HEALTH EFFECTS FROM WELDING EXPOSURES:

2020-2021 LITERATURE UPDATE

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List of Acronyms and Abbreviations

AM	Additive Manufacturing
ASME	American Society of Mechanical Engineers
AWS	American Welding Society
BMI	Body Mass Index
CAT	Catalase
CI	Confidence Interval
CO	Carbon Monoxide
COPD	Chronic Obstructive Pulmonary Disease
EBC	Exhaled Breath Condensate
ELISA	Enzyme-linked Immunosorbent Assay
FA	Fractional Anisotropy
FCW	Flux-cored Wires
FEV1	Forced Expiratory Volume in 1 sec
FVC	Forced Vital Capacity
GP	Globus Pallidus
GSH	Glutathione
GST	Glutathione-S-transferase
GTF	Grinding Time Fraction
HR	Hazard Ratio
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IL-6	Interleukin-6
LDCT	Low Dose Computed Tomography
LTB4	Leukotriene B4
LTC	Leukotrienes
MDA	Malondialdehyde
MRI	Magnetic Resonance Imaging

NPC	Nasopharyngeal Carcinoma
OR	Odds Ratio
PD	Parkinson’s Disease
PEF	Peak Expiratory Flow
PGE2	Prostaglandin E2
PGF2 α	8-iso-prostaglandin F2-α
PM	Particulate Matter
PPE	Personal Protective Equipment
RBC	Red Blood Cells
SN	Substantia Nigra
SOD	Superoxide Dismutase
SOHAS	Stainless or High Alloy Steel
TAC	Total Antioxidant Capacity
TNF-a	Tumor necrosis factor alpha
UFP	Ultra fine particles
WBC	White Blood Cells
WF	Welding Fume
WS	Welding Slag
XRF	X-ray Fluorescence

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 2020 and 2021 (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 years 2020-2021 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 1,174 citations. We further refined the search to include "health" and this reduced the number of citations to 167. The 167 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 2020-2021.

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 2019 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	12
Epidemiology and controlled human exposure	19
Animal	0
Mechanistic/cell/*in vitro*	15
Reviews	0
Overall Total	**46**

3.0 EXPOSURE STUDIES

We identified 12 exposure-related studies or studies related to regulation or health and safety in welding occupational groups published from 2020-2021 (*i.e.*, particle characterization and exposure). Some studies were published online in 2020 (*i.e.*, 2020 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.

Berger et al. (2021) assessed the concentration of nanoparticles from welding activities including manual arc welding and automatic welding. Particle number concentrations (size range 20-1000 nm) and mass of PM1 fractions were measured using various particle counters (i.e., NanoScan SMPS 3910, Optical Particle Sizer OPS 3330, P-TRAK 8525 and DustTrak DRX 8534) at 15 min intervals near the welding activity. The authors reported particle number concentration ranges of 84×10^3-176×10^3 #/cm^3 and 96×10^3-147×10^3 #/cm^3 for electric arc welders and welding machine operators, respectively. An average particle number concentration of 179×10^3 #/cm^3 was reported for welding locksmiths. Overall, the range in concentrations of PM1 was 0.45-1.4 mg/m^3. Occupational exposure limits for nanoparticle number concentrations were exceeded numerous times during welding activities. The authors concluded that exhaust ventilation and the use of appropriate personal protective equipment should be used to reduce exposures.

Cieslak et al. (2021) presented the results from use of a novel high-frequency and ultrasound personal exposimeter that can be used to assess exposures to ultrasonic noise in the workplace. The device was tested in a laboratory using several common industrial scenarios including the use of an ultrasonic welding machine. The sound level detection capabilities of the prototype device were compares with an ultrasound level meter that was previously tested. The results showed that the simulated sounds varied from 10 kHz to 40 kHz with a frequency range of 60 dB to 90 dB in amplitude. The authors found good agreement between the two devices used with the louder range of sound. The portability of the device, which would have to be worn by a person all day, gives the new device some advantages. The authors noted that the uncertainty in the measurements depends on the individual measurement setup and further study of the device under real-world scenarios is needed.

Dain et al. (2021) evaluated results from testing of welding curtains and screens, which are used to protect workers other than welders, under laboratory conditions to assess compliance with international and national standards. Results from spectral transmittance testing (ultraviolet, visible, and infrared) of 21 samples were evaluated by comparing them to standards. The authors reported only a small number of samples that passed the ultraviolet (10) and visible/infrared (4) standards (across all international and national standards). Overall, the authors found that the Australian/New Zealand standards were the most stringent for ultraviolet and blue-light regions, but the derivation of the standards is not well documented. The authors concluded that some curtains that comply with international standards may still transmit potentially hazardous levels of blue-light and that all standards should be reviewed and potentially revised.

Kato et al. (2022, epub 2021) presented results from an analytical method used to characterize the elemental distribution of welding fume (WF) and welding slag (WS) from stainless steel flux-cored arc welding process. The authors analyzed fluxing elemental distribution near the surfaces of the WS and WF using scanning electron microscopy and energy-dispersive X-ray spectroscopy. They found that micron-sized spherical particles grew from nanosized primary particles. The spherical particles had different composition of metals, with either a distribution of elements, a striped pattern, or a dotted pattern. The authors concluded that the results from the analysis of both WF and WS could be used for establishing exposure assessment protocols to help protect workers.

