Metalworking fluids
– allergens, exposure, and skin and respiratory effects

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People and Work
Research Reports 85

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To Sirkka-Liisa, Kimi, Vilho and Helvi
SUMMARY

About 20,000 machinists are employed in the fabrication of machine parts and other metallic objects in Finland. Machinists are exposed to metalworking fluids (MWF) that are used for cooling and lubricating the machining process, and for washing away metal chippings and other contaminants from between the machining tool and the work piece surface. The purpose of this study was to enhance knowledge related to machinists’ skin and respiratory exposure to MWFs, and to study the adverse health effects caused by MWFs.

Statistics on occupational skin and respiratory diseases of machinists were analysed, based on the Finnish Register of Occupational Diseases (FROD) and the patient register of the Finnish Institute of Occupational Health (FIOH) during 1992–2001. The frequency of skin and respiratory symptoms was inquired in a cross-sectional telephone interview of 757 machinists and 84 office workers (controls) in 64 metal companies. Working conditions were assessed and total aerosols were measured with a real-time aerosol photometer in 60 of the companies participating in the cross-sectional study. Detailed measurements of skin and respiratory exposure were carried out in ten companies: standardized methods were used to measure oil mist, inhalable dust, volatile organic compounds (VOC), aldehydes and microbial contaminants in the workplace air. New methods were developed for quantifying alkanolamines in the air and on the skin. 17 MWF concentrates were analysed for their skin-sensitizing components, and the results were compared with the information in the safety data sheets (SDS).

A total of 279 occupational skin diseases were diagnosed in machinists during 1992–2001. Skin diseases were found to be the second commonest occupational disease of machinists after strain injuries, and they
accounted for 27% of all occupational diseases. The incidence of skin diseases was 1.6 cases per 1000 persons per year. Machinists had about a three-fold incidence of occupational skin diseases compared to the total working population. Most of the occupational skin diseases were contact dermatoses, namely irritant contact dermatitis and allergic contact dermatitis. The most common causative agents of allergic contact dermatitis were MWFs and their ingredients. One out of five machinists in the telephone interview reported recurring or prolonged hand or forearm dermatitis during the past 12 months. The risk of hand or forearm dermatitis was about two-fold compared to the office workers (controls), and the risk of dermatitis elsewhere than on the hands or forearms was about four-fold compared to the controls. Skin atopy was an important risk factor of both hand or forearm dermatitis, and dermatitis occurring elsewhere.

Altogether 34 allergic respiratory diseases were reported in machinists during 1992–2001, constituting 3% of all occupational diseases in machinists. The incidence of respiratory diseases was 0.2 cases per 1000 persons per year, which is about the same as in the total working population. Most of the cases (85%) were asthma. The commonest causative agents were metal dusts and fumes, plastic chemicals, and MWFs and their ingredients. In the telephone interview, 31% reported suffering from some recurring or prolonged respiratory symptom within the past 12 months, even when the workplace air was found to be fairly clean according to total aerosol measurements. The risk of any respiratory symptom was 2.5-fold compared to that of the office workers, and especially the risk of upper respiratory symptoms was high, about four-fold. Among machinists, exposure to aerosol levels above the median concentration of 0.17 mg/m³ in the general air was related to both upper and lower respiratory symptoms. Furthermore, machinists with 15 or more years' work history had more cough and chronic bronchitis than those with a shorter work history.

In the workplace assessments, the quality of workplace air was found to be reasonably good according to the total aerosol measurements. However, there was considerable variation in exposure control measures, as only one third of the machines were equipped with functional local ventilation and enclosure. Protective gloves were not used systematically, and many of the gloves were made of materials not optimal for MWFs.
In the detailed exposure measurements conducted in ten machine shops, the concentrations of chemicals, microbes and inhalable dust were low, being clearly below the current occupational exposure limits (OEL) in most samples. VOCs were the most abundant contaminant with an average concentration of 1.9 mg/m³. The average concentrations of inhalable dust, oil mist, alkanolamines and aldehydes were 0.78 mg/m³, 0.14 mg/m³, 0.11 mg/m³ and 0.10 mg/m³, respectively. Exposure to alkanolamines was found to occur mainly through the skin. The alkanolamines quantified from the skin of the hands corresponded to 1–2 ml of MWF retained on the skin during two hours of working. All MWFs analysed were found to contain skin-sensitizing components, of which formaldehyde, alkanolamines and iodopropynyl-butylcarbamate were the most common. Skin sensitizers were poorly declared in the SDSs of the MWFs.

