Characterisation of the biological effect of ultrafine particles in welding fumes after controlled exposure – Effect of the MIG welding of aluminium and the MIG brazing of zinc-coated materials

Long-time exposure to welding fumes is supposed to be responsible for lung disease in some cases [1]. Whether welding fume exposure leads to an impairment of human health seems to be dependent on various factors like fume concentrations, ventilation of the workshops [2, 3], use of personal protection equipment [4-6] and presence of co-factors like cigarette smoking [7]. From different epidemiological and toxicological studies, it is also known that ultrafine particles which are produced by many thermal processes such as welding are able to induce inflammatory processes not only in the lung but also systemically [8-15], thus inducing not only lung injury but also impairment of the cardiovascular system. However, it seems to be evident that health effects of welding fumes also depend on the nature of the fumes, on welding techniques and on base and filler materials. In order to improve the prevention of welding-related diseases, it would be helpful to have better knowledge about the relationship between the potential to induce lung diseases and those welding-related factors (welding techniques and materials).

1 Introduction

The development of lung disease is a process ongoing over many years in which risk factors are difficult to record and to evaluate. It would be more efficient if the health effects of welding fumes could be estimated from the reaction of the human body after an initial short-time contact with the fumes. This task seems to be achievable by monitoring inflammatory reactions in the human body after contact with the fumes. These inflammatory reactions are natural responses of the body to exposure to external, potentially harmful material. Usually, these reactions are terminated after some time and there is no irreversible damage to lung tissue. However, if the exposure persists over long periods and inflammation, although minimal, becomes chronic, this may gradually lead to disease.

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At the same time, the Aachen Workplace Simulation Laboratory was developed [16-18] in order to overcome problems arising from real workplace conditions like heterogeneous exposure conditions (complex mixtures of emissions from different sources like welding, grinding, soldering or chemical solvents) or typical workplace conditions like ventilation, space, head/body position, individual behaviour or the use of personal protection equipment in field studies – taking into account previous considerations of the Working Group “Effect-Related Factors” of the “Iron and Metal I” expert committee in the employers’ liability insurance association, Section “Hazardous Substances in Welding and Allied Processes”. This laboratory makes it possible to perform exposure studies on human subjects under controlled conditions using the emission of one single working process and to establish exposures with controlled concentration time courses in order to assess the short-term effects of various workplace emissions which are comparable among different subjects.

Thus, an interdisciplinary research programme of the Institute of Occupational and Social Medicine and the ISF - Welding and Joining Institute of the Aachen University of Technology in Aachen/Germany was designed in close cooperation with the Expert Committee “Metal and Surface Treatment” of the employers’ liability insurance association which supported this study. Different welding techniques and materials were evaluated in respect to their potential to induce inflammation after the short-term exposure of human subjects to welding fumes under controlled, experimental conditions.

The studies presented in this paper focus on two different welding processes and material combinations: the MIG welding of aluminium and the MIG brazing of zinc-coated steel were part of this research project.

2 Methods
2.1 The Aachen Workplace Simulation Laboratory

While observing workplace threshold limits, controlled exposures of healthy human subjects are performed in the Aachen Workplace Simulation Laboratory [19]. This device consists of two different units: the emission room in which the welding fumes are generated and the exposure laboratory in which the test subjects are exposed (Fig. 1). Both units are connected by a ventilation system. The air containing welding fumes enters the exposure laboratory via four ceiling diffusers which have a vortex flow and ensure a homogeneous aerosol distribution throughout the laboratory.

An experienced welder performs the welding below a funnel-shaped fume hood. Welding is usually performed for 40 s about every 10 min. The intervals between each welding episode as well as the flow rates given by the ventilation system determine the average particle mass concentration within the exposure room which can be varied over a wide range of concentration.

The exposure conditions are monitored on line in respect to many physical fume properties. The particle mass concentration (PM$_{10}$) is measured continuously using a tapered-element oscillating microbalance (TEOM – series 1400A, Thermo Scientific, USA). The particle number/size distribution and the total number are measured using a fast-mobility particle sizer (FMPS – model 3091, TSI, USA). Additionally, welding-related gases are measured for NO, CO, and CO by electrochemical sensors (Ados, Germany) and a UV photometrical sensor for ozone (Thermo Scientific, model 49i, USA). The elemental composition of the welding fume particles was measured using atomic absorption spectrometry (AAS).

2.2 Effect parameters

Appropriate inflammation markers have to be available in order to quantify inflammatory reactions after the exposure of humans to welding fumes. Different markers which are supposed to assess inflammation either topically (within the lung) or systemically (in the whole body) are used in this research programme. Systemic inflammation can be assessed by collecting exhaled breath condensate and condensing the fluid contained in the exhaled air using a condensation trap. In this fluid, nitrosative and oxidative stress can be detected by measuring nitrate and a U V photometrical sensor for ozone (Thermo Scientific, model 49i, USA). The elemental composition of the welding fume particles was measured using atomic absorption spectrometry (AAS).

