures should be tailored to each process.

Ljungkvist et al. (2022) reported on a novel method for measuring the metal particle dose (chromium, manganese, and nickel) to the lungs from welding compared to air monitoring. The method, Particles in Exhaled Air (PExA), measures the particles that enter the small airways in the lung. The authors collected exhaled air samples in 19 stainless steel workers before and after their work shift. Concurrently air monitoring was conducted, and blood samples were also collected. The authors reported no significant difference between the before and after exhaled air metal concentrations. The authors speculate that the samples were subject to a significant amount of contamination during sampling and high background metal concentrations that affected the results. In conclusion, the authors noted that the new method is promising, but background and contamination issues need to be resolved.

Nalugya et al. (2022) conducted a cross-sectional study to evaluate the practice of using personal protective equipment (PPE) in small metal workshops in the Nansana Municipality in Uganda. The authors used questionnaires to collect information from 329 welders and also conducted interviews. The data were analyzed using Poisson regression. The authors reported that 61.4% of the welders were knowledgeable with regards to PPE use, but 68.7% had a negative attitude towards the use of PPE. Only 37.1% of welders used appropriate PPE. Associations were found between knowledge of PPE use and training, while attitude was related to education, knowledge, and duration of work experience. Use of appropriate PPE was associated with training and attitude. The authors concluded that although welders had good knowledge of PPE use, the majority had a bad attitude that resulted in poor PPE use practices. A better understanding of health impacts from welding exposures would help with the welding attitude and improve PPE use.

Ndaw et al. (2022) used data from the human biomonitoring for Europe initiative (HBM4EU) to assess various biomarkers for use to determine exposures to hexavalent chromium (CrVI) from stainless steel processing, chrome plating and other occupational activities (including welding). The authors measured CrVI concentrations in red blood cells (RBC) and plasma (P) in 345 exposed workers and 175 controls including how concentrations are affected by job task. Higher Cr concentrations in P were found in all workers compared to controls, whereas only chrome platers and paint application workers had higher Cr levels in RBCs compared to controls (not welders). Similarly, the authors reported significant correlations between CrVI in inhalable dust and chromium concentrations in P and RBCs for most occupations, but not in welders. The authors concluded that more studies were needed to verify the usefulness of blood biomarkers for assessing CrVI occupational exposures.

Paridokht et al. (2023, epub 2022) used computational fluid dynamics (CFD) to assess occupational exposures to metal fumes from shielded metal arc welding (SMAW). The concentrations and size of the metal fumes were measured in a galvanized steel chamber to compare with simulated results and evaluate the efficiency of ventilation systems for reducing exposures. The authors reported that the highest concentrations measured were from iron metal fumes (3045 $\mu g/m^3$, 0.25 μm diameter) and that a traditional ventilation system with local exhaust can reduce the exposures to workers. Moreover, CFD was useful in estimating metal fume concentrations and evaluating the efficiency of the ventilation systems. The authors concluded that more research in this area would be helpful for assessing additional welding fume exposures, including of gases.

Sauvé et al. (2022) used data from two large occupational exposure studies, COLCHIC and SCOLA, to evaluate co-exposures to multiple air pollutants. The authors selected a total of 118 chemicals, including 31 carcinogens, for which more than 100 measurements were available above the respective limits of detection from 2010-2019. Measurements were grouped by working scenarios (combination of occupational sector, task and year) and analyzed for the most common co-exposures. With regards to welding, the authors reported that electric arc welding had one of the highest percentages of co-exposure to carcinogens (37%). The authors noted the importance of considering co-exposures, particularly of carcinogens in the workplace.

Shang et al. 2022 assessed the switching time requirements for automatic welding filters (AWFs) for meeting optical radiation limits established by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) or the American Conference of Governmental Industrial Hygienists (ACGIH). In a welding environment, the authors evaluated single and cumulative exposures of retinal thermal and blue light exposures. Results indicated that maximum switching time was inversely proportional to the exponent of the shade number difference, and estimated switching times are up to 1/10th smaller than current international limits for effective blue light. The authors also noted that AWFs are effective for limiting hazardous radiation levels in a dark state.

Viegas et al. (2022) assessed whether risk management measures (RMM) contributed to the reduction in hexavalent chromium (CrVI) in a cohort of 399 workers and 203 controls that were part of the HBM4EU project that spanned nine European countries. The authors evaluated urinary total chromium (U-Cr), Cr and CrVI in personal inhalable and respirable dust, and Cr on hand wipes. The RMM were assessed using a questionnaire. Regression analyses were conducted to evaluate the relationship between inhalation results and U-Cr in different workers. The authors reported good correlations between inhalation and U-Cr. For welders, a reduction in U-Cr was found with the use of personal protective equipment, use of local exhaust ventilation and training.

Wang et al. (2022) experimentally determined emission rates for metal fumes (total chromium (Cr), iron (Fe), lead (Pb), manganese (Mn), and nickel (Ni)) from gas meal arc welding and flux cored arc welding and estimated exposures in workers at a shipyard using these values in a Near-Field/Far-Field mathematical model together with a Bayesian decision analysis methodology. The model was further evaluated using a welding simulation experiment and measured data at a shipyard. The authors found that there was a strong correlation (R^2 = 0.81-0.94) between the predicted exposures using the mathematical model and the field measurements. Importantly, estimated long-term worker exposures to Mn, Fe and Pb exceeded health-based limits, which indicated that protective measures were needed. The authors concluded that the prediction model was a valid method for assessing exposures, especially when there were limited personal measurements available.