The present study suggests that occupational skin diseases are commonly reported to the FROD, but that some cases may nevertheless be missed from the statistics because not all work-related skin problems are identified at primary health care units or because some of the affected workers may change to another job without seeing a doctor. More attention should be paid to the skin symptoms and skin exposure of machinists, and suitable protective gloves, such as textile gloves coated partly with nitrile rubber, should be available in workplaces. It was also demonstrated that total exposure to alkanolamines can be reduced considerably by minimizing skin exposure. Skin patch test series should be updated to comply with the formulations of MWF to ensure reliable diagnosing of allergic contact dermatitis. Both chemical analysis of the patients' own MWFs and patch testing with the ingredients may be needed to discover contact allergies to MWF.

Although respiratory diseases were rarely diagnosed as occupational diseases, respiratory symptoms were abundant even in fairly clean work environments according to the total aerosol concentrations. Most of the reported respiratory symptoms were likely to be due to unspecific irritation. However, some cases of occupational asthma may be missed from the statistics because their work-relatedness is not identified, or because MWFs cause asthma with an unknown mechanism, thus making the diagnosing difficult. Also, the affected workers may transfer to cleaner jobs instead of seeking medical care. It was also shown that
other exposures than MWF may cause asthma in machinists. As there is very little knowledge on the specific, asthma-causing agents in MWF, provocation tests with individual ingredients should be considered if the MWF itself has provoked a positive reaction, and if the patient’s condition allows it.

The study demonstrated that improvements in occupational hygiene, such as increasing protective measures, improving working habits and developing new methods of cleaning air, are still needed. New methods of exposure assessment should be applied as well. For example, total aerosol content is indicative of overall air contaminants, and alkanolamines proved to be useful markers of exposure to all water-miscible MWFs. OELs for oil mist, alkanolamines and formaldehyde should be lowered to comply better with current concentrations at workplaces, or at least new target values clearly below current OELs should be established.
Suomessa on noin 20 000 metallintyöstäjää, jotka valmistavat koneistamalla erilaisia osia ja rakenteita metallista ja muista materiaaleista. Käytettyjä koneistustekniikoita ovat esimerkiksi sorvaus, poraus ja hionta. Metallintyöstö nesteitä eli lastuamisnesteitä käytetään yleisesti mm. työstöprosessin jäähdyttämiseen ja voiteluun sekä poistamaan työstöterästä ja -kappaleista irronnutta kiinteää metallijätettä. Tämän tutkimuksen tarkoituksena oli selvittää metallintyöstäjien ihon ja hengitysteiden altistumista metallintyöstö nesteille sekä tutkia työstö nesteiden aiheuttamia terveyshaittoja.


Vuosina 1992–2001 metallintyöstäjillä todettiin kaikkiaan 279 ammatti-ihotautia. Ihotaudit olivat toiseksi yleisin ammattitauti me-
TIIVISTELMÄ (FINNISH SUMMARY)