2.3 Study design

The studies performed in this research programme take place as crossover studies with twelve healthy male subjects. Crossover study means that each subject is exposed to different welding fumes and a control exposure in which the subjects are exposed to clean air free from welding fumes. Each subject is exposed for six hours. Endpoint parameters are usually measured before exposure, after exposure, and after one week. Every 60 min, each subject cycled on an ergometer at 80 W inside the exposure laboratory for 15 min in order to simulate a workout as would occur during a work shift.
2.4 Statistical analysis

In order to identify any differences in the biological effects among different welding techniques, the differences between the value after exposure versus before exposure, the differences between the value 24 h after exposure versus before exposure and the differences between the value one week after exposure versus before exposure were calculated for each end-point parameter. The parametric analysis of variance and the non-parametric Kruskal-Wallis test were used in order to identify dependencies of these differences from the exposure scenario.

3 Study I: MIG welding of aluminium and MIG brazing of zinc-coated steel

This study was performed as threefold crossover study in which three different exposures were compared:
1. reference exposure to clean air (zero),
2. exposure to the emissions of a metal inert gas welding process on aluminium (MIG-aluminium) and
3. exposure to the emissions of a metal inert gas brazing process on hot-dip zinc-coated steel [22].

3.1 Welding

The following materials were used:

- **Metal inert gas welding (MIG welding) on aluminium alloys**: base material: aluminium, EN 573-2: EN AW-5754 (AlMg3), filler metal: AlMg3 (97% aluminium, 3% magnesium), EN ISO 18273 – SA l5754, shielding gas: argon, DIN EN ISO 14175 – I1 - Ar. The welding process was in the pulsed-arc mode.

- **Metal inert gas brazing (MIG brazing) on zinc-plated base material**: base material: hot-dip zinc-coated steel sheet EN 10346: DX51D+Z275, filler metal: CuSi3Mn1 (96% copper, 1% manganese, 3% silicon), ISO 24373 – S Cu 6560, shielding gas: argon, DIN EN ISO 14175 – I1 - Ar.

3.2 Results

Concerning the chemical composition of welding fumes, the investigations showed the following:

- fumes from MIG brazing contained 60.1% zinc, 16.7% copper, 0.9% iron and 0.3% manganese
- fumes from the MIG welding of aluminium generated 51.4% aluminium, 4.6% magnesium and 0.1% manganese

Concerning ozone during MIG brazing, the measured value stayed below 50 µg/m³. On the contrary, high ozone concentrations (up to 250 µg/m³) were observed during the MIG welding of aluminium. The concentrations of NO, CO₂ and CO were negligible.

Fig. 2 shows the particle number/size distribution for MIG brazing and MIG welding. On Figs. 3 and 4, the time course of the particle number and the mass concentrations are shown as examples for one day of each exposure.

- **Fig. 2** • Particle number/size distribution for MIG brazing and MIG welding [22].
- **Fig. 3** • Time course of particle number and mass concentrations within the exposure laboratory on a study day with exposure to MIG brazing emissions. The dashed line represents the given value [22].
- **Fig. 4** • Time course of particle number and mass concentrations within the exposure laboratory on a study day with exposure to MIG welding emissions. The dashed line represents the given value [22].
scenario. As can be seen, the given values for the average mass concentration of 2.5 mg/m³ welding fumes could be kept with good accuracy. Chemical analysis has shown that 1.9 mg/m³ zinc oxide and 1.5 mg/m³ zinc were present in the welding fumes.

During MIG brazing, the mean particle number concentration was $6.0 \times 10^5$ particles/cm³ (the average of the peak maxima was $1.8 \times 10^5$ particles/m³) for a mass concentration of 2.51 mg/m³ (4.07 mg/m³ for the mass concentration, corresponding to the max. particle number concentration). During the MIG welding of aluminium, the average particle number concentration was at a level similar to that in MIG brazing with $4.01 \times 10^5$ particles/cm³ and the mass concentration was 2.52 mg/m³. The average of the peak maxima number concentration was $1.3 \times 10^6$ particles/cm³ for a mass concentration of 4.29 mg/m³. Without fume exposure, the mean number concentration was $3.7 \times 10^3$ particles/cm³ for a mean mass concentration of 17 µg/m³.