Wippich et al. (2022) presented an analysis of measured concentrations of cobalt in inhalable and respirable dust fractions to determine if a conversion function can be determined for application between the two size fractions. A conversion function would be useful for retrospective analyses of occupational exposures. The authors used 639 parallel measurements of cobalt concentrations in inhalable and respirable dust fractions obtained from the MEGA databased (maintained by the Institute for Occupational Safety and Health of the German Social Accident Insurance). The data were split into groups based on the type of data (stationary of personal) and three activity groups (the occupational activities 'high temperature processing', 'filling/transport/storage', and 'machining/abrasive techniques'). The 'high temperature processing' and 'machining/abrasive techniques' were further subdivided into welding and grinding categories. Based on evaluation of these data, the authors developed conversion functions for estimating the amount of cobalt in the respirable dust fraction out of the cobalt concentration in the inhalable fraction. In the paper the authors highlight the uncertainties associated with these conversion functions.

4.0 HEALTH EFFECTS STUDIES

4.1 Studies in Humans

We identified studies in humans that assessed various health effects related to welding fume exposures. These health effects included neurological effects (3 studies), respiratory effects (12 studies), cancer (3 studies), eye effects (3 studies), musculoskeletal effects (3 studies), reproductive effects (2 studies), and other health effects (4 studies). Summaries of these studies are provided below.

4.1.1 Neurological Effects

de Freitas et al. (2022) evaluated the effects of metal fume exposures on multi-finger synergy and posture-stabilizing synergy while standing. The authors obtained information on workers occupational history, a Magnetic Resonance Imaging (MRI) scam, and results from performance-stabilizing synergy for multi-finger force production and load releasing while standing. The subjects included 29 welders and 19 controls (matched by age and gender). Brain iron and manganese concentrations were estimated using R2* and R1 relaxation rates and brain microstructural integrity was also assessed. The results showed higher R2* in welders in various regions of the brain compared to controls. No difference between welders and controls was found for the multi-finger synergy test, but welders did have lower performance during the load releasing postural task, compared to controls. The effects did not appear to affect job performance, but the reduced performance was correlated with increased R2*. Therefore, the authors noted that these results could be indicative of neurotoxicity associated with the welding fume exposures.

Ma et al. (2022) presented a case of a carbon dioxide (CO_2) arc welder suffering from encephalopathy likely from carbon monoxide (CO) poisoning due to his welding work. The 40-year-old man had worked as a welder for 15 years. He was taken to the hospital and his symptoms included a tremor, involuntary urination, and speaking nonsense. In addition, he suffered from headaches and memory loss. A brain magnetic resonance image showed that he had encephalopathy. Treatment in a hyperbaric chamber relieved some of his symptoms. The authors concluded that the encephalopathy was due to the workers extended exposure to CO from welding and urged more awareness related to this potential danger.

Prado-Rico et al. (2022) evaluated the potential for lead co-exposures in welders. Because lead has been found to impact iron regulation, the authors assessed the association between blood lead levels and iron accumulation in 42 welders and 29 controls. The authors collected whole blood metal concentrations and obtained magnetic resonance images. The R2*(1/T2*) and R1 (T1 relaxation rate) were used to estimate iron and manganese concentrations, respectively. Regression analyses were conducted, adjusting for potential confounders. The authors reported higher whole blood levels of lead, manganese, iron and copper compared to controls. In addition, welders had higher R2* levels in the red nucleus (RN) but not R1. The R2* in the RN was significantly correlated with whole blood lead levels. The authors concluded that the results suggest that R2* levels in the RN may be a biological marker for elevated lead exposures. They recommend further studies to support these conclusions and note that lead is also a neurotoxin, and co-exposures can have important health implications for workers exposed to welding fumes.

4.1.2 Respiratory Effects

Abdel-Rasoul et al. (2022) evaluated correlations between respiratory health disorders and workplace exposures in Egyptian welders. The authors randomly selected 110 welders and 110 controls between January 2019 and February 2021. Personal measurements of total welding fume, respirable dust and manganese air concentrations were collected along with spirometry measurements, manganese concentrations in whole blood, and respiratory symptoms. Personal air concentrations across all measurements exceeded international occupational levels. Compared to controls, welders had increased respiratory symptoms (rhinitis, cough, expectoration, wheezing, dyspnea, and chronic bronchitis) as well as reduced spirometry measures (FVC%, FEV_1%, FEV_1/FVC%, and FEF_{25-75}%). Manganese concentration in blood were also higher in welders than controls (3.35 ± 0.5 and 1.81 ± 0.79 ng/mL; respectively). Longer work hours were correlated with increased respiratory symptoms, and use of personal protective equipment (PPE) was correlated with reduced symptoms. The authors concluded that based on their study welders in Egypt were exposed to welding fume levels that exceeded occupational standards and these exposures were associated with respiratory symptoms and compromised lung function. They urged that workers wear adequate PPE and that regular occupational and health monitoring be conducted to improve workers' health.

Cha et al. (2022) reported on a case of a 54-year-old welder that developed flu-like symptoms after arc welding of galvanized steel in a poorly ventilated area. The man had elevated urine zinc levels (3579 ug/24 hr; normal range 0-616 ug/24 hr). Treatment with antibiotics was ineffective. A chest x-ray revealed consolidation, ground-glass opacity and right pleural effusion, indicating extensive lung inflammation that was successfully treated with corticosteroid treatment. The authors noted that the likely zinc oxide fume exposure produced metal fume fever and chemical pneumonitis in the welder.

Dawson et al. (2022) reported on an investigation of two cases of "welder's anthrax" to determine the source of exposure. Welder's anthrax is the result of infection with *Bacillus cereus* group of bacteria that have genes that produce the anthrax toxin. Infection can result in fatal pneumonia. The authors conducted an environmental monitoring campaign at the workplace of the two reported cases, including taking samples of soil and dust. Samples were analyzed using polymerase chain reaction (PCR) and cultures to determine if any were positive for the bacteria. Of 100s of samples collected and tested, only 8% of the samples for one of the cases tested positive and was successfully cultured for the suspect bacteria. The authors noted that all cases should be investigated thoroughly to determine the source of exposure and a workplace hazard assessment should be conducted to reduce the workplace risks [See also review by De Perio et al. (2022) in Section 4.4].

