HHS Public Access

Author manuscript

J Occup Environ Hyg. Author manuscript; available in PMC 2019 June 01.

Published in final edited form as:

J Occup Environ Hyg. 2019 June ; 16(6): 372–377. doi:10.1080/15459624.2019.1587172.

Influence of Welding Fume Metal Composition on Lung Toxicity and Tumor Formation in Experimental Animal Models

Patti C. Zeidler-Erdely[#1,2], **Lauryn M. Falcone**[1,2], and **James M. Antonini**[#1]

[1]Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV

[2]West Virginia University, School of Medicine, Morgantown, WV

[#] These authors contributed equally to this work.

Abstract

Millions of workers in the US and worldwide are exposed to complex, metal-rich welding fumes. Although welding is a crucial industrial process, the generated fumes are known to cause acute and chronic health effects when inhaled. The International Agency for Research on Cancer (IARC) classified welding fumes as *carcinogenic to humans* (Group 1) in 2017, based on sufficient epidemiological evidence and limited evidence in animals, an upgrade from the former Group 2B (*possibly carcinogenic to humans*) classification. There is human evidence that both iron-abundant mild steel as well as chromium- and nickel-containing stainless steel welding fumes contribute to an increased risk of lung cancer. Recent animal studies show that welding fumes may act as lung tumor promoters, regardless of the presence or absence of potentially carcinogenic metals, such as chromium and nickel. The goal of this manuscript was to examine the pulmonary responses associated with welding fumes by reviewing a series of recent experimental animal studies that assessed the influence of welding fume metal composition (e.g., stainless steel versus mild steel welding fume) on markers of lung toxicity and tumor development. Additional *in vivo* laboratory studies are needed to further explore the association between welding and lung cancer and to help advance our understanding of a potential mechanistic link.

Keywords

welding; lung cancer; A/J mice; chromium; iron

Welding Processes and Characterization

Approximately 11 million workers worldwide are regularly exposed to welding fumes. [1, 2] Given the variety of welding processes used in the workplace, welders are a diverse and heterogeneous group. The most common metal fusion process is electric arc welding.

Address for correspondence: Patti C. Zeidler-Erdely, PhD, National Institutes for Occupational Safety and Health, Health Effects Laboratory Division, 1095 Willowdale Road (M/S L2015), Morgantown, WV 26505, Tel: 304-285-5881; Fax: 304-285-5938. paz9@cdc.gov.

Specific types of arc welding include manual metal arc welding [MMAW; also known as shielded manual metal arc welding (SMAW)], gas metal arc welding (GMAW), flux-cored arc welding (FCAW), gas tungsten arc welding (GTAW), submerged arc welding (SAW), and plasma arc welding (PAW).[1] In arc welding, high temperatures of 5,000°C or more melt the joint between two metal work pieces as well as a filler material placed between them.[3] These extremely high temperatures are produced when an electric arc is established between the work pieces and a consumable wire electrode. As temperatures cool, the bond solidifies, firmly fusing the work pieces together. The bond created by welding is unique in that it is a mixture of the metal work pieces and the electrode filler material, making the bond extremely strong as it retains the strength of both initial metal parts.[1, 3]

Welding fumes are a byproduct of the process and generally arranged as chain-like agglomerates of nanometer-sized primary particles when generated.[4] The size of the welding particles formed varies depending on the process but can range from 10 nm - 20 μm. However, the mass median aerodynamic diameter of most welding fumes has been measured to be 0.2 - 0.5 μm.[5–8] The welding aerosol composition also varies depending on the specific type of welding process and materials used (e.g., stainless steel versus mild steel consumables). However, it is typically composed of a combination of a mixture of vaporized metal oxides from the electrode and/or flux material used.[3] Surface coatings or paint on the base metal or electrode can also contribute to the fume. Due to the contribution by the flux, the morphology of particles generated during MMAW welding is different and more complex than GMAW welding particles.[5, 6] Also, because of the presence of alkali metals in the flux, MMAW particles are more soluble (and thus potentially more biological reactive due to the availability of solubilized metals) compared to GMAW fumes which are relatively insoluble.[9]