Koh et al. (2021) developed an exposure database specific to South Korea of potential carcinogenic exposures across various industries. The authors selected 20 known carcinogens and three national databases (the Work Environment Measurement Database, the Special Health Examination Database, and the Work Environment Condition Survey) to obtain exposure prevalence estimates. The results were reviewed by professional industrial hygienists to obtain final exposure estimates. The estimated number of exposed workers was then calculated by multiplying the exposure estimates by the total number of workers in each industry. The results showed that the largest population of workers were exposed to welding fumes (326 822 workers), then ultraviolet radiation, (168 712 workers), and mineral oil mist (146 798 workers). The authors concluded that these estimates provide important information for the potential prevention of occupational cancers.

Lotah et al. (2022) measured concentrations of heavy metals, lead (Pb), nickel (Ni), cadmium (Cd), and manganese (Mn) in hair and nail samples of welders in the United Arab Emirates. The authors evaluated the association between levels of heavy metals and other variables including smoking habits, exposure/day, years of experience and use of protective personal equipment (PPE) in exposed and non-exposed workers. Concentrations were determined using atomic absorption spectrophotometry. The authors reported that heavy metal concentrations were higher in nail samples compared to hair in both groups. Mn in hair was higher in the exposed group and among smokers. In subjects with 8 hrs/day or greater exposure, Cd in hair and Ni in nails was higher. Cd and Ni in hair was also higher with increased experience and highest in those with > 20 years of working. The authors concluded that heavy metal measurements in hair and nails are useful biomarkers for evaluating welder's exposures.

Mitra et al. (2021) assessed the adequacy of using a filtering (N95) facepiece or a pleated (N95) particulate respirator for protection against ultrafine (0.1-0.5 μm) or submicron (<0.1 μm) particle exposures in welding and asphalt production facilities. The facepieces were tested on a manikin using two TSI Nanoscan SMPS nanoparticle counters (10-420 nm in size range) from inside of the mask at commercial and academic manufacturing sites including a welding site. The authors reported that particle sizes ranged from 40 to 200 nm. Results varied depending on the particle size, but under sealed conditions both facepieces filtered the desired 95% of particles. For unsealed conditions, only the pleated N95 respirator achieved 95% filtration, whereas the filtering N95 facepiece only achieved 60% filtration.

Newton et al. (2021) conducted an exposure assessment in a stainless steel welding facility to evaluate the personal and area concentrations of inhalable PM_{10} and bioavailable metals. For two consecutive shifts, personal samples for 18 welders were taken. In addition, X-ray fluorescence spectrometry was used to collect area samples in different work areas. Inductively coupled plasma mass spectrometry (ICP-MS) was used to analyze the samples. The authors reported median personal concentrations of chromium, nickel, and manganese across all shifts of 66 (range: 13–300) $\mu g/m^3$, 29 (5.7–132) $\mu g/m^3$, and 22 (1.5–119) $\mu g/m^3$), respectively. With regards to bioavailability, manganese was the most bioavailable metal (16 ± 3%), followed by nickel and chromium (1.2 ± 0.08% and 2.6 ± 1.2%, respectively). The authors concluded that measurement of personal concentrations and assessment of bioavailability can be used to target approaches for controlling worker exposures.

Rafiee et al. (2022) conducted a systematic review of the efficacy of respirators for reducing metal particle exposures in workplaces. The authors identified 983 references (463 after removing duplicates) across five bibliographic databases (Embase, Web of Science, Medline, Scopus, and CINAHL) for the years 1900 – April 2019, and the gray literature. A total of 70 articles were reviewed in full, and from these 8 were selected for inclusion. The authors reported that the geometric mean metal concentrations in the worker's breathing zone were 9.4 and 1,777 $\mu g/m^3$ for iron, 1.1 and 139 $\mu g/m^3$ for lead, 2.1 and 242 $\mu g/m^3$ for zinc, and 27 and 1,398 $\mu g/m^3$ for manganese oxide with and without the respiratory, respectively, noting a significant difference is the personal exposures for workers using a respirator. Authors also reported that N95 masks provided significantly less protection compared to half facepieces, full-face respirators, and powered airpurifying respirators. Overall, the authors noted the need for more studies to evaluate the effectiveness of respirators.

Santonen et al. (2022, epub 2021) evaluated occupational exposures to hexavalent chromium [Cr(VI)] across different industries, including stainless steel welding. The study included nine European countries and 399 workers across the different industries, with 203 controls for establishing background exposure levels of Cr(VI). In addition to obtaining personal exposure measurements of inhalable and respirable Cr(VI), the authors reported collecting biomarkers of exposure including chromium in urine, red blood cells (RBC) and exhaled breath condensate (EBC). Hand wipe samples to assess dermal exposures were also collected. The authors reported that the highest Cr(VI) exposures were found in workers involved in electrolytic bath plating and that welding workers had significantly lower exposures in comparison. Chromium in urine was highly correlated with air and dermal concentrations, whereas the RBC and EBC measurements were not. The authors concluded that chromium in urine was the best biomarker to use for assessing occupational exposures to Cr(VI).