Fan et al. (2022) evaluated the incidence of pneumoconiosis in cases of workers in the non-coal mining industry in the Jiangsu Province in China. The authors reported that 7019 cases of pneumoconiosis were identified from January 1956 to December 2019 using the Jiangsu Pneumoconiosis Follow-up Network Reporting System. Data on the workers gender, employer, duration of dust exposure, and details on the type and diagnosis date of the pneumoconiosis were obtained. Statistical analyses of the data revealed that most of the cases were reported in 2007 and primarily in two cities Wuxi (41%) and Suzhou (28%). About 61% of the cases were workers in the non-metallic mining industry and the most common type of pneumoconiosis was silicosis (96%). The authors noted that welders on average were diagnosed at a younger age (about 45 years old) and had the shortest duration of dust exposure (about 17 years). The authors concluded that welders, in particular, should be the focus of improved health management including the use of personal protective equipment.

Hendricks (2022) present two cases of severe pneumonia in welders with diagnosed *Bacillus anthracis*, which has traditionally been associated with anthrax exposures. The disease has been reported in welders that are infected with *Bacillus cereus*, which have genes that produce anthrax toxins. The author describes the risks factors for infection and treatment options [See also review by De Perio et al. (2022) in Section 4.4].

Li et al. (2022a) assessed lung-related disease risk in a population of workers exposed to welding fume in a vehicle factory in Wuhan, China. The workers with the highest exposures included welders in the maintenance workshop. Compared to non-welders, overall welders had about a two-fold increased relative risk of lung disease (RR= 2.17, 95% confidence interval [CI]: 1.31–3.57, $p < 0.05$), with male welders having a slightly higher risk (RR= 2.24, 95% CI: 1.34–3.73, $p < 0.05$), and smoking welders an even higher risk (RR=2.44, 95% CI: 1.32–4.51, $p < 0.01$). The authors concluded that their study showed that the welders with high fume exposures were at increased risk of lung disease.

Li et al. (2022b) investigated the incidence of pneumoconiosis in the city of Ningbo, China from 1967 to 2019. Data were obtained from different Disease Prevention and Control Centers and supplemented with other relevant information as available (i.e., from employers). A total of 1715 cases were reported, including 40 cases of welder's pneumoconiosis. Cases were primarily male (75.6%), including all cases of welder's pneumoconiosis. The average age of the workers was 49.7 years old and the average length of employment was 10.98 years. The authors concluded that there is a need to supervise and manage industries in this city to reduce exposures and incidence of pneumoconiosis.

Lucas et al. (2022) presented a case of a 55 year old welder that was hospitalized with difficulty breathing. Pulmonary function was compromised, and a chest x-ray indicated damage to the bronchioles (small airways of the lung) with a diagnosis of obliterans bronchiolitis (also known as "popcorn lung"). A biopsy, however, revealed that the patient had pulmonary siderosis or "welder's lung" and was likely due to an acute and high exposure of iron particles. The authors note that the symptoms in this case were not necessarily consistent with welder's lung and only after biopsy they were able to make the diagnosis, which was consistent with the likely occupational exposure.

Rahimimoghadam et al. (2022) evaluated the effects on pulmonary function of metal fume exposures in a cohort of 98 welding and casting workers. Air monitoring was conducted using NIOSH 0500 method. Dust samples were analyzed by gravimetry and metals by atomic absorption. Lung function was determined via spirometry for the years 2010 to 2016. Multivariate regression analyses were conducted. The authors also estimated the cancer and non-cancer risks to the workers. The results showed that average workplace dust and iron concentrations were 15.95 ± 6.65 mg/m^3 and 13.18 ± 3.06 mg/m^3, respectively. Lung function significantly declined over the 6-year work period in welders including forced vital capacity (FVC), peak expiratory flow rate (PEFR) and forced expiratory volume in 1 second (FEV1). The variables that were correlated with lung function deficits included body mass index and work history. The lifetime cancer risk associated with hexavalent chromium exposures was 708 per million and the non-cancer hazard quotient was 19.6. The authors concluded that metal fume exposures contributed to lung function deficits and results indicated a high estimated risk of both cancer and non-cancer health effects.

Song et al. (2022) investigated the survival rate of occupational pneumoconiosis in China, noting that prevalence has increased since 1990 worldwide. The authors reported a total of over 15,000 cases in China, of which 3.8% were welder pneumoconiosis. Overall, the survival rate was 14.7 years, and the life expectancy was 34 years. The total mortality rate was 19.9%. Survival was related to dust exposure period, the pneumoconiosis stage (stage 1, less severe and stage III, most severe). The authors concluded that prevention and delaying stage progression were the most important factors for increasing survival rates.

Wu et al. (2022) assessed the effects on pulmonary function of metals exposure in a group of 186 welders in Anhui, China in 2019. Metal concentrations in end-of-shift urine samples were analyzed using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and lung function measurements were collected including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow (PEF). The authors used complex statistical analyses including elastic-net regression, multivariate linear regression, Bayesian kernel machine regression, and quantile g-computation models in order to determine which metals are correlated with poor lung function. High lead and cadmium concentrations were correlated with lower FVC and FEV1, while high nickel and chromium concentrations were associated with lower PEF. Overall, the authors concluded that metals individually and as a mixture adversely impacted lung function in this cohort of welders, but results indicated that the primary metals linked to poor lung function were lead, cadmium and nickel.