The most common metals present in generated welding fumes are listed in Table 1. Iron (Fe) is the primary metal in most welding fumes and usually composes >80 % of mild steel fumes. Fume primarily made up of Fe has long been considered a nuisance dust with a small likelihood of causing chronic lung diseases. Fe has been shown to accumulate in the lungs of long-time welders and often causes a mostly benign lung condition known as siderosis.[10] Manganese (Mn), a known neurotoxicant, is a common component of most welding fumes as it improves metallurgical properties and acts as a deoxidizing agent to increase hardness and strength of the resultant weld.[11] Chromium (Cr) is common in SS welding fumes, existing in both Cr^{3+} and Cr^{6+} oxidation states.[12] Cr^{3+} cannot enter cells as readily and has low toxicity, whereas Cr^{6+} easily passes into cells, is highly toxic and classified as a carcinogen.[13] The permissible exposure limit (PEL) of Cr was lowered from 52 to 5 $\mu g/m^3$ in 2006 due to its harmful effects.[14] Nickel (Ni) also is a component of stainless steel welding fume and classified as a human carcinogen.[15] Ni alloys are becoming increasingly popular in welding as a potential alternative to Cr-containing materials.[16]

Lung Cancer in Humans

Recently, the International Agency for Research on Cancer (IARC) has classified welding fumes as carcinogenic to humans (Group 1), an upgrade from the Group 2B (possibly carcinogenic to humans) classification of welding fumes in 1989.[17] This reclassification for

welding fumes was based on sufficient evidence in humans for lung cancer and limited evidence in experimental animal studies. A majority of the cohort and case-control studies across different countries, time periods, and occupational settings reported an elevated risk of lung cancer for workers employed as welders or have reported being exposed to welding fumes. Potential confounders, such as tobacco smoking and asbestos exposure, were considered important, however, co-exposure to either agent could not explain all of the observed excess risk of lung cancer among welders. It has been suggested that welding with mild steel consumables, which account for the majority of all welding, posed little risk for lung cancer development because of the absence of carcinogenic metals, such as Cr and Ni, in the generated fume. However, numerous worker studies have been unable to associate an elevated risk of lung cancer directly with Cr-and Ni-containing stainless steel welding compared to mild steel welding.[18–20] Based on the conclusions of the IARC review, an increased risk of lung cancer was observed regardless of the welding process/method or material/consumable used, and there was no evidence that the increased cancer risk was limited to exposure to Cr-and Ni-containing stainless steel welding fumes.[17] However, because a majority of welders often used multiple processes and consumables, the observed results of the reviewed studies may reflect other underlying and unexplained workplace differences, thus making these associations difficult. To further define the pulmonary responses to welding fumes, a series of experimental animal studies were performed by which the exposure to specific welding fumes were well-controlled. The overall goal of the studies was to examine the influence of welding fume metal composition (e.g. stainless steel versus mild steel welding fume) on lung toxicity and tumor development.

Lung Toxicity in Experimental Animal Models

An initial study characterized markers of lung toxicity after exposing lung tumor-susceptible (A/J) and tumor-resistant (C57BL/6) mice by inhalation to Cr- and Ni-containing stainless steel welding fume.[21] Both strains of mice were exposed to GMAW-stainless steel at 40 mg/m^3 × 3 hours/day × 10 days. A significant and sustained lung response without recovery, as evidenced by an increased influx of polymorphonuclear leukocytes (PMN) and cytotoxicity, was found in both mouse strains. In a follow-up study of the same design, the lung toxicity profile of an Fe-abundant mild steel welding fume, which lacks carcinogenic metals, was evaluated.[22] Unlike with the stainless steel welding fume, no significant lung response occurred after exposure to the mild steel welding fume up to 84 days. A similar pattern of response was observed using a rat inhalation model. Male Sprague-Dawley rats were exposed to GMAW-stainless or mild steel welding fumes (40 mg/m^3 × 3 hours/day × 3 days).[23] Inhalation to the Fe-abundant mild steel welding fume had no significant effect on the lungs at any time point compared to controls, whereas lung toxicity was significantly increased and persisted up to 21 days after exposure to the Cr- and Ni-containing stainless steel fume. Importantly, the two welding fumes generated for all the above mentioned studies were nearly identical in particle size, solubility, and morphology.