Singh et al. (2022, epub 2021) evaluated occupational exposures to lead (Pb), aluminum (Al), and zinc (Zn) in 120 factory workers compared to 100 healthy controls (18-78 years of age) in north-western India. Blood Pb, and serum Al were analyzed using graphite furnace atomic absorption spectrophotometry and serum Zn was analyzed using flame atomic absorption spectrophotometry. The authors reported that the levels of these metals were significantly higher in workers compared to controls, and there were no significant differences based on age or duration of exposure. Also, painters were found to have elevated levels of blood Pb, whereas welders had elevated serum Al and Zn levels. The authors concluded that these data should be considered in the development of effect industrial hygiene approaches to protect workers from potential health effects associated with metal exposures.

Specht et al. (2022, epub 2021) presented results of a methodology for a novel portable x-ray fluorescence (XRF) meter for use in taking in vivo toenail metal measurements on intact nails. This methodology would replace typical methods of using toenail clippings and analysis by inductively coupled plasma mass spectrometry (ICP-MS). To compare the efficacy of the method, a 3-min measurement using XRF was conducted on intact nails of 16 welders to assess manganese exposure and 10 workers from a nail salon to assess mercury exposure. Toe nail clippings were collected after the XRF measurements and analyzed by ICP-MS. The authors reported that there was good correlation between the ICP-MS measurements and the XRF measurements for manganese ($R=0.59$, $p=0.02$) and mercury (R= 0.74, $p < 0.001$). The detection limits for the XRF measurements were 2.6 µg/g for manganese and 0.5 µg/g for mercury. The authors concluded that these XRF measurements could be effectively used for assessing occupational exposures to metals and was a cost-effective alternative. However, they recommended further testing of the methods and evaluation of ways to improve the detection limits.

Wippich et al. (2021) presented an analysis of measured concentrations of nickel 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 551 parallel measurements of nickel 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 occupational activities. For example, for welding, there were groups for ‘welding (grinding time fraction [GTF] < 5%)’ and ‘welding (GTF > 5%).’ Based on evaluation of these data, the authors developed conversion functions for estimating the amount of nickel in the respirable dust fraction out of the nickel 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 (2 studies), respiratory effects (5 studies), cancer (3 studies), eye effects (2 studies), and multiple or other health effects (7 studies). Summaries of these studies are provided below.

4.1.1 Neurological Effects

Bast-Pettersen et al. (2022) presented a review of studies of workers that are occupationally exposed to aluminum (Al). The authors identified 559 papers and included 24 relevant studies in their evaluation. Overall, the authors did not find consistent associations between occupational exposures to aluminum and any neuropsychological deficits, although there was some suggestion of worse performance for tests related to information processing speed and memory tests for Al-exposed workers. The authors found the data too limited to draw any conclusions regarding an association between Al exposure and neuropsychological function.

Lee et al. (2022) investigated whether welders that were asymptomatic for manganese (Mn)-induced parkinsonism showed differences in the substantia nigra (SN) region of the brain and other regions related to Parkinson's disease (PD). The authors collected occupational exposure histories for 43 welders and 31 matched controls and conducted brain Magnetic Resonance Imaging (MRI) scans. The MRI markers included diffusion tensor imaging fractional anisotropy (FA; estimate of microstructural integrity) and R2* (estimate of iron and other PD-related brain differences) in the SN and globus pallidus (GP). The authors compared the exposed results to the controls and also assessed if there was an association between the MRI markers in the welders. The authors reported differences for FA, but not R2*, in the GP of welders with low-level but chronic exposures to Mn compared to controls. FA in both SN and GP were statistically significantly associated with cumulative lifetime welding exposures. The authors concluded that although more data were needed, the results suggest that lifetime exposures to even low levels of Mn can result in neurotoxicity as evidenced by associations with FA in the GP and SN regions of the brain.

4.1.2 Respiratory Effects

Chung et al. (2021) evaluated data from lung cancer screening of shipyard workers in Korea. Screenings have been conducted using low-dose computed tomography (LDCT) as part of a data system called Lung-RADS. The authors collected data from 6,326 workers at a single shipyard that had a health screening and LDCT from January 2010 to December 2018. The workers were categorized into groups depending on exposure levels (high, low or no exposure) to nickel, chromium, and welding fumes and job type. To assess associations between exposure levels and LDCT category (> 3), the authors used Cox proportional hazards regression analyses. Only a small percentage of the workers (1.5%) or 97 workers were classified as having an LDCT category >3, and 7 (0.1%) were diagnosed with lung cancer. The authors reported that the hazard ratio for a LDCT rating of >3 was 1.4 (95% confidence interval [CI]: 0.91-2.31) and 1.7 (95% CI: 1.01-2.84) for the low and high-exposure groups, respectively. The HR was statistically significant only for the high-exposure group when adjusted for age and smoking (pack-years), HR: 1.69 (95% CI: 1.00-2.84). The authors concluded that high occupational exposures are associated with greater risk of developing cancer.