Zhou et al. (2022) conducted a cross-sectional study in 384 Chinese workers to assess the correlation between blood and urinary metal concentrations and welder's pneumoconiosis as well as lung function. Metal concentrations were determined using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and lung function parameters were measured with a spirometer. The concentrations of metals in respirable and total dust were also measured. The authors reported poor lung function in workers with pneumoconiosis including lower forced vital capacity (FVC) and forced expiratory volume in 1s (FEV1). Data analysis using logistic regression and adjusted for age, body mass index, working duration, welding dust exposure, and smoking indicated that blood levels of chromium and zinc were significantly correlated with pneumoconiosis (odds ratio [OR] = 4.98, 95% confidence interval [CI]: 1.73–21.20, $p = 0.009$ and OR = 5.23, 95%CI: 1.56–41.08, $p = 0.033$, respectively). Metal concentrations in blood (cadmium and lead) and urine (cadmium and iron) were associated with decreased lung function in cases of pneumoconiosis. Overall, welders had significantly higher metal concentrations in blood and urine and higher exposures to respirable and total dust compared to non-welders. The authors concluded that chromium and zinc were primarily correlated with pneumoconiosis, whereas cadmium and lead were associated with decreased lung function in pneumoconiosis cases.

4.1.3 Cancer

Ahmadi et al. (2022) assessed the risk of testicular cancer in the offspring of workers exposed to heavy metals and welding fumes, The authors identified 454 cases and 670 controls from a French case-control study and used a job-exposure matrix (INTEROCC) to estimate exposures to metals (chromium, cadmium, iron, nickel, and lead) and welding fumes based on the father's job. Conditional logistic regression was used to determine the odds ratios for testicular cancer using three analytical approaches – single agent analysis, analysis by group, and principal component analysis. The authors found no association between heavy metal or welding fume exposures and risk of testicular cancer in the worker's offspring.

Behrens et al. (2023, epub 2022) reviewed and pooled data from 14 case-control studies in Europe and Canada to assess the correlations between lung cancer risk and exposures to hexavalent chromium (CrVI) and nickel. The dataset included 16,901 lung cancer cases and 20,965 controls. Exposures were estimated using a job-exposure matrix matched to the subjects' occupational history. The authors analyzed the data using logistic regression and adjusting for the specific study, age of subjects, smoking, and exposures to other occupational carcinogens. Results identified positive and significant lung cancer risks from CrVI and nickel, odds ratio (OR) = 1.32 (95% confidence interval [CI] 1.19-1.47) and 1.29 (95% CI 1.15-1.45), respectively for the highest cumulative exposure group in men. Risks in women were generally smaller and were not statistically significant, OR = 1.04 (95% CI 0.48-2.24) and 1.29 (95% CI 0.60-2.86), for CrVI and nickel, respectively. Also, the authors reported synergistic effects from CrVI and nickel exposure and smoking that were more than additive. Overall, the authors found associations between CrVI/nickel exposures and increased lung cancer risks, especially in men. However, the authors also noted the potential for measurement or exposure misclassification errors that could have biased the results.

Collatuzzo et al. (2022) evaluated the potential disparities worldwide related to socioeconomic status and occupation. The authors analyzed various different factors that could contribute to disparities including participating in cancer screening programs and risk of cancer by occupation depending on a worker's education and race/ethnicity. The authors analyzed data from a multi-center lung cancer study that included an evaluation of lung cancer risks associated with diesel exhaust, silica and welding fumes exposures. The authors noted the importance of considering different factors that could contribute to disparities in the association between cancer and occupation including income, access to health insurance as well as occupational exposures. All of these factors are critical to aspects of cancer control and outcomes.

4.1.4 Eye Effects

Liou et al. (2022) evaluated the correlation between welding metal fume exposures and dry eye metrics in a cross-sectional study of 59 welders and 25 administrative staff (controls) in a shipyard in Taiwan (September and October 2020). The authors collected the worker's information, measured $PM_{2.5}$ concentrations, and concentrations of metals in urine and toenails. Dry eye measurements were conducted via questionnaires and using an ocular surface analyzer. The authors reported higher concentrations in the exposed workers of vanadium (V) and chromium (Cr) in urine, and V, Cr, manganese (Mn), iron (Fe), nickel (Ni), zinc (Zn), arsenic (As), cadmium (Cd), and lead (Pb) in toenails compared to the control group. Dry eye measurements were significantly correlated with urinary Cd and toenail Pb concentrations. The authors concluded that welders had significantly higher levels of metals compared to controls and metals were found to potentially contribute to dry eye.

Owczarek et al. (2022) evaluated the use of protective filters (welding filters and infrared protection filters) and intraocular lenses (IOL, with and without yellow chromophore) for reducing risks from harmful optical radiation. The purpose of the study was to determine if workers that use IOLs need to also use protective filters, or if the type of protective filter differs when using an

IOL. The authors found that using IOLs together with protective filters did not affect the level of protection of the filter. There was also no difference in the type of IOL used (with or without yellow chromophore). The authors concluded that IOLs can safely be used with adequate protective filters to safeguard from harmful optical radiation during welding.

Praveena et al. (2022) assessed the prevalence of ocular disorders in 90 arc welders compared to 90 non-welders (mean age was about 33 years old for each group). In this cross-sectional study, the authors collected sociodemographic information for the study population and performed ophthalmological examinations. The authors reported that the majority of the welders (93%) had at least one ocular issue, higher than in the non-welder group (27%). In welders, conjunctivitis was the most common ocular issue (36%). Phototoxic maculopathy was also much higher in welders (57%) compared to non-welders (8%). Welders used googles as the principal protective equipment (PPE), and those that used PPE regularly had lower prevalence of maculopathy compared to non-welders. Use of PPE was not correlated with any of the sociodemographic variables. The authors concluded that ocular disorders are associated with welding work and that strict policies should be implemented regarding the use of PPE to reduce prevalence of these disorders.