Using intratracheal instillation, a method by which a welding fume suspension was delivered directly to the lungs of rats, Taylor et al.[24] compared the potential of three different welding fumes and their soluble and insoluble fractions to cause pulmonary toxicity. GMAW-stainless steel and mild steel fumes were compared in the study as well as a more

chemically complex and highly water-soluble MMAW-stainless steel fume. Male Sprague-Dawley rats were exposed to 2 mg/rat of each welding fume suspension or the saline vehicle control. The results indicated that welding fumes of differing metal composition caused varied responses in the lungs of rats. It also was observed the stainless steel fume from the MMAW process induced the greatest lung response of three fumes and in most cases was dependent on both the soluble and insoluble fractions of that fume. The mild steel fume caused negligible lung toxicity that was significantly less compared to both stainless steel fumes which confirmed the findings from previous studies.[23, 25] The overall conclusion from both the mouse and rat studies was that stainless steel welding fumes cause a greater pulmonary toxicity compared to mild steel, likely due to the presence of potentially toxic and carcinogenic metals (e.g., Cr, Ni). Also, stainless steel fumes that were more soluble, such as those that are generated from MMAW processes, are likely to be the most acutely toxic.

Lung Carcinogenesis in Experimental Animal Models

Predicated on a document from an IARC advisory group on the Monograph priorities for 2010–2014 that listed welding fume as a high priority agent for further evaluation of carcinogenic risk to humans, a series of studies examining welding fume and lung tumorigenesis in experimental animals was initiated at the National Institute for Occupational Safety and Health.[26] In 2008, Zeidler-Erdely et al.[27] compared lung tumor-susceptible (A/J) and tumor-resistant (C57BL/6J) mouse strains exposed to GMAW-mild steel, GMAW-stainless steel, and MMAW-stainless steel via oropharyngeal aspiration in four separate bolus doses. The oropharyngeal aspiration exposure technique is one in which the welding fume samples are suspended in saline and aspirated into the lungs by the animal after a small volume of the suspension is placed at the base of the tongue.[28] Lung toxicity was assessed at 2, 7, and 28 days post-exposure, and gross lung tumor counts and histopathological analysis were done at 48 and 78 weeks. GMAW-stainless steel induced an acutely greater and more prolonged inflammatory response in the lungs of A/J mice, persisted in the lungs for the longest period of time, and caused a trend towards increased tumor incidence as compared to the other two welding fumes. It was also concluded that the GMAW-stainless steel fume did not appear to be a potent initiator for the induction of lung tumors using this particular experimental model and exposure regime.

Based on this finding, the next study focused on whether GMAW-stainless steel fume acted as a lung tumor promotor using a two-stage (initiation-promotion) mouse model. Male A/J mice were treated with a chemical initiator, 3-methylcholanthrene (MCA), or a corn oil vehicle control and were exposed 1 week later to different doses of GMAW-stainless steel via oropharyngeal aspiration 1/week × 5 week.[29] After 30 weeks post-initiation, lung tumors were enumerated. MCA initiation followed by GMAW-stainless steel promotion significantly increased lung tumor number compared to MCA/air-exposed controls (12.1 ± 1.5 tumors/mouse for low dose GMAW-stainless steel and 14.0 ± 1.8 tumors/mouse for high dose GMAW-stainless steel versus 4.77 ± 0.7 tumors/mouse in MCA/air). This study provided support for the theory that a stainless steel welding fume could act as lung tumor promoter.

To confirm the results of the oropharyngeal aspiration study, a similar two-stage (initiation-promotion) study using inhalation as the exposure route with GMAW-stainless steel fumes was done in A/J mice. Inhalation is the preferable route for animal studies because it more closely simulates workplace welding fume exposure with respect to particle size and surface properties of the generated fume. Furthermore, it has been shown previously that “freshly-generated” GMAW-stainless steel welding fume is more reactive and toxic to the lungs than “aged” welding fume that is commonly used for oropharyngeal aspiration studies.[30] Male A/J mice were treated with intraperitoneal injections of corn oil or MCA and then were exposed 1 week later to air or GMAW-stainless steel fume (40 mg/m^3 × 8 hours/day × 4 day/week × 9 weeks).[31] At 30 weeks post-initiation, average tumors per mouse lung were determined. Mice initiated with MCA and then promoted with GMAW-stainless steel had significantly greater average lung tumor numbers compared to MCA/air-exposed controls (16.11 ± 1.18 versus 7.93 ± 0.82). Taken together, the findings from these studies provided strong support that a Cr- and Ni-containing stainless steel welding fume acts as a lung tumor promoter in an animal model.