Työperäisten sairauksien rekisteriin ilmoitettiin 34 metallintyöstäjien hengitystieallergiaa vuosina 1992–2001. Hengitystieallergioiden ilmaantuvuus oli 0,2 tapausta 100 henkilöä kohti vuodessa; ilmaantuvuus oli suunnilleen sama kuin koko työväestössä. Suurin osa (85 %) hengitystieallergioista oli astmoja. Astma yleisimmat aiheuttajat olivat metallipölyt ja -huurut, muovikemikaalit, ja metallintyöstönestet ja niiden aineosat. Puhelinhaastattelussa 31 % metallintyöstäjistä ilmoitti kärseineensä jostain toistuvasta tai pitkittyneestä hengitystieoireesta viimeisten 12 kuukauden aikana siitä huolimatta että työpaikan ilman kokonaisaerosolipitoisuus oli melko pieni raja-arvoihin nähden. Riski saada mitä tahansa hengitystieoireita oli noin 2,5-kertainen ja ylähengitystieoireiden riski oli noin nelinkertainen vertailuryhmään nähden. Sekä ylä- että alahengitystieoireiden riski oli suurempi niillä, jotka altistuivat keskimääräistä aerosolipitoisuutta (0,17 mg/m³) suuremmalle pitoisuudelle, kun taas vähintään 15 vuotta työskennelleillä metallintyöstäjillä oli enemmän yskää ja kroonista bronkiittia kuin alle 15 vuotta työskennelleillä.

Kokonaisaerosolipitoisuuksien perusteella koneistustyöpaikkojen ilmanlaatu oli melko hyvä. Suojatuomisessa oli kuitenkin suuria vaihteluita, ja vain noin kolmasosassa koneista oli toimiva paikallispoisto ja kotelointi. Suojakäsineiden käyttö oli vaihtelevaa, ja monet suojakäsineistä olivat tehty metallintyöstönesteille soveltumattomasta materiaalista. Kymmenessä yrityksessä, jossa tehtiin tarkat työhygieeniset mittaukset, kemikaalien,
hengittyvän pölyn ja mikrobiepäpuhtauksien keskiarvopitoisuudet olivat selvästi raja-arvoja pienemmät. Haihtuvien organisten yhdisteiden (VOC) kokonaiskeskiarvopitoisuus oli 1,9 niiden pitoisuus oli selvästi suurempi kuin muiden epäpuhtauksien pitoisuudet. Hengittyvän pölyn keskiarvopitoisuus oli 0,78 mg/m³,öljysumun 0,14 mg/m³, alkanolamiinien 0,11 mg/m³ ja aldehydien 0,10 mg/m³. Työntekijät altistuivat alkanolamiineille enimmäkseen ihon kautta. Käsien iholta mitattut alkanolamiinit vastasivat 1–2 ml:n lastuamisnestejäämää käsissä kahden tunnin työskentelyn jälkeen. Kaikki analysoitut lastuamisnesteen sisällöltä ihoa heristäviä aineosia. Yleisimpiä olivat formaldehidi, alkanolamiinit ja jodipropynyylibutyylikarbamaatti. Ihoa heristävät aineet olivat merkitty puutteellisesti kaikkien lastuamisnesteenä KTT:een.

aineosista on hyvin vähän tietoa, altistuskokeita yksittäisillä aineosilla tulisi harkita potilailla, joiden altistuskoe omalla metallintyöstönesteellä on positiivinen ja jotka ovat riittävästi hyväkuntoisia jatkotutkimuksiin.

ACKNOWLEDGEMENTS

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The participating companies, their workers and occupational health units, and distributors of metalworking fluids are greatly appreciated for their positive attitude and collaboration throughout the project. This study was carried out in collaboration with the Finnish Metalworkers’ Union and the Federation of Finnish Technology Industries. The study was supported financially by the Finnish Work Environment Fund, for which I am indebted.

Finally, I owe my warmest thanks to my family: my parents and parents-in-law for their constant encouragement and practical help while I was occupied with this study. I am deeply grateful to my husband Kim for his amazingly solid love and support, and to our children Vilho and Helvi for helping me understand what’s best in life.