Dev et al. (2021) investigated the prevalence of respiratory symptoms and lung function impairment in 283 welders (18-55 years old) in Punjab, India. A questionnaire was administered to all workers to assess respiratory symptoms. Lung function tests were conducted in a subset of 50 male welders, and 50 male non-welders. The authors reported that all welders had respiratory symptoms including chronic cough (38.86%), phlegm (38.86%), shortness of breath (33.56%), wheezing (32.15%), chest tightness (36.40%,) and sputum (34.27%). Lung function results did not differ significantly between the exposed and non-exposed groups. Mean forced vital capacity (FVC) was 3.37±0.175 and 3.70±0.15 for welders and non-welders, respectively. The forced expiratory volume in 1s (FEV1) was 2.59±0.16 and 3.05±0.25 for welders and non-welders, respectively. And the FEV1/FVC ratios were 76.63±6.16 and 82.49±7.62 for welders and non-welders, respectively. Nevertheless, the authors noted that welders in India work long hours, are not well educated, and often work under poor conditions, and therefore, workplace safety and protection need to be a priority for these workers.

Grahn et al. (2021) evaluated the association between occupational particulate exposures and risk of developing chronic obstructive pulmonary disease (COPD) in cohort of subjects that responded to a Health Survey between 2002 and 2014 in Stockholm, Sweden. Using population census data, the subjects were linked to a quantitative job exposure matrix using occupational titles. Subjects with COPD were identified either by medication usage information or a confirmed diagnosis by a physician. The authors analyzed the data using a proportional hazards regression model, adjusted for age and tobacco-smoking. The authors reported increased risk of COPD (adjusted for smoking) for men exposed to silica (HR 1.46, 95% CI 1.13–1.90), gypsum and insulation material (HR 1.56, CI 1.18–2.05), diesel exhaust (HR 1.18, 95% CI 0.99–1.41), asphalt/bitumen (HR 1.71, 95% CI 1.06–2.76), and welding fumes (HR 1.57, 95%CI 1.12–2.21). There was a significant positive exposure-response trend for men exposed to silica, iron dust, gypsum and insulation material, and diesel exhaust, but the trend was not statistically significant for welding fume. The authors concluded that COPD was significantly associated with various different occupational exposures, including welding fumes (although the exposure-response trend was not significant).

Li et al. (2021b) conducted a study to evaluate the short-term effects of welding fume exposures on lung function in 36 male welders (mean age 31 years old) and employed for an average of 4 years. Lung function tests, including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and peak expiratory flow (PEF) of welders, were conducted before and after a working shift and welding fumes were also measured. The authors reported average welding fume concentration of 1.27±0.49 mg/m^3. Lung function measurements (FVC, FEV1, and PEF) were significantly lower than measurements before the shift. Changes in FVC and FEV1 were significantly associated with welding fume exposures. The authors found that for every 1 mg/m^3 exposure to welding fume, FVC decreased by 1.02% and FEV1 decreased by 1.56%. The authors concluded that welding fume exposures can decrease lung function in workers. However, the clinical significance of these small changes in lung function are unknown.

Liu et al. (2021) conducted an epidemiological study to better understand the characteristics, including survival time of workers diagnosed with pneumoconiosis in Guangzhou City from 1958 to 2018. The authors collected data on all cases, including the number of cases, type of pneumoconiosis, industries, survival status, and dust exposures. There were 1194 cases of pneumoconiosis reported between 1958 and 2018, mostly in men (96.1%) and mostly silicosis (60.1%, 718 cases) and welder's pneumoconiosis (21.5%, 257 cases). The industries with the most reported cases included construction (25%, 151 cases), railway, ship and aerospace equipment manufacturing (16.1%, 192 cases), and non-metal mining (15.7%, 187 cases). The authors reported that the mean age at diagnosis was 47.8 years old, and the mean dust exposure duration was 12.3 years. Follow-up (as of December 2019) was conducted on 963 cases, of which 48.5% survived

(467) and 51.5% (496) died. The authors concluded that the focus for prevention of pneumoconiosis should be on the top industries identified in the survey. Better dust exposure data and reporting of cases is also needed.

4.1.3 Cancer

Chen et al. (2021) examined the role of occupational exposures on the risk of developing nasopharyngeal carcinoma (NPC) in a population-based case-control study in China. The study was based on 2514 NPC cases and 2586 randomly selected population controls from 2010 to 2014. A questionnaire was used for self-reporting of occupational history and other variables (e.g., age, sex, educational level, family history of cancer, and smoking). The authors used multivariate logistic regression for the analysis. The authors reported statistically significant risks of NPC associated with a range of occupational exposures including to dusts, chemical vapors, exhaust and smoke. Specifically for welding "smoke" the authors reported an odds ratio (OR) of 1.35 (95% confidence interval, 1.01-1.81). Much larger ORs were reported for chemical vapors (organic solvents, formaldehyde, dyes), asphalt, and acid/alkali substances. The authors conclude that the study results show that occupational exposures contribute to the incidence of NPC and that occupational hygiene programs should be implemented to reduce exposures.