Because results of epidemiology studies suggest that welders exposed to mild steel welding fumes also were at an increased risk for lung cancer, the potential of an Fe-abundant GMAW-mild steel fume to promote lung tumors in the A/J mouse two-stage model was examined in a recent study.[22] Male A/J mice received a single intraperitoneal injection of corn oil or MCA and were exposed 1 week later by inhalation to GMAW-mild steel aerosols (34.5 mg/m^3 × 4 hours/day × 4 days/week × 8 weeks). At 30 weeks post-initiation, GMAW-mild steel welding fumes significantly promoted lung tumors in A/J mice initiated with MCA (21.86 ± 1.50) compared to MCA/air-exposed mice (8.34 ± 0.59). Importantly, this study demonstrated that inhalation of Fe-abundant GMAW-mild steel fume promoted lung tumors in an animal model and aligned with findings from worker studies that showed mild steel welders were at risk for lung cancer, even with less or no exposure to carcinogenic metals, such as Cr and Ni.

Conclusions and Future Directions

Welding fumes currently have no workplace exposure limit. Recent emphasis has been placed on regulating exposures in the workplace to the most toxic metals contained in welding fume, such as Cr. However, this may not be the best practice as questions remain in regards to other metals associated with welding fumes that have been believed to be or classified as less toxic or a nuisance, such as Fe. Two main topics that need to be further evaluated in future experimental animal models: (1) the contribution of the individual welding fume metals or combination of metals in the development of lung toxicity and tumor formation; (2) the mechanisms by which welding fume and the associated metals cause tumorigenesis.

To address the first topic, a preliminary study has been completed.[32] The primary goal was to compare the pulmonary toxicity of the metal oxides commonly found in GMAW-stainless steel welding fume. The secondary goal was to examine the potential of the different metal oxides to promote lung tumors using the two-stage (initiation-promotion) model. In the first set of experiments, lung tumor-susceptible A/J mice were exposed by oropharyngeal

aspiration (1 ×/week for 5 weeks) to vehicle, GMAW-stainless steel fume (1.7 mg), or different doses of surrogate metal oxides based on the weight percent of each metal in the fume: Cr_2O_3 + $CaCrO_4$ (366 + 5 μg and 731 + 11 μg), NiO (141 and 281 μg), or Fe_2O_3 (1 and 2 mg), and lung toxicity was examined at 1, 7, 28, and 84 d post-aspiration. It was observed that the ranking for the lung inflammatory response of the metal oxides was Fe_2O_3 > Cr_2O_3 + $CaCrO_4$ > NiO. Overall, lung toxicity was negligible for NiO, acute but not persistent for Cr_2O_3 + $CaCrO_4$, and persistent for the Fe_2O_3 exposures. Importantly, however, lung toxicity was the greatest for the total GMAW-stainless steel welding fume compared to the individual metal oxide components, suggesting a possible synergistic effect of the metals in combination. This is consistent with the findings of previous studies which have reported the metal components to be less toxic than the total welding fume.[27, 33]

In a second set of experiments from the recent Falcone et al.[32] study, A/J mice were initiated with MCA or corn oil and then exposed by oropharyngeal aspiration (1 ×/week for 5 weeks) with the different metals. Lung tumors were counted at 30 weeks post-initiation. Results indicated that Fe_2O_3, but not Cr_2O_3 + $CaCrO_4$ or NiO significantly promoted lung tumors. Although these findings demonstrated that none of the metals besides Fe_2O_3 promoted lung tumors, previous studies have shown that GMAW-stainless steel welding fume promoted lung tumors after oropharyngeal aspiration and inhalation exposure (Zeidler-Erdely et al., 2013; Falcon et al., 2017).[29, 31] In addition, Falcone et al.[32] observed histopathological changes only in the lungs of the animals exposed to the total GMAW-stainless steel fume that were not present after exposure to the individual metals, including Fe_2O_3. Moreover, the changes in the inflammatory mediators were the greatest in the lavage fluid recovered from the lungs for the GMAW-stainless steel group compared to the individual metals. It may be possible that Fe is the primary component that drives the persistent or more chronic lung responses (e.g., cancer) to welding fume, whereas Cr and Ni may have the greatest effect on the more acute cytotoxic lung effects (e.g., inflammation). Overall, these findings provide further evidence that Fe is an important mediator of welding fume toxicity and support previous epidemiology and the recent IARC re-classification for welding fume.