Helsinki, January 2009

Katri Suuronen
## ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ACD</td>
<td>allergic contact dermatitis</td>
</tr>
<tr>
<td>ACGIH</td>
<td>American Conference of Governmental Industrial Hygienists</td>
</tr>
<tr>
<td>ARD</td>
<td>allergic respiratory disease</td>
</tr>
<tr>
<td>ASTM</td>
<td>American Society for Testing and Materials</td>
</tr>
<tr>
<td>BAL</td>
<td>bronchoalveolar lavage</td>
</tr>
<tr>
<td>BPT</td>
<td>bronchial provocation test</td>
</tr>
<tr>
<td>CAD</td>
<td>computer aided design</td>
</tr>
<tr>
<td>CATI</td>
<td>computer assisted telephone interview</td>
</tr>
<tr>
<td>CEN</td>
<td>European Committee for Standardization</td>
</tr>
<tr>
<td>CFU</td>
<td>colony forming unit</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CU</td>
<td>contact urticaria</td>
</tr>
<tr>
<td>DE</td>
<td>dermatitis elsewhere than on the hands or forearms</td>
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<tr>
<td>DEA</td>
<td>diethanolamine</td>
</tr>
<tr>
<td>DREAM</td>
<td>dermal exposure assessment method</td>
</tr>
<tr>
<td>ESCD</td>
<td>European Society of Contact Dermatitis</td>
</tr>
<tr>
<td>EU</td>
<td>endotoxin unit</td>
</tr>
<tr>
<td>FEV1</td>
<td>forced expiratory volume in one second</td>
</tr>
<tr>
<td>FIOH</td>
<td>Finnish Institute of Occupational Health</td>
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<td>FROD</td>
<td>Finnish Register of Occupational Diseases</td>
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<tr>
<td>FVC</td>
<td>forced vital capacity</td>
</tr>
<tr>
<td>GC-MS</td>
<td>gas chromatography-mass spectrometry</td>
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<tr>
<td>HD</td>
<td>hand dermatitis; hand or forearm dermatitis</td>
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<tr>
<td>HSE</td>
<td>Health and Safety Executive</td>
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<tr>
<td>ICD</td>
<td>irritant contact dermatitis</td>
</tr>
<tr>
<td>IgE</td>
<td>immunoglobulin E</td>
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<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>IPBC</td>
<td>iodopropynyl-butylcarbamate</td>
</tr>
<tr>
<td>IR</td>
<td>infra red</td>
</tr>
<tr>
<td>ISCO</td>
<td>International Standard Classification of Occupations</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
</tr>
<tr>
<td>LC-MS</td>
<td>liquid chromatography-mass spectrometry</td>
</tr>
<tr>
<td>LC-UV</td>
<td>liquid chromatography-ultraviolet detection</td>
</tr>
<tr>
<td>LOD</td>
<td>limit of detection</td>
</tr>
<tr>
<td>MAK</td>
<td>maximale arbeitsplatz konzentration (maximum workplace concentration)</td>
</tr>
<tr>
<td>MDBGN</td>
<td>methyl-dibromoglutaronitrile</td>
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<tr>
<td>MDEA</td>
<td>methyldiethanolamine</td>
</tr>
<tr>
<td>MEA</td>
<td>monoethanolamine</td>
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<tr>
<td>MHHPA</td>
<td>methylhexahydriptalic acid anhydride</td>
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<tr>
<td>MWF</td>
<td>metalworking fluid</td>
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<tr>
<td>NIOSH</td>
<td>National Institute for Occupational Safety and Health</td>
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<tr>
<td>OCD</td>
<td>occupational contact dermatitis</td>
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<tr>
<td>ODTS</td>
<td>organic dust toxic syndrome</td>
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<td>OEL</td>
<td>occupational exposure limit</td>
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<td>OR</td>
<td>odds ratio</td>
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<tr>
<td>ORD</td>
<td>occupational respiratory disease</td>
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<tr>
<td>OSD</td>
<td>occupational skin disease</td>
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<tr>
<td>OSHA</td>
<td>Occupational Safety and Health Administration</td>
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<tr>
<td>PAH</td>
<td>polyaromatic hydrocarbons</td>
</tr>
<tr>
<td>PEF</td>
<td>peak expiratory flow</td>
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<tr>
<td>RAST</td>
<td>radio allergy sorbent test</td>
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<tr>
<td>REL</td>
<td>recommended exposure limit</td>
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<tr>
<td>SDS</td>
<td>safety data sheet</td>
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<tr>
<td>SFS</td>
<td>The Finnish Standards Association</td>
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<tr>
<td>SWORD</td>
<td>surveillance system for work-related or occupational respiratory disease</td>
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<tr>
<td>TEA</td>
<td>triethanolamine</td>
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<tr>
<td>VITAE</td>
<td>video imaging technique for assessing dermal exposure</td>
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<tr>
<td>VOC</td>
<td>volatile organic compound</td>
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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on investigations carried out at the Finnish Institute of Occupational Health. It is a summary of the following publications, which are referred to in the text by their Roman numerals.