4.1.5 Musculoskeletal Effects

Chen et al. (2022) assessed the prevalence of wrist injuries in 15 different industries and different jobs in China including factors that contributed to the injuries. The authors collected demographic information, wrist posture during work, and pain metrics. They applied logistic regression to analyze the data and identify significant factors associated with wrist injuries. Overall, the prevalence of injuries across all industries was about 13%. Wrist injuries were most prevalent in the toy, auto, shoe and biopharmaceutical manufacturing industries as well as the animal husbandry industry. Among the types of tasks that accounted for the highest rates was welding (31%). The authors identified numerous factors that increased the risks, including years of service (> 6 years), female gender, frequency of upward and downward flexion, placement of the wrist on the edge of an angular object, squeezing objects tightly while working, prolonged wrist flexion and position of the hand above the shoulder for an extended amount of time. The odds ratios were all statistically significant and ranged from 1.11 (> 6 years of service) to 1.86 from prolonged wrist flexion. The authors concluded that these industries and specific job tasks require special attention in order to reduce wrist injuries.

Elvis et al. (2022) investigated the prevalence, severity, and risk factors associated with work-related musculoskeletal disorders (WRMDs) in 128 welders (33 ± 10.5 years old) from three urban cities in Zimbabwe. The authors used questionnaires based on the Modified Cornell Musculoskeletal Questionnaire and conducted evaluations using the Quick Exposure Check and Rapid Entire Body Assessment (REBA) for postural risks. The authors reported that the most common reported disorders were lower back pain (78%), shoulder pain (66%), and wrist pain (61-62%). The severity of the back pain was high in 48% of cases, mild in 24% and low in 4%. Also, REBA scores were elevated and correlated with self-reported complaints in various regions of the body. Regression analyses identified several risk factors including long working hours, lack of physical activity, and smoking. Protective factors included job satisfaction and frequent breaks. The authors concluded that there was a high prevalence of WRMD among welders and that they would benefit from ergonomics education, but that individual risk factors also contributed to these disorders.

Yao et al. (2022) assessed the prevalence and risk factors associated with neck musculoskeletal disease (MSD) in a random sample of 677 welders that worked in an automobile factory in Shiyan City, China. The authors used a questionnaire to collect the data and analysis using logistic regression to determine contributing factors. They reported that the prevalence of neck MSD in the cohort of welders was 54.8% (371/677). The main risk factors included gender, age, educational level, length of employment, smoking, neck tilting motions, and uncomfortable postures. Rest was found to be protective. The authors concluded that there was a high prevalence of neck MSD in welders and that the results could guide interventions for preventing injury.

4.1.6 Reproductive Effects

Cherry et al. (2022) assessed the correlation between ergonomic demands in a job and the risk of fetal loss. A total of 447 female welders and 438 in an electrical trade for a total of 885 women were part of the cohort and were identified through the Canadian Women's Health in Apprenticeship Trades- Metals and Electrical (WHAT-ME) study. Employment and reproductive histories were collected at the beginning of the study and every 6 months for 5 years. The authors recorded what job the workers had at conception and any fetal loss as a result of ergonomic activities. Of the recruited women, 574 reported at least one pregnancy and a total of 756 pregnancies were evaluated. There was no statistically significant difference in the fetal loss percentage between welders and electrical workers (31.2% vs. 27.6%). The authors reported that risk of fetal loss was increased in welders with whole-body vibration (prevalence ratio [PR] = 2.14, 95% confidence interval [CI] 1.39-3.31) and hand-arm vibration for over 1 hour/day (PR = 2.15, 95% CI 1.33-3.49), with risks reduced with ventilation. The authors concluded that there was no difference in fetal loss risk by job category (welding vs electrical trades), but vibrations and extended work hours were found to increase fetal loss risks.

Galarneau et al. (2022b) evaluated the outcome of pregnancy for exposed female welders recruited for the Worker's Health in Apprenticeship Trades-Metal and Electrical (WHAT-ME) study. The welders were followed for up to 5 years and questionnaires were collected every 6 months to establish work details, including welding activities, ergonomic factors, perception of noise, heat and cold and estimates of welding fume exposure based on welding process and base metals used (see Galarneau et al., 2022 in Section 3). The authors used multivariable models to evaluate the effects of welding on pregnancy outcomes. Out of 242 pregnancies in the welding cohort, 122 pregnancies in 90 welders were included in the analysis. A total of 91 live births were recorded of the 122 pregnancies (mean birth weight of 3365 g, and gestation of 39.4 weeks), and there were 31 losses (27 miscarriages and 4 stillbirths). The authors reported increased odds of fetal loss with manipulation of heavy objects (Odds Ratio – OR = 5.13, 95% Confidence Interval (CI) 2.04-12.92), whole-body vibration (OR = 5.86, 95% CI 1.81-18.92) and increased noise (OR=1.52, 95% CI 1.24-1.85). Odds of fetal loss decreased with increased ventilation (OR = 0.20, 95% CI 0.03-1.18). Gestation decreased with increased perceived heat, and birth weight was lower with whole body vibration. Gestation and birth weight were not associated with any of the metal or particulate matter measurements. There was some association between aluminum and to a lesser extent nickel and particulate matter and fetal loss, but these variables were not significant in the full statistical model. The authors concluded that pregnancy outcomes were primarily influenced by the physical characteristics of welding work (heavy loads, vibration, heat and noise), and no independent effect of welding fume exposure was identified.

4.1.7 Other Health Effects

Bainin et al. (2022) assessed the levels of heavy metals and hematological profile of welders and nonwelders in Ghana. In this case-control study, the authors used questionnaires to collect demographic data from both welders (N=40) and nonwelders (N=40). They also collected blood samples and analyzed the blood for cell counts as well as concentrations of manganese (Mn), iron (Fe), lead (Pb), and zinc (Zn). The authors reported no significant differences between welders and nonwelders in concentrations of Mn, Zn, and Fe (0.53 vs. 0.23 mg/L,0.41 vs. 0.15, 1.82 vs. 1.11, respectively). They reported significantly lower Pb levels in welders compared to nonwelders, however (0.09 vs. 0.3 mg/L). Cell counts including, white and red blood cells, and hemoglobin were not significantly different between the two groups. Only the mixed cell fraction was significantly higher in welders compared to nonwelders. All blood cell counts were, however, within normal physiological limits. The authors concluded that any differences between the groups were not clinically significant.