In the other topic that needs further evaluation in experimental animal studies is the examination of the mechanism by which welding fumes cause lung cancer. To date, this mechanism is mostly unknown. It has been hypothesized that the likely primary carcinogenic characteristics of welding fume include their ability to cause immunosuppression and chronic inflammation.[34] Epidemiology clearly demonstrates that that welders are more susceptible to the development of respiratory tract infections and immunosuppression compared to the general population.[35–37] In agreement, inhalation to both GMAW-stainless steel and GMAW-mild steel welding fumes suppressed the ability of the lungs to clear a bacterial pathogen in rats.[38–39] In regards to welding fume causing chronic inflammation, GMAW-stainless steel fume has been shown to cause sustained inflammatory cell influx in the lungs in rodent studies.[21, 27, 39] More recently, Fe_2O_3 also was found to be toxic to the lungs with both local and systemic inflammatory responses reported.[32] These potential mechanisms possibly contribute to development of lung cancer associated with welding fume exposure. Obviously, more studies are needed to evaluate these mechanisms in greater detail.

References

(1). Antonini JM: Health Effects Associated with Welding In Comprehensive Materials Processing, Volume 8, Bassim N (ed.). Oxford, UK: Elsevier Ltd., 2014 pp. 49–70, 2014.

(2). Guha N, Loomis D, Guyton KZ, Grosse Y, El Ghissassi FE, Bouvard V, Benbrahim-Tallaa L, Vilahur N, Muller K, and Straif K: Carcinogenicity of welding, molybdenum trioxide, and indium tin oxide. Lancet Oncology. 18(5):581–582 (2017). [PubMed: 28408286]

(3). The James F Lincoln Arc Welding Foundation: Arc-welding Fundamentals In The Procedure Handbook of Arc Welding, Fourteenth Edition, The James F. Lincoln Arc Welding Foundation (ed.). Cleveland, OH, 2000, p. 1.3–1.

(4). Antonini JM, Keane M, Chen BT, Stone S, Roberts JR, Schwegler-Berry D, Andrews RN, Frazer DG, and Sriram K: Alterations in welding process voltage affect the generation of ultrafine particles, fume composition, and pulmonary toxicity. Nanotoxicology. 5:700–710 (2011). [PubMed: 21281223]

(5). Zimmer AT: The influence of metallurgy on the formation of welding aerosols. J. Environ. Monit 4(5):628–632 (2002). [PubMed: 12400906]

(6). Jenkins NT, Pierce WM-G, and Eagar TW: Particle size distribution of gas metal and flux cored arc welding fumes. Weld. J 84:156s–163s (2005).

(7). Antonini JM, Afshari AA, Stone S, Chen B, Schwegler-Berry D, Fletcher WG, Goldsmith WT, Vandestouwe KH, McKinney W, Castranova V, and Frazer DG: Design, Construction, and Characterization of a Novel Robotic Welding Fume Generation and Inhalation Exposure System for Laboratory Animals. J. Occup. Environ. Hyg 3:194–203 (2006). [PubMed: 16531292]

(8). Sowards JW, Ramierz AJ, Dickinson DW, and Lippold JC: Characterization of welding fume from SMAW electrodes. Weld. J 89:82s–90s (2010).

(9). Antonini JM, Lawryk NJ, Murthy GG, and Brain JD: Effect of welding fume solubility on lung macrophage viability and function in vitro. J. Toxicol. Environ. Health, Part A 58(6):343–363 (1999). [PubMed: 10580758]

(10). Kalliomaki PL, Junttila ML, Kalliomaki K, Lakomaa EL, and Kivela R: Comparison of the retention and clearance of different welding fumes in rat lungs. Am. Ind. Hyg. Assoc. J 44(10): 733–738 (1983). [PubMed: 6650394]

(11). Harris MK, Ewing WM, Longo W, DePasquale C, Mount MD, Hatfield R, and Stapleton R: Manganese exposures during shielded metal arc welding (SMAW) in an enclosed space. J. Occ. and Environ. Hyg 2(8):375–382 (2005).