I INTRODUCTION

A lubricant is a substance used to reduce friction and wear between two moving surfaces. It provides a protective film which allows two touching surfaces to be separated and smoothed so that they are able to pass each other with as little friction as possible.

Lubrication, in its many forms has been used throughout human history. However, widespread use of industrial lubricants including metalworking fluids (MWF), which are used in the fabrication of metal parts, was initiated along with automobile and aircraft manufacturing in the beginning of the 1900s. Mineral oils and mixtures of water and soap had been used for lubrication already since the mid-1800s, but the first mineral oil containing, water-miscible MWFs came onto the market in the early 1900's. They were subsequently accompanied with semi-synthetic and modern synthetic MWFs by the 1950s (McCoy 1994). Since then, the need for more technically appropriate and safe products has led to the development of MWF formulations with a wide variety of additives to provide the best performance in various applications.

Since the mid-1900s, a multitude of investigations have addressed the adverse skin and respiratory effects of water-miscible MWF (Pryce et al. 1989; NIOSH 1998; Geier and Lessmann 2006). Occupational contact dermatoses of machinists are common in dermatological units, whereas occupational respiratory diseases in machinists have been diagnosed relatively seldom. This study was conducted to investigate the skin and respiratory ill-health of Finnish machinists caused by chemical exposures at work. The aim was to learn more about the causative factors and to find means to prevent the disorders. The special emphasis was placed on exposure to modern water-miscible metalworking fluids and their harmful effects.
II REVIEW OF THE LITERATURE

2.1. Metalworking fluids

2.1.1. Use

In Finland, there are about 20,000 machinists who fabricate machine parts and other objects according to workshop drawings from metal or other materials with various machining techniques such as turning, milling and grinding (Statistics Finland 2007). In machining, high speed cutting tools are used. The resulting heat, friction and pressure between the work piece and the tool can lead to welding and deformation of the work piece as well as reduced tool life, and therefore cooling and lubrication is needed. These are provided by metalworking fluids (MWF), which also carry away the chips formed, and protect the cut surfaces from corrosion. MWFs are either supplied manually, or circulated in one machine or in several machines connected to a centralized fluid system. The circulating MWF is sprayed or flowed to the cutting zone via a nozzle or through the tool edge, after which it is usually collected and led to a container, and re-used after filtering, skimming or other cleaning systems (NIOSH 1998). Control measures such as follow-up of concentration, pH and oil level are taken to observe the performance and quality of MWF. Water, MWF concentrate or other chemicals such as antimicrobial agents or defoamers may be added to the fluid while they are used. The fluid containers and the machines are cleaned and re-charged typically once or twice a year, or according to the recommendations of the MWF supplier. During the machining process, MWFs are splashed, evaporated and sprayed to the surroundings. Despite increased automation, machining still requires the close presence of an operator,
II REVIEW OF THE LITERATURE

and a lot of work done by hand, such as the handling of work-pieces and machine tools, and maintaining and servicing the machines. Consequently, the machinists’ skin and respiratory tract frequently come into contact with MWFs.

According to the head association of European lubricant manufacturers (Europalub), the annual domestic market of MWF in the European Union was about 270,000 tons in 2005. In Finland, there are no specific figures on MWFs, but according to the statistics of Europalub, the estimated overall market of metalworking oils including quenching oils and corrosion prevention oils was 4700 tons in 2005, of which, the majority were MWFs.