Dauter et al. (2022) evaluated changes in biomarkers associated with cancer in welders exposed to low-to-moderate concentrations of welding fumes from mild steel welding. Swedish male non-smoking welders (N=171) and controls (N= 167) were recruited, and 78 welders/96 controls were also included in a follow-up after 6 years. The authors collected data on respirable dust, welding years and cumulative exposures. The biomarkers included DNA methylation of specific cancer-related genes (AHRR, F2RL3, and B3GNTL1), number of mitochondrial DNA copies, and telomere length. Analyses were conducted using multivariate regression. The authors reported respirable dust median concentrations of 0.7 mg/m^3 (adjusted for use of personal protective equipment), and a statistically significant decreased in DNA methylation of two of the genes (B3GNTL1, F2RL3). Exposures to welding fume were significantly associated with decreased methylation for one of the genes (F2RL3). The authors concluded that welding fume exposures can cause changes in these early markers for cancer. However, the clinical significance of these changes is unknown. That is, these small genetic changes may contribute to increased risk, but do not necessarily indicate that a worker will get cancer as a result of exposure.

Koutsoumplias et al. (2022 epub 2021) evaluated the health risks from exposures to workers in a shipyard in Greece by assessing genetic damage in samples of oral mucosa epithelium (cheek cells). A total of 38 workers were recruited, of which most were welders (30) with an average age of 50 years old. A total of 29 controls (office workers) were also included in the study with an average age of 40 years old. Most of the welders were smokers (23), and the average working duration was 22.5 years (range 5-40 years). The authors analyzed the buccal cells to assess DNA and cellular damage using the buccal micronucleus cytome assay. Results indicated that there were statistically significant differences in the cell types and the amount of DNA damage in exposed workers compared to nonexposed workers. The authors concluded that these results indicate that exposed workers are at increased risk of cancer from their exposures and that efforts should be made to reduce exposures. As with other biomarker studies, however, it is unclear if the differences are large enough to be clinically significant (i.e., result in development of cancer).

4.1.4 Eye Effects

Kyriakaki et al. (2021) reviewed the literature related to trauma to the eyes to evaluate the common causes and associations with occupation and socioeconomic status. The authors also evaluated approaches to care, prevention and treatment. A literature search was conducted in PubMed and overall, 72 articles were found out of which 25 were found to be relevant. The majority of the studies were retrospective and cross-sectional and were related to occupational injuries. Welders were one of the occupations identified as high risk for eye injuries. Other occupations included farmers, metalworkers and grinding, construction and manufacturing. The most prevalent injuries were foreign objects and corneal abrasions. Use of personal protective equipment (PPE) was found to be the most useful preventive measure, but lack of adherence to use of PPE was a common issue. The authors found that more could be done for prevention of eye injuries in the workplace.

Sughra et al. (2021) reported on the results from an occupational survey conducted from January- June 2018 in 158 welders in Pakistan to assess the prevalence of ocular injuries in the workplace. Welders were at least 20 years old and worked as a welder for at least a year. The authors reported that topical ocular anesthetic was used in 45.6% of the welders. Statistical analysis indicated that work experience was the best predictor of knowledge and practice of workplace safety.

4.1.5 *Other Health Effects*

Cherry et al. (2021) examined the rates of dermatitis in men and women in welding and electrical occupations and associations with nickel exposures. A total of 1885 participants (welders; 447 women, 554 men: electrical trades; 438 women, 446 men) were recruited from workers that were entering welding or electrical apprenticeships. The authors used questionnaires that were administered upon entry into the study and every 6 months for 5 years. Data was collected on any dermatitis and whether work exacerbated the condition. Additional information was collected from welders including the process and base metal used. Nickel concentrations in urine were also measured. The authors applied statistical models to analyze the prevalence and severity of dermatitis in the cohort. New onset of dermatitis was most prevalent in women that were entering the welding profession compared to workers entering the electrical trades [odds ratio (OR) = 1.54; 95% confidence interval (CI) 1.02-2.32], and compared to men entering the welding trade (OR = 1.85; 95% CI 1.15-2.96). Welding with stainless or high alloy steel (SOHAS) as a base metal was found to be associated with dermatitis that was made worse by the work, but controlling for the use of SOHAS still resulted in greater risks in women compared to men. The authors concluded that women in the welding profession were at increased risk of dermatitis and preventive measures should be considered to reduce the prevalence of this condition.

Dueck et al. (2021) evaluated exposures to metals in welding fumes in 43 welding apprentices compared to 41 controls from other trades in Northern Alberta, Canada. The authors collected ambient and personal samples on days 0,1, 7 and 50 of the training program. Samples were analyzed for metal concentrations using coupled plasma mass spectrometry. The authors reported significant variability in the particle and metal concentrations of the apprentice welders, with increased exposures associated with increased time in the program. Variability was attributed to improper use of ventilation, amount of time welding, the welding process used, and overall welding experience. Higher particle exposures were associated with metal core arc welding compared to gas arc welding. Specifically, the apprentice welders were found to be at risk from exposures to elevated manganese levels. The authors concluded that better workplace protections are needed to reduce risks in apprentice welders.

Itiakorit et al. (2021) evaluated the prevalence and factors associated with occupational injuries in welders in Uganda. Questionnaires were used to collect data on 327 randomly selected welders from 20 different metal workshops. The authors reported a high prevalence of self-reported occupational injuries (87.8%), primarily cuts/burns (84.3%) and eye injuries (62.7%). The two factors that were significantly associated with injuries included lack of training and working long hours. The authors concluded that there was a high risk of injuries to small-scale workers in Uganda, and these workers would benefit from better training and reduced working hours in order to reduce the risk of injuries.