(12). Keane M, Stone S, Chen B, Slaven J, Schwegler-Berry D, and Antonini J: Hexavalent chromium content in stainless steel welding fumes is dependent on the welding process and shield gas type. J. Environ. Monit 11:418–424 (2009). [PubMed: 19212602]

(13). Cohen MD, Kargacin B, Klein CB, and Costa M: Mechanisms of chromium carcinogenicity and toxicity. Crit. Rev. Toxicol 23(3):255–281 (1993). [PubMed: 8260068]

(14). “Occupational exposure to hexavalent chromium. Final rule,” Federal register 71:39 (2006). pp. 10099–10385.

(15). International Agency for Research on Cancer: Chromium, nickel, and welding In IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, World Health Organization (ed.). Geneva, 1990, pp. 447–525.

(16). Sowards JW, Liang D, Alexandrov BT, Frankel GS, and Lippold JC: A new chromium-free welding consumable for joining austenitic stainless steels. Weld. J 90:63s–76s (2011).

(17). International Agency for Research on Cancer: Welding, Molybdenum Trioxide, and Indium Tin Oxide In IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Voulme 118, World Health Organization (ed.). Lyon, France, 2018, pp. 36–265.

(18). Sorensen AR, Thulstrup AM, Hansen J, Ramlau-Hansen CH, Meershon A, Skytthe A, and Bonde JP: Risk of lung cancer according to mild steel and stainless steel welding. Scand. J. Work Environ. Health 33:379–386 (2007). [PubMed: 17973064]

(19). Moulin JJ: A meta-analysis of epidemiologic studies of lung cancer in welders. Scand. J. Work Environ. Health 23:104–113 (1997). [PubMed: 9167233]

(20). Langard S: Nickel-related cancer in welders. Sci. Total Environ 148:303–309 (1994). [PubMed: 8029707]

(21). Zeidler-Erdely PC, Batelli LA, Stone S, Chen BT, Frazer DG, Young S-H, Erdely A, Kashon ML, Andrews R, and Antonini JM: Short-term inhalation of stainless steel welding fume causes sustained lung toxicity but no tumorigenesis in lung tumor susceptible A/J mice. Inhal. Toxicol 23:112–120 (2011). [PubMed: 21309664]

(22). Falcone LM, Erdely A, Kodali V, Salmen R, Battelli LA, Dodd T, McKinney W, Stone S, Donlin M, Leonard HD, Cumpston JB, Cumpston JL, Andrews RN, Kashon M, Antonini JM, and Zeidler-Erdely PC. Inhalation of iron-abundant gas metal arc-mild steel welding fume promotes lung tumors in mice. Toxicol. 409:24–32 (2018).

(23). Antonini JM, Roberts JR, Stone S, Chen BT, Schwegler-Berry D, Chapman R, Zeidler-Erdely PC, Andrews RN, and Frazer DG: Persistence of deposited metals in the lungs after stainless steel and mild steel welding fume inhalation in rats. Arch. Toxicol 85:487–498 (2011). [PubMed: 20924559]

(24). Taylor MD, Roberts JR, Leonard SS, Shi X, and Antonini JM: Effects of welding fumes of differing composition and solubility on free radical production and acute lung injury and inflammation in rats. Toxicol. Sci 75:181–191 (2003). [PubMed: 12832661]

(25). Antonini JM, Krishna Murthy GG, Rogers RA, Albert R, Ulrich GD, and Brain JD: Pneumotoxicity and pulmonary clearance of different welding fume particles after intratracheal instillation in the rat. Toxicol. Appl. Pharmacol 40:188–199 (1996).

(26). International Agency for Research on Cancer: Report of the advisory group to recommend priorities for IARC. Monographs during 2010–2014 Lyon, France: Internal report 08/001 (2008).

(27). Zeidler-Erdely PC, Kashon ML, Battelli LA, Young S-H, Erdely AD, Roberts JR, Reynolds SH, and Antonini JM: Lung inflammation and tumor induction in lung tumor susceptible A/J and resistant C57BL/6J mice exposed to welding fume. Particle Fibre Toxicol. 5:12 (2008).