2.1.2. Classification

Metalworking fluids, also called e.g. cutting fluids, coolant oils, cutting oils or metal removal fluids, can be divided into four main categories according to their chemical composition and use (NIOSH 1998; Bartels et al. 2008).

1) Neat oils, also called straight oils, are used as such without dilution to water. The main component of neat oils is mineral oil derived from petroleum oil (Table 1). Other lubricant bases are animal, vegetable or synthetic oils: these may also be used in combinations with mineral oil. The main additives used in neat oils consist of viscosity index improvers, extreme pressure additives, antioxidants, anti-welding agents, surface wetting agents and corrosion inhibitors. As there is no water, antimicrobial agents or emulsifiers are not needed. Neat oils are typically used for slow-speed machining and more easily cut materials for which lubrication is more important than cooling, and when a high flow rate of the fluid is not needed.

2) Emulsifiable oil MWFs, or soluble oils, are supplied as concentrates that are mixed with water to form usually a 2–10% emulsion. Soluble oils contain 30%–85% mineral oil (Table 1). Other lubricants, such as vegetable oils or fatty acids, may be combined with mineral oils. The rest of soluble oils consist of emulsifiers, corrosion inhibitors,
antimicrobial agents, extreme pressure additives, pH adjusters and a wide variety of other additives to provide the best properties in various applications.

3) Semi-synthetic MWFs are also water-miscible concentrates. They contain up to 30% mineral oil or other lubricant oil, and they may also contain synthetic lubricating components such as hydrocarbons, esters, polyglycols, etc. The additives are largely similar to those in emulsifiable oil MWFs. The cooling and flow properties are better while the lubricating ability is poorer than in the soluble oils.

4) Synthetic MWFs are water-miscible concentrates that contain no mineral oil. They usually form a clear or opalescent solution rather than an emulsion. Synthetic MWFs contain synthetic lubricating component and various organic and inorganic salts in water. Synthetic MWFs provide good cooling and a large flow volume, and are used mainly for grinding and high-speed cutting.

According to the Europalub, neat oils formed about 60% of the market in the European Union in 2005, and the rest was composed of the three types of water-miscible MWF, supplied as concentrates.

2.1.3. Additives

All MWFs, but especially water-miscible MWFs (emulsifiable oil, semi-synthetic and synthetic MWFs) contain varying amounts of additives that represent a wide range of organic and inorganic compounds, many of which have several functions in the fluid (NIOSH 1998; Bartels et al. 2008). The additives of water-miscible MWFs are generally used in 1–35% concentration each, and the fluids typically contain up to 40% of additives in total. Some additives are available on the market as ready-made mixtures. Certain additives, such as antimicrobial agents or anti-foaming agents, may be available at workplaces as separate products that are added to MWF emulsions during their use. The components and their amounts in the four classes of MWF concentrates are outlined in Table 1.
Table 1. Components of metalworking fluids (adopted from (Childers 1994) (NIOSH 1998) and (Bartels et al., 2008)).