Lei et al (2021) evaluated noise hazards in metal processing industries in China. A total of 737 workers from three metal processing plants were included. The authors measured noise intensity (equivalent continuous A-weighted noise exposure level normalized to an 8 h-working-day, L(Aeq, 8 h) using individual noise meters. The authors reported that exposed workers were primarily 18-40 years old (71.5%), male (77%), and had a high school education (56%). Most of the workers (77.6%) had a noise exposure intensity greater than 85 dB, and had been exposed less than 8 years (86%). One of the activities associated with elevated noise was welding. The authors identified significant noise hazards in the industries that were studied and highlighted the need for insulation and engineering controls to reduce these risks.

Lourenço et al. (2021) evaluated whether there was a higher incidence of musculoskeletal disorders in a sample of 40 Portuguese welders compared to 42 non-welders and if this higher incidence was associated with a reduced quality of life. The authors used surveys to collect information from the workers. They reported statistically higher incidence of disorders in the cervical, dorsal, lumbar, and wrists and hands of welders compared to non-welders. In particular, disorders in the lumbar region were associated with chronic pain and reduced quality of life. The authors concluded that welders are at greater risk of developing musculoskeletal disorders that can results in decreased quality of life and this issue needs to be better addressed.

Lucas et al. (2021) commented on the study by Dueck et al. (2021), and added the results of their unpublished study of welding fumes and metals in welders conducting ship repair tasks. They reported the following air concentrations of particulate matter and metal concentrations from 89 8-hr samples:

- Overall: 4.5 mg/m^3 total particles, 2.73 µg/m^3 hexavalent chromium, and 0.13 mg/m^3 manganese.
- Flux core arc welding mean (maximum): 9.3 (22.6) mg/m^3 total particles, 0.26 (1.2) mg/m^3 manganese.

- Metal core arc welding mean (maximum): 1.7 (3.5) mg/m^3 total particles, 4.8 (27.5) $\mu g/m^3$ hexavalent chromium and 0.05 (0.17) mg/m^3 manganese.
- Tungsten inert gas welding mean (maximum): 0.7 (1.3) mg/m^3 total particles, 0.5 (0.08) $\mu g/m^3$ hexavalent chromium, 0.01 (0.01) mg/m^3 manganese.

Similar to Dueck et al. (2021) the authors reported variations dues to the position of the welder and local ventilation, noting that ventilation is difficult to achieve in the confined spaces of ships. The authors emphasized the need to reduce exposures in welders throughout their working life in order to prevent potential welding-related disease such a respiratory or cardiovascular diseases.

Pilat et al. (2021) conducted a pilot study to assess the performance of an ergonomic welding torch designed to reduce the physical load and improve welding quality for novice welders. The authors recruited 10 novice welders to conduct a welding trial using both the ergonomic and the traditional welding torches. The welders performed the welding task at chest height (ASME code 1G) and overhead (ASME code 4G). Surface electromyography and changes in isometric peak force were used to measure skeletal muscle load and fatigue and information on pain sensation, perceived exertion and the welding quality were also collected. The authors reported lower muscle load response in three out of eight muscles for welders using the ergonomic torch, as well as lower pain and higher quality welding. These results indicated promising results for the ergonomic torch with regards to reducing ergonomic disorders in welders.

4.2 Animal Studies

No animal studies were identified in this literature search.

4.3 Mechanistic/cell/*In vitro*

We identified 15 mechanistic/cell/*in vitro* study that evaluated the potential health effects of welding fume exposures.

Assenhöj et al. (2021) evaluated the use of non-invasive sampling of nasal lavage fluid (NLF) to determine whether exposures in welders or additive manufacturing (AM) operators resulted in changes to inflammatory protein markers. The samples were collected from six welders and five AM operators at the beginning and end of a workweek in year 1. Preventive interventions were applied and samples were collected again in year 2. The samples were analyzed for a panel of 71 inflammatory protein markers. Different protein markers were influenced for AM operators compared to welders in the first year. After preventive measures, there were no significant differences in the protein markers. Overall, the authors identified several protein markers that could serve as good markers for exposure in future studies.

Boudjema et al. (2021) assessed the effects of ultrafine particles (UFP, $\leq$ 0.25 μm) derived from stainless steel gas metal arc welding on human lung cells (BEAS-2B cells). The UFPs were enriched with iron, chromium, manganese and silica. The authors reported activation of signaling pathways related to oxidative stress, inflammation, and cell death with exposures to 1.5 and 9 $\mu g/cm^2$ for 24 hours or with repeated exposures at 0.25 and 1.5 $\mu g/cm^2$, 3 × 24 hours. The authors concluded that the results indicate the importance of considering the toxicity of metal-enriched UFP and the need for occupational standards to protect workers from these exposures.

Buonaurio et al. (2021) evaluated the levels of exposure and oxidative stress biomarkers in the urine of workers in a metal carpentry industry. Levels of metals including barium (Ba), mercury (Hg), lead (Pb), strontium (Sr), rubidium (Rb), tellurium (Te), vanadium (V), beryllium (Be), and copper (Cu) were measured along with oxidation products of RNA and DNA metabolism and compared with control groups. The authors reported that the metal concentrations in urine were well below occupational exposure limits, but exposed workers had levels that exceeded controls by as much as a factor of four. Several of the metals were correlate with oxidative stress biomarkers. The authors concluded that measurements of biomarkers could be used to identify occupationally exposed workers, even at low exposure levels and could be useful for evaluation of potential health effects associated with these exposures.