(28). Rao GVS, Tinkle SS, Weissman DN, Antonini JM, Kashon ML, Salmen R, Battelli LA, Willard PA, Hoover M, and Hubbs AF: Efficacy of a technique for exposing the mouse lung to particles aspirated from the pharynx. J. Toxicol. Environ. Health, Part A 66:1441–1452 (2003). [PubMed: 12857634]

(29). Zeidler-Erdely PC, Meighan TG, Erdely A, Battelli LA, Kashon ML, Keane M, and Antonini JM: Lung tumor promotion by chromium-containing welding particular matter in a mouse model. Particle Fibre Toxicol. 10:45 (2013).

(30). Antonini JM, Clarke RW, Krishna Murthy GG, Sreekanthan P, Jenkins N, Eagar TW, and Brain JD: Freshly generated stainless steel welding fume induces greater lung inflammation in rats as compared to aged fume. Toxicol. Lett 98:77–86 (1998). [PubMed: 9776564]

(31). Falcone LM, Salmen R, Erdely A, Battelli LA, Meighan TG, McKinney W, Stone S, Cumpston A, Andrews RN, Kashon M, Antonini JM, and Zeidler-Erdely PC: Inhalation of gas metal arc-stainless steel welding fume promotes lung tumorigenesis in A/J mice. Arch. Toxicol 91:2953–2962 (2017). [PubMed: 28054104]

(32). Falcone LM, Erdely A, Salmen R, Keane M, Battelli L, Kodali V, Bowers L, Stefaniak AB, Kashon ML, Antonini JM, and Zeidler-Erdely PC: Pulmonary toxicity and lung tumorigenic potential of surrogate metal oxides in gas metal arc welding– stainless steel fume: iron oxide as a primary mediator compared to chromium and nickel oxides; PLoS One. Submitted.

(33). Antonini JM, Taylor MD, Zimmer AT, and Roberts JR: Pulmonary responses to welding fumes: Role of metal constituents. J. Toxicol. Environ. Health., Part A 67:233–249 (2004). [PubMed: 14681078]

(34). Guyton KZ, Rusyn I, Chiu WA, Corpet DE, van den Berg M, Ross MK, Christiani DC, Beland FA, and Smith MT: Application of the key characteristics of carcinogens in cancer hazard identification. Carcinogenesis. 39(4):614–622 (2018). [PubMed: 29562322]

(35). Lockey JE, Schenker MB, Howden DG, Desmeules MJ, Saracci R, Sprince NL, and Harber PI: Current issues in occupational lung disease. Am. Rev. Respir. Dis 138:1047–1050 (1988). [PubMed: 3202432]

(36). Palmer KT, Poole J, Ayres JG, Mann J, Burge PS, and Coggon D: Exposure to metal fume and infectious pneumonia. Am. J. Epidemiol 157:227–233 (2003). [PubMed: 12543622]

(37). Coggon D and Palmer KT: Are welders more at risk of respiratory infections? Thorax. 71(7): 581–2 (2016). [PubMed: 27103350]

(38). Antonini JM, Stone S, Roberts JR, Chen B, Schwegler-Berry D, Afshari AA, and Frazer DG: Effect of short-term stainless steel welding fume inhalation exposure on lung inflammation, injury, and defense responses in rats. Toxicol. Appl. Pharmacol 223:234–245 (2007). [PubMed: 17706736]

(39). Antonini JM, Roberts JR, Stone S, Chen BT, Schwegler-Berry D, and Frazer DG: Short-term inhalation exposure to mild steel welding fume had no effect on lung inflammation and injury but did alter defense responses to bacteria in rats. Inhal. Toxicol 21:182–192 (2009). [PubMed: 18925477]

Table 1.

Metal Composition of Common Welding Fumes

Welding Fume Samples	Metal (weight %)*	Soluble/Insoluble Ratio
GMAW-mild steel	Fe 85 Mn 14	0.020
GMAW-stainless steel	Fe 57 Mn 13.8 Cr 20.2 Ni 8.8	0.006
Shielded MMAW-stainless steel	Fe 41 Cr 29 Mn 17 Ni 3	0.345 **Soluble metals:** Cr 87% Mn 11%

* Relative to all metals analyzed; modified from Antonini et al.(9)