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
<th>Neat oils</th>
<th>Emulsifiable oil MWF</th>
<th>Semi-synthetic MWF</th>
<th>Synthetic MWF</th>
<th>Examples of chemical agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Acts as coolant, solvent and diluent</td>
<td>–</td>
<td>Usually more than 80% in diluted MWF</td>
<td>Usually more than 90% in diluted MWF</td>
<td>Usually more than 90% in diluted MWF</td>
<td>Naphthenic or paraffinic mineral oil, lard oil, rapeseed oil</td>
</tr>
<tr>
<td>Petroleum, vegetable or animal oil</td>
<td>Lubricates</td>
<td>60–100%</td>
<td>30–85%</td>
<td>5–30%</td>
<td>–</td>
<td>Glycol ethers and esters, polyglycols, fatty acids</td>
</tr>
<tr>
<td>Synthetic lubricant</td>
<td>Lubricates</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>5–30%</td>
<td>Fatty acid soaps, fatty acid alkanolamides, petroleum sulfonates</td>
</tr>
<tr>
<td>Emulsifier, surface active agent</td>
<td>Emulsifies, forms a stable emulsion with water</td>
<td>–</td>
<td>5–20%</td>
<td>5–10%</td>
<td>5–10%</td>
<td>Zinc dialkyl-dithiophosphates, chlorinated or sulfurized hydrocarbons</td>
</tr>
<tr>
<td>Extreme pressure additive</td>
<td>Improves pressure durability of the lubricant film</td>
<td>0–40%</td>
<td>0–20%</td>
<td>0–10%</td>
<td>0–10%</td>
<td>Fatty acid alkanolamides and other fatty acid derivatives, alkanolamine borates</td>
</tr>
<tr>
<td>Corrosion inhibitor</td>
<td>Prevents rusting</td>
<td>0–10%</td>
<td>3–10%</td>
<td>10–20%</td>
<td>10–20%</td>
<td>Alcoxylated alcohols and phenols</td>
</tr>
<tr>
<td>Surface wetting agent</td>
<td>Improves coverage of the metal surfaces for lubrication</td>
<td>0–10%</td>
<td>5–20%</td>
<td>10–20%</td>
<td>10–20%</td>
<td>Chlorinated or sulfurized paraffin</td>
</tr>
<tr>
<td>Anti-welding agent</td>
<td>Prevent welding</td>
<td>0–20%</td>
<td>0–20%</td>
<td>0–10%</td>
<td>0–10%</td>
<td>Fatty acids, glycol ethers</td>
</tr>
<tr>
<td>Coupling agent</td>
<td>Stabilizes the emulsion</td>
<td>–</td>
<td>1–3%</td>
<td>1–3%</td>
<td>1–3%</td>
<td></td>
</tr>
</tbody>
</table>

continues...
Table 1. continues...

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
<th>Neat oils</th>
<th>Emulsifiable oil MWF</th>
<th>Semi-synthetic MWF</th>
<th>Synthetic MWF</th>
<th>Examples of chemical agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH adjuster</td>
<td>Acts as buffer control and stabilizes pH</td>
<td>–</td>
<td>2–5%</td>
<td>2–5%</td>
<td>2–5%</td>
<td>Alkanolamines, alkali hydroxides</td>
</tr>
<tr>
<td>Chelating agent</td>
<td>Stabilizes, binds free metal ions in the fluid</td>
<td>–</td>
<td>0–1%</td>
<td>0–1%</td>
<td>0–1%</td>
<td>Ethylenediamine tetra-acetic acid (EDTA)</td>
</tr>
<tr>
<td>Antimicrobial agent</td>
<td>Prevents bacterial and fungal growth, preserves</td>
<td>–</td>
<td>0–2%</td>
<td>0–2%</td>
<td>0–2%</td>
<td>Formaldehyde liberators, isothiazolinones</td>
</tr>
<tr>
<td>Antifoam agent</td>
<td>Prevents foam formation</td>
<td>0–500 ppm</td>
<td>0–500 ppm</td>
<td>0–500 ppm</td>
<td>0–500 ppm</td>
<td>Silicon oils, waxes</td>
</tr>
<tr>
<td>Dye</td>
<td>Dyes, leak detection</td>
<td>*</td>
<td>0–500 ppm</td>
<td>0–500 ppm</td>
<td>0–500 ppm</td>
<td>Azo-dyes</td>
</tr>
<tr>
<td>Viscosity index improver</td>
<td>Maintains viscosity</td>
<td>*</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Polyolefins</td>
</tr>
<tr>
<td>Detergent</td>
<td>Prevents deposit formation and improves phase mixing</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Fatty acid soaps</td>
</tr>
<tr>
<td>Plasticizer</td>
<td>Reduces tackiness</td>
<td>–</td>
<td>*</td>
<td>–</td>
<td>–</td>
<td>Polymeric ethers</td>
</tr>
<tr>
<td>Anti-mist agent</td>
<td>Reduces misting</td>
<td>*</td>
<td>*</td>
<td>–</td>
<td>–</td>
<td>Acrylate copolymers</td>
</tr>
<tr>
<td>Odorant</td>
<td>Masks odour</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Pine oil, limonene</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>Prevents oxidation of the lubricant oil</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>–</td>
<td>Aromatic amines</td>
</tr>
</tbody>
</table>