Kozłowska et al. (2022) evaluated associations between changes in metabolic pathways and hexavalent chromium (CrVI) exposure in a population of 220 male workers and 102 controls across several countries (Belgium, Finland, Poland, Portugal and the Netherlands) that were part of the HBM4EU Chromates Study. Metabolites in urine were measured using liquid chromatography mass spectrometry, and principal components analysis was used to determine differences between post-shift concentrations and controls. The authors reported changes in metabolic indicators between workers involved in the application of chromate, including welders, and controls that could not be explained by smoking status or alcohol consumption. The authors could not discount other work-related factors, other than exposure to CrVI that could have impacted these metabolic changes. The authors concluded that more studies were needed to better understand the observed changes and to assess whether these metabolic markers can be used as indicators of adverse effects of CrVI exposure.

Lucas et al. (2022) evaluated the impact of welding fume exposures and noise on the cardiovascular system using measures of heart rate variability (HRV) in a group of 16 welders and eight airport workers (controls). The authors administered electrocardiograms, measured welding fumes (WF) using a dust track, and measured noise with a calibrated noise dosimeter. Statistical analyses were conducted to assess correlations between HRV measurements and noise levels. The authors reported significantly higher measures of HRV in welders, which the authors interpreted as an imbalance between the sympathetic and parasympathetic nervous system. Several of the HRV measures were also significantly associated with noise in welders, but not in the control group. They also reported a significant interaction between noise and WF exposures in welders. The authors concluded that there was evidence of an imbalance in the nervous system of welders and that this could be attributed to noise exposures or a synergistic effect of noise and WF exposures.

Vergara-Murillo et al. (2022) conducted a cross-sectional study of workers in Cartagena, Columbia to assess whether there were any correlations between chronic exposure to lead (Pb) and cadmium (Cd) and general health or clinical parameters (e.g., elevated body mass index, cholesterol, blood glucose, blood pressure). The workers included mechanics, battery and garbage recyclers, and welders with a median age of 45 years. Elevated blood lead level (BLL, > 5 ug/dl) were found predominantly in the battery recyclers (82.1%), whereas a much smaller percentage of welders had elevated BLL (24.8%). All the occupations had higher percentage of BLL > 5 ug/dl than the controls (15.3%) except for the garbage recyclers (11.5%). The percentage of workers that had Cd blood levels >5 ug/dl was similar across all occupations and the control group. The only clinical parameter that was significantly impacted by greater BLL was a decrease in platelet counts in workers with > 5 ug/dl BLL. The authors concluded however, that these workers were at high health risks from metal exposures, particularly the battery recyclers. They recommended further studies and increased awareness regarding these risks.

4.2 Animal Studies

We identified two studies in animals that assessed various health effects related to welding fume exposures.

Sani et al. (2023, epub 2022) conducted a toxicity study in rats to assess potential health effects of metal fume exposures in a population in Kano, Nigeria with widespread metal works operations. Laboratory rats were exposed intratracheally to different doses of metal fumes, which were representative of metal workers' exposures for 2, 4 or 8 hours and for 3, 5, 10 and 20 years. After rats were euthanized, whole blood samples were collected and tested for liver function markers. The authors reported mortality in the rats associated with the higher doses of metal fumes. In addition, metal fume exposures were associated with impaired liver function. Based on the results from the study, the authors established a no-observed-adverse-effect level (NOAEL) for welding fumes of 25.7 mg and an LD_{50} (lethal dose causing 50% of animals to die) of 270 mg. This dose corresponds to a metal worker doing a 4 hour shift for 5 years. The authors concluded that monitoring should be conducted to limit exposures below these recommended doses.

Zeidler-Erdely et al. (2022) assessed pulmonary deposition and toxicity of copper-nickel fumes from gas metal arc welding in male A/J mice (6-8 weeks old). Copper-nickel has been recommended as a substitute consumable to reduce exposures to chromium in stainless steel welding. Mice were exposed to metal fumes for 2 or 4 hours per day for 10 days, representing low and high exposures, respectively. Bronchoalveolar lavage (BAL), macrophage function, and histopathology analyses were done at different timepoints post-exposure. The authors reported that particles were between 0.1 and 1 um in diameter and a mixture of 76% copper and 12% nickel. Exposure to metal fumes resulted in diminished macrophage function and lung inflammation and cytotoxicity. These effects were resolved about 28 days post-exposure. The authors concluded that exposures to copper-nickel fumes were acutely toxic and may not be a less toxic alternative to consumables that contain chromium.

4.3 Mechanistic/cell/*In vitro*

We identified 6 mechanistic/cell/*in vitro* study that evaluated the potential health effects of welding fume exposures.

Akram et al. (2022) evaluated the associations between arsenic exposures and differential hypoxanthine phosphoribosyl transferase (HPRT) and 8-oxoguanine DNA glycosylase (OGG1) gene expression and DNA damage in industrial workers including welders (n= 60). The HPRT gene is important for encoding enzymes that are involved in purine recycling (purines are necessary building blocks of DNA) and the OGG1 gene is involved in DNA repair after oxidative damage. The authors collected blood samples from workers and controls to evaluate gene expression and DNA damage and to measure arsenic levels in blood. The authors reported higher arsenic levels in blood in all workers compared to controls. In addition, workers had downregulated expression of both genes compared to controls, together with increased DNA damage. DNA damage was also greater in welders compared to controls and other industries. The authors conclude that the study results indicate that these workers had altered expression of key genes, which would exacerbate oxidative stress and negatively impact DNA repair, therefore resulting in an increased risk of DNA damage and potential cancer.