Dos Santos Oliveira et al. (2021) reviewed studies that examined DNA methylation (DNAm) as a biological marker associated with potential cardiac autonomic dysfunction. The authors found 22 studies that met the inclusion criteria, including 18 human studies. They found that methylation of certain genes was associated with certain psychosocial stressors. In welders, the methylation of the gene *GPR133* was observed. This gene is associated with effects on heart rate's deceleration capacity, which is the capacity of the cardiovascular system to respond to physical and psychological stimuli. The authors concluded that DNAm can serve as a biological marker for assessing autonomic dysfunction as a result of various stressors.

Gao et al. (2021) investigated the metabolic profiles of 74 welders recruited from a training center in Quincy, Massachusetts. Blood samples were collected before and after a working shift and on a non-welding day. A total of 665 metabolites were measured using liquid chromatography-mass spectrometry in plasma. Two-way analysis of variance was applied to evaluate significant time (afternoon compared with morning) and day (welding/non-welding) interactions. The authors reported that sphingosine 1-phosphate and sphingasine 1-phosphate exhibited significant interaction effects between day and time (p values of 0.03 and <0.01, respectively). Specifically, trends over time were similar for both metabolites, with high relative levels on a non-welding day in the morning and declining by afternoon, and lower starting levels on a welding day with no decline. The authors concluded that these metabolites were altered as a result of welding. Further investigation is warranted, as these metabolites have many vital roles, and the clinical implications of these alterations are unclear.

Goyal et al. (2021a) evaluated the impacts of occupational exposures to cadmium on biomarkers of oxidative stress and inflammation. The authors recruited 100 workers in the metal manufacturing and welding industries working in Jodhpur, Rajasthan. Blood levels of Cd were measured using atomic absorption spectroscopy. The oxidative stress markers in serum included Total Antioxidant Capacity (TAC), Catalase (CAT), Superoxide Dismutase (SOD), and Malondialdehyde (MDA) levels analyzed by a colorimetric method. The inflammatory biomarkers included serum IL-6 and TNF-α analyzed using Enzyme-linked Immunosorbent Assay (ELISA). The authors reported median blook Cd levels of 2.4 μg/L. Welders had significantly higher levels of Cd than metal workers. TAC and CAT were both lower and MDA was higher in the most exposed workers. There were no observed associations with the inflammatory biomarkers. The authors concluded that relatively low level exposures to Cd can result in decreased oxidative stress capacity as evidenced by lower TAC and CAT in the more highly exposed workers.

Goyal et al. (2021b) evaluated the association between cadmium (Cd) exposure and changed in miRNA associated with inflammation and carcinogenesis. The author recruited 106 workers involved in metal handicraft or that worked as welders, and 80 non-exposed controls.

Cadmium concentrations in blood (BCd) were analyzed as well as levels of miRNA and pro-inflammatory markers. The authors reported higher BCd levels in exposed workers compared to controls, along with higher pro-inflammatory markers and miRNA. Duration of employment was positively associated with increased miRNA. The authors concluded that miRNA was a potentially a good marker for Cd toxicity in exposed workers.

Kahl et al (2021) reviewed 15 studies that evaluated telomere length (TL) and associations with occupational exposures, including to metals (lead [Pb] and mixtures) and particulate matter (PM). TL is a biomarker that has been associated with many health outcomes. Specifically shorter TL has been associated with adverse health outcomes. There was limited information on associations between TL and length of employment or age and gender. The authors reported that results varied with occupational exposures, but that the majority (53%) of the studies reported decreased TL with higher exposures to welding fumes, coal (from mining), and Pb and PM exposures. Reduced TL was also associated with DNA damage in 7 or 8 studies that evaluated measured this outcome, and with increased oxidative damage in 4 of 5 studies that evaluated this. The authors concluded that TL can be used as a good biomarker in occupational risk assessment.

Lai et al. (2021) presented a long-term study of health effects of shipyard workers, specifically welders, and repeated exposures to $PM_{2.5}$. The authors collected personal air samples of $PM_{2.5}$ and analyzed for different metal species for 49 welders and 20 office workers and also measured metal concentrations in urine samples, with a follow-up after one year. Biomarkers of oxidative stress and inflammation were analyzed for associations with exposure measurements. The authors reported different composition of PM exposures for welding workers (primarily iron, zinc and manganese) and office workers (primarily lead, copper and zinc). Exposures were associated with increased oxidative stress biomarkers, urinary 8-iso-prostaglandin F2-α (PGF2α) and 8-hydroxy-2'-deoxy guanosine (8-OHdG). Other biomarkers, such as IL-6 and cortisol were decreased with exposures to $PM_{2.5}$ and other metals. Overall, the authors concluded that exposures to metal fumes from welding were associated with increased levels of inflammatory biomarkers and decreased levels of cortisol, which could be indicative of adverse health effects.