As an example, Fig. 2 shows the particle number as well as the mass concentration for the MIG brazing of zinc-coated steel over one day. Fig. 3 shows the average particle number/size distribution for the two different exposure fumes. For the MIG brazing of a zinc-coated workpiece, the welding fume particle size distribution showed that 33% of the particles are smaller than 100 nm and the modal size was 124 nm whereas the mode derived for the MIG welding of aluminium material was 143 nm with 15% of the particles being smaller than 100 nm. More details on the particle size distribution and the fume composition can be found in [22].

The analysis of the markers for systemic inflammation in the blood showed no change between the value before and after exposure to the emissions from the MIG welding of aluminium alloys. A significant increase in hsCRP ($p < 0.001$) was observed for the exposure to MIG brazing fumes containing zinc oxide (Fig. 6). Compared with the mean value of 0.3 mg/l before exposure, the mean value one day after the exposure was 2.75 mg/l. However, although this increase was nearly tenfold, most values remain within the normal range (< 5 mg/l) and the subjects experienced no symptoms. The neutrophil concentration in the blood showed a similar pattern although this data failed statistical significance ($p > 0.05$) (Fig. 7). Blood coagulation factors VIII and ristocetin co-factors showed significant increases either directly after exposure or after seven days.

No indications of local inflammation within the lungs were found in any exhaled breath condensate samples.

### 3.3 Discussion

This study has shown that, even at low fume concentrations which are in compliance with German workplace threshold limits, the inhalation of the emissions from a MIG brazing process on zinc-coated steel is able to induce a distinct inflammatory reaction within the human body. Since it is well-known that the inhalation of zinc fumes is able to induce metal fume fever at high fume concentrations [23-25], it may be speculated that zinc (zinc ox-
ide), in addition to copper oxide, is responsible for the observed effect. These effects may be understood if it is considered that zinc plays an important role in the regulation of immune reactions within cells [26, 27]. An excess amount of zinc in cells may lead to disproportionate immune reactions as was observed in this study. However, it may be suspected that this reaction is able to induce lung injury after long-term exposure to low concentrations of fumes containing zinc but this still has to be proven.

4 Study II: Assessment of the no observed effect level for welding fumes from the MIG brazing of zinc-coated materials

The results shown in the previous section are especially important in consideration of the ongoing debate about workplace threshold limits for zinc. The German WTL Commission has recently proposed a threshold limit of 0.1 mg/m³ zinc in the air (1.5 mg/m³ in the study reported above). This proposal was based on data reported by Beckett et al. [28] who exposed human subjects to 0.5 mg/m³ zinc oxide for two hours. In this study, they found no changes in haematological parameters, inflammation markers or cardiac physiology. This exposure was considered as safe and extrapolated to an eight-hour work shift. Therefore, it was concluded that 0.1 mg/m³ zinc should be safe for eight hours too. However, it is very likely that even higher concentrations of zinc fumes would be safe. The experimental setup of the Aachen Workplace Simulation Laboratory gives the possibility to assess the threshold for the onset of biological effects (no observed effect level – NOEL) systematically and to make a contribution to the determination of evidence-based workplace threshold limits.

The study addressing this issue was performed in an adaptive study design [29]. This means that an interim analysis is performed after the first out of three exposures and it is tested whether an increase in hsCRP in the blood could be detected. If an effect is observed, the second exposure is performed with a lower concentration. If no effect is observed, the second exposure is performed with a higher concentration – and so on (Fig. 8). The welding fume concentration at which the onset of signs of systemic inflammation can be observed can be approximated in this way.

4.1 Results

The first exposure was performed with a fume concentration of 1.43 mg/m³ containing 0.9 mg/m³ zinc as zinc oxide. No increase in hsCRP was observed 24 h after this exposure (Fig. 9). Therefore, the next exposure was performed with 2 mg/m³ fumes containing 1.2 mg/m³ zinc in the form of zinc oxide. A statistically significant increase in hsCRP was observed this time (p<0.001). The third exposure was therefore performed with 2.5 mg/m³ and 1.5 mg/m³ zinc. As seen before, an increase in hsCRP was observed after this exposure but it was less pronounced than in the previous study. More details can be found in [29].
Obviously, welding fumes from the MIG brazing of zinc-coated materials are able to induce signs of systemic inflammation which may be considered as a precursor of metal fume fever. Although it is not known if the chronic exposure to welding fumes containing zinc is able to induce lung injury, the welding of such materials should be performed using fume exhaust systems at the source and personal protection equipment in addition.

The Aachen Workplace Simulation Laboratory seems to be a powerful tool to assess the biological effects of different welding techniques. The research programme introduced in this paper makes provision for further studies in which other materials and welding techniques will be investigated in respect to their impact on workers’ health. Furthermore, the effect of welding parameters on the biological parameters should be investigated in order to optimise welding safety.

Literature