Fleck et al. (2022) determined the oxidative potential (OP) of welding fumes compared to other construction activities. In addition to measuring personal and area particulate matter (PM) concentrations, the authors assessed OP using an ascorbate assay (OPAA) and by determining the oxidative burden (OBAA). The OBAA was estimated by multiplying the OPAA and PM concentrations. The authors reported that the median PM concentrations (25^{th} to 75^{th} percentiles) was 900 (672-1730) mg/m^3 from welding, which was higher than other construction activities 432 (345-530) mg/m^3. Welding also was associated with higher OP (OPAA = 3.3 pmol/min-ug, OBAA 1750 pmol/min-m^3) than construction activities (OPAA = 31.4 pmol/min-ug, OBAA 486 pmol/min-m^3). The authors noted that OPAA was not dependent on the sampling strategy, whereas the OBAA was influenced by higher PM levels found in the personal samples. The authors concluded that the OP exceeded levels found in more typical environmental studies and should be further explored as a potentially important metric in occupational studies.

Koutsoumplias et al. (2022) assessed potential risks to shipyard workers in Greece from exposures to welding fumes, solvents and paints. The authors collected oral samples from the workers mouths and measured potential genetic damage using the micronucleus cytome assay. The authors reported higher induced micronuclei compared to office workers (controls), indicating potential genetic damage. Smoking also contributed to the observed genetic damage. The authors concluded that working conditions needed to be improved to protect workers, including use of personal protective equipment.

Scheurer et al. (2022) studied the changes in noncoding RNAs (IncRNAs) in macrophages exposed to ultrafine zinc/copper (Zn/Cu) from welding fumes. These IncRNAs have been found linked to cardiovascular disease, inflammation, and lung disorders. Specific IncRNAs were measured in exposed macrophages after 1, 2, and 4 hours. In addition, the authors took blood samples to measure the levels of these IncRNAs in 14 volunteers that were exposed to Zn/Cu welding fumes (2.5 mg/m3) for 6 hours. Samples were collected before exposure and at 6,10, and 29 hours post-exposure. All but 1 of the 4 IncRNAs were elevated in the macrophages. In the blood samples, increases of 2 of the 4 IncRNAs were reported, and a decrease in another. The last IncRNA was unchanged. The authors concluded that the observed increases of most the studied IncRNAs contribute to an understanding of inflammation from metals exposures, in particular Zn/Cu mixtures.

Suárez et al. (2022) investigated the mechanism by which inhalation of metal fumes, in particular zinc (Zn), contributed to metal fume fever (MFF), which is an inflammatory condition driven by oxidative stress. The authors explored two different mechanisms, 1) a photocatalytic production of hydrogen peroxide (H2O2) from ZnO and 2) production of hydroxyl radicals from a Fenton reaction involving magnetite nanoparticles. The authors used a multiscattering-enhanced absorbance device (photocatalysis) and degradation of bromophenol blue using microplate photometry (Fenton reaction products). They reported that H2O2 was produced at a rate 3 to 4 times higher in the presence of both ZnO and UV radiation. They also found Fenton reactions associated with magnetite, Fe(II), and Fe (III) nanoparticles. These results indicate that oxidative stress in the lungs occurs when iron nanoparticles are found in the lungs and exacerbated by photocatalysis of ZnO, which occurs during welding of galvanized steel. Overall, the authors report a plausible mechanism for MFF onset in welders.

Ye et al. (2022) assessed whether manganese poisoning could be determined based on measurements of specific biomarkers in the blood of exposed workers. The biomarkers of interest in this study included glutamate–cysteine ligase (γ-GCS) mRNA expression and glutathione peroxidase (GSH-PX) activity. The authors recruited 115 welders and 65 administrative office workers, with the welders divided into a high (N=43) and low (N=72) exposure group based on whether the exposures exceeded occupational standards. The authors compared levels of γ-GCS mRNA expression and GSH-PX among the different exposed and non-exposed workers. They reported that γ-GCS mRNA expression and GSH-PX activity differed between the exposed and non-exposed groups, with exposed workers showing higher γ-GCS mRNA expression and lower GSH-PX activity. The γ-GCS mRNA expression was positively correlated with increased concentrations of manganese in air and urine, while GSH-PX activity was negatively correlated with increase manganese in air and urine. The authors concluded that these biomarkers would be useful early indicators of potential manganese poisoning.

4.4 Reviews

De Perio et al. (2022) reviewed cases of severe pneumonia reported since 1997 that have symptoms similar to those exposed to anthrax. The authors report that nine cases have been found, mostly welders, but including also other metal workers and a review the literature on the *Bacillus cereus* group infections that the author's have termed "welder's anthrax" because the infectious agent produces anthrax toxins. The review includes health risks from exposures to welding fumes, potential mechanisms of infection and preventive measures to reduce welding fume exposures and prevent disease transmission among welders.

Dirandeh et al. (2022) conducted a review of occupational exposures to manganese (Mn), clinical symptoms associated with exposure, and the relationship between exposure and Parkinsonism in workers. The authors noted that Mn is an essential element required for normal growth and development, but that elevated exposures via inhalation, dermal absorption or ingestion are associated with neurotoxicity and symptoms of Parkinsonism.

Fishwick et al. (2022) assessed the incidence of occupational respiratory disease in the UK over a 20-year period using data from the Surveillance of Work Related Occupational Respiratory Diseases (SWORD) database. The authors reported that there were 172 actual cases, which they estimated equaled about 502 cases when adjusted for frequency. Incidence of respiratory disease decreased from 1.7 per million in the first 5-year period to 0.5 per million in the last 5-year period. Welding was among the top occupations responsible for about 35% of all cases. A total of 4.7% of cases were from welding.