Li et al. (2021a) evaluated the association between metals exposures, chromium (Cr), manganese (Mn) and lead (Pb) in welding fumes and effects on blood parameters including white blood cell counts (WBC), lymphocytes, monocytes, eosinophils, neutrophils, and hematocrit (Hct) after work compared to after 3 weeks of exposure cessation. A total of 86 male welders were recruited. Metal levels in urine were measured after a work day. Blood parameters were measured after 3 weeks of exposure cessation. Workers were divided up based on occupation (welder vs non-welder) and metal levels in the urine (low vs high). Data was analyzed using linear regression to determine associations between metal concentrations and blood parameters controlling for age, body mass index (BMI), and smoking status. The authors reported that welders had higher urinary Mn and Cr levels (Mn: 0.96 vs 0.22 ug/g creatinine, $p < 0.001$; Cr: 0.63 vs 0.22 ug/g creatinine, $p < 0.01$) and higher Hct (44.58 ± 2.84 vol% vs 43.07 ± 3.31 vol%, $p = 0.026$). Lower WBC were found in the high Mn group vs the low Mn group (6.93 ± 1.59 X 106 Cell/ml vs 7.90 ± 2.13 X 106 Cell/ml, $p = 0.018$). Other blood parameters were not significantly different among the groups. The authors concluded that welders had 3 to 4 times higher Mn and Cr urine concentrations and that Mn exposure was associated with changes in WBC counts. The clinical implications, however, are unknown.

McCarrick et al. (2021) evaluated the genotoxicity and inflammatory characteristics of stainless steel welding fume particles using standard or Cr(VI)-reduced flux-cored wires (FCW) in human lung cells (HBEC-3kt, 5-100 µg/mL) and macrophages (THP-1, 10-50 µg/mL). The authors characterized the welding fume particles and tested for toxicity (cell viability, DNA damage and inflammation). They reported that use of standard FCW released more Cr(VI) and was more cytotoxic than the Cr(VI)-reduced FCW, which had < 3% Cr(VI). No DNA damage was found using the Cr(VI) FCW. Both particles, however, caused an inflammatory response. Overall, the authors noted that the toxicity of welding fume particles can be reduced by substituting the FCW with the Cr(VI)-reduced FCW.

Monsé et al. (2020) evaluated the effects of short-term controlled exposures to nano-sized zinc oxide (ZnO) on airway inflammatory markers in 16 healthy non-smokers (8 men and 8 women). Volunteers were exposed to either filtered air or ZnO (0.5, 1.0, and 2.0 mg/m^3) for 4 hours. The authors collected exhaled breath condensate (EBC) and measured the amount of zinc and various biomarkers (leukotriene B4 (LTB4), peptide leukotrienes (LTC4/D4/E4), 8-iso-PGF2α, pH, and prostaglandin E2 (PGE2)) in the EBC. The authors found that none of the biomarker concentrations that were detectable were correlated with ZnO exposures and therefore concluded that EBC was not a good way to gauge exposures to ZnO.

Pereira et al. (2021) reviewed studies on the adverse effects of chromium exposures and male reproductive outcomes (changes in testosterone-producing cells, spermatogenesis, and sperm quality). The authors highlight that chromium (specifically hexavalent chromium CrVI) is common exposure in various industries, including welding. Animal studies have shown that exposures to CrVI impair spermatogenesis and the mechanism appears to be related to oxidative stress. The authors stress the need to further investigate the associations between chromium exposures and male reproductive health outcomes.

Vinnikov et al. (2022, ePub 2021) measured exhaled nitric oxide (FeNO), biomarker of inflammatory, exhaled carbon monoxide (CO) and pulmonary function (spirometry) in a cohort of 80 metalworking factory workers (median age 51.5 years of age) in Kazakhstan. The workers were placed into 3 categories: machine operators (41%), welders and assemblers (33%), and others (including administrative staff, 26%). The authors also collected information on occupational history, smoking, air pollution sources at home, respiratory symptoms, and comorbidities via questionnaires. Mixed-effects statistical models were used to assess associations between FeNO and occupational groupings, adjusting for other variables. The authors reported statistically significant associations between FeNO and occupational groups ($p < 0.01$), current smoking ($p < 0.05$), and age ($p < 0.05$). The highest exposure group was the machine operator group, followed by the welders and others. However, the welding group had significantly higher levels of measured FeNO (44.8 ppb, 95% confidence interval (CI): 33.8-55.9 ppb) compared to the machine operators (24.6 ppb, 95% CI: 20.5-28.7) and others (24.3 ppb, 95% CI: 17.7-30.9). The authors concluded that the high FeNO observed for welders may indicate respiratory inflammation that could be associated with welding fume exposures.

Zhang et al. (2021) examined the effects of iron oxide nano particles, which can be formed from welding processes, on respiratory cells with respect to glutathione (GSH) and glutathione-S-transferase (GSTs). GSH and GST are two key enzymes that are associated with the oxidative stress response from both acute and chronic exposures to environmental pollutants. Low concentrations of iron oxide nanoparticles (≤100 µg/ml) resulted in reduced GSH and GST activity in respiratory cells. The results appear to suggest a potential early marker for toxicity warranting further research.

4.4 Reviews

No general reviews of welding exposure and health effects were identified in this literature search, topic specific reviews are presented in the sections above.

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