Karyakina et al. (epub 2023) conducted a literature review to assess evidence regarding the correlations between airborne manganese (Mn) concentrations and concentrations of Mn in biological media, particularly in blood. The authors also evaluated evidence of an association between Mn blood levels and subclinical neurological outcomes. Of the over 6000 references, the authors identified 76 articles with relevant data. The authors found that the evidence of an association between airborne Mn concentrations and Mn levels in blood was limited and inconsistent. There was also limited and inconsistent evidence of an association between Mn blood levels and adverse neurological indicators. Overall, comparisons across studies were difficult because of the variation in sources of Mn exposure, methodologies used, and poor reporting of key information. However, the authors noted that of the different biomarkers reported (e.g., Mn levels in blood, urine, saliva, nails, hair), Mn levels in blood appeared to be the most useful for use in biomonitoring or risk assessment studies.

Loomis et al. (2022) conducted a systematic review and analysis of the correlations between prevalence, incidence and mortality from trachea, bronchus, and lung cancer and welding fume exposures to inform estimates for Work-related Burden of Disease and Injury that the World Health Organization (WHO) and the International Labor Organization (ILO) produces jointly. The authors developed a systematic review protocol and systematic review framework for the work. The review included searches of multiple databases including Medline, EMBASE, Web of Science, CENTRAL and CISDOC, grey literature, internet searches, and consultation with reference lists from major reviews. Inclusion criteria were all studies of working age (> 15 years old) workers in the WHO/ILO member states that had estimates of any welding exposure compared to no exposure and trachea, bronchus, and/or lung cancer incidence and mortality. All studies were reviewed by two people for inclusion, data extraction, risk of bias, and quality and strength of the evidence. Forty studies met the inclusion criteria. Of these, 29 were case control studies and 11 were cohort studies that included over 1.2 million workers (≥22,500 females) in 21 countries in the Americas, Europe, and Western Pacific. Most of the studies reported exposures based on job title or self-reported and health outcomes based on administrative or medical records. The authors reported an increased risk in trachea, bronchus or lung cancer of 48% (Relative Risk [RR] = 1.48, 95% confidence interval [CI] 1.29-1.70) based on 23 studies and > 57,900 workers compared to workers with no exposure. They also reported increased mortality associated with welding fumes of 27% (RR 1.27, 95 % CI 1.04-1.56) in workers with any welding fume exposure compared to no exposure, although based only on 3 studies and > 8,600 workers. Although risk of bias was generally deemed to be low, there were several studies that were rated high for risk of bias based on potential exposure misclassification and/or confounding. The authors concluded that there was sufficient evidence for increased incidence of trachea, bronchus, and lung cancer associations with welding fume exposures, but limited evidence of increased mortality. The pooled estimates were deemed to be sufficient for inclusion in the WHO/ILO estimates for Work-related Burden of Disease.

Sjögren et al. (2022, epub 2021) present important issues related to setting an occupational exposure limit (OEL) for welding fumes, noting that the current limit of 5 ug/m^3 as an 8-hour weighted limit is not protective enough to ensure health protection for the approximately 11 million people worldwide that work as welders. The authors note that they welcome a new proposed health-based OEL from the European Chemical Agency (ECHA) for the European Union. Welding fumes are process-based and therefore are not regulated under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Soltanpour et al. (2023, epub 2022) reviewed studies conducted in Iran from 1900 to 2020 related to welding exposures and health effects. The authors assessed the cancer and non-cancer risks from welding fume exposures using Monte Carlo methods. They reported metal fume concentrations ranging from 1.8 to 1061 ug/m^3 and 54.9 to 4883 ug/m^3 for gas welding and arc welding, respectively. Average concentrations of metal fumes were below the exposure limits recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) except for manganese in both gas and arc welding, and aluminum in arc welding. The risk assessment results indicated that the cancer risk from nickel exposures from both gas and arc welding were greater than 1 x 10^{-6}, but less than 1 x 10^{-4}, which the authors noted was a “probable” risk. Elevated non-cancer risks were found for cadmium exposures from gas welding (hazard quotient (HQ) greater than 1). The authors concluded that welders were exposed to levels of welding fumes that were hazardous to health and protective measures were needed to reduce these risks.

Torén et al. (2022) conducted a review of the history of pneumococcal pneumonia from occupational exposures to metal fumes and dust. The historical research included a manual search for articles in the library of the Surgeon General in addition to PubMed, and consulting reference lists in articles that were published before PubMed. The authors found that early literature dating from the 1890s recognized pneumonia from exposures to “Thomas slag,” which was a steel industry byproduct that contained iron and manganese. Metal-dust occupations, mainly using manganese, were reported by researchers to have increased incidence of pneumococcal pneumonia. Furthermore, in the 1930s an outbreak of pneumococcal pneumonia was attributed to manganese fume exposures. Post World War II, there was renewed interest in occupational pneumonia that was assumed to be related to exposure to Potassium permanganate, but this was later attributed to chemical pneumococcal pneumonia. It was not until two decades later that risk of pneumococcal pneumonia was once again highlighted in the literature as occupationally related to welding fume exposures, however, the risks specifically associated with manganese exposures appears to be overlooked, according to the authors. The authors concluded that it is important to review historical documentation of occupational disease to obtain a better understanding of potential disease correlations.

Tavares et al. (2022) conducted a risk assessment of metals mixture exposures associated with welding and other occupations. Data were derived from the European Human Biomonitoring Initiative (HBM4EU), which provided published biomonitoring data for hexavalent chromium (CrVI), nickel (Ni), and polyaromatic hydrocarbons. Risks were characterized based on dividing exposures to health risk factors (i.e., levels of exposure that are determined to be associated with lower risk) to obtain a Risk Quotient (RQ) and the sum of Risk Quotients (SRQ) for mixtures of two or three compounds. Based on studies that reported urinary concentrations of Cr and Ni from welding exposures the authors found SRQ > 1 from combined exposures indicating higher health risks. The authors noted that although single pollutant exposures could have a RQ< 1 the combined exposures could result in SRQ > 1, and that this shows that risks based on mixtures should be considered.

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