* usually present in the MWF class
2.1.4. Contaminants

Water-miscible MWFs provide an excellent growing medium for bacteria and fungi. The microbial species in MWFs are largely the same as those in natural water systems (Veillette et al. 2004). However, the species may vary depending on the antimicrobial agents used, pH, temperature and other changes in the fluid (Virji et al. 2000; Veillette et al. 2004). The most common bacterial genus has been the gram-negative species *Pseudomonas* (Thorne and DeKoster 1996a; Woskie et al. 1996a), although other species have also been identified (Linnainmaa et al. 2003; Woskie et al. 2003). Also mycobacteria and fungi (Laitinen et al. 1999; Veillette et al. 2004) have been reported to contaminate MWFs. In addition to microbes themselves, endotoxins, i.e., lipopolysaccharide-protein complexes in the cell wall of gram-negative bacteria, are commonly found in MWFs (Thorne and DeKoster 1996a; Linnainmaa et al. 2003; Gordon 2004). Endotoxins appear in the fluid mainly as a result of the death or injury of the bacterial cell, and thus they remain in the bulk fluid even if antimicrobial agents are added (Laitinen et al. 1999).

MWFs become contaminated also with the leaking machine lubricants, often referred to as tramp oils, and other lubricants such as protective oils on metal surfaces. Other contaminants include chemicals from preceding, following and surrounding processes, machine cleaners and various solid contaminants (NIOSH 1998). In addition, cutting tools and fabricated metals such as alloyed steel and hard metal may release soluble metal ions, e.g. those of nickel, chromium and cobalt, into the fluid (Einarsson et al. 1975; Einarsson et al. 1979; Sjogren et al. 1980).

2.1.5. Skin exposure

The need for quantification of skin exposure to MWF and to its harmful components such as alkanolamines has been emphasized (NIOSH 1998; Woskie et al. 2003), but the reports are few. The reported studies have utilized surrogate skin methods (Sprince et al. 1996; Roff et al. 2004; van Wendel de Joode et al. 2005), trace chemical methods (van Wendel de Joode et al. 2005) and observational methods (Wassenius et al. 1998; van Wendel de Joode et al. 2005), whereas use of hand wiping or rinsing methods has been suggested as another possible means for quantifying exposure to MWF (Roff et al. 2004).
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In the study by Roff and co-workers (Roff et al. 2004), surrogate skin materials were analysed for boron or mineral oil hydrocarbons. Boron was used as a marker of water-miscible MWFs and mineral oil hydrocarbons as markers of neat oils. The median surface loading rate of total extractable MWF was 62 μg/m²/h in over-suits, and 2900 μg/m²/h in gloves worn inside protective gloves. This finding supports the general idea that the hands are the most heavily exposed skin area of machinists, even when protective gloves are used. The most exposed other body parts were the left leg and middle body. Based on visual observations, the authors suggested that this was due to the fact that the workers frequently wiped their soaked hands on their legs.

In the Netherlands, three different skin exposure assessment methods were used in a cross-sectional study on dermatitis (van Wendel de Joode et al. 2005). The purpose was to compare the methods in their ability to group workers according to their skin exposure. One of the methods was a surrogate skin method, one was a trace chemical method employing video imaging called VITAE (video imaging technique for assessing dermal exposure) and one was a semi-quantitative method consisting of visual observation and an interview performed by an occupational hygienist, i.e., DREAM (dermal exposure assessment method). The surrogate skin method was found to detect differences in skin exposure poorly, while the DREAM was found to work best. The VITAE method was considered to be fairly expensive, and another limitation is that addition of trace chemicals to MWFs is not always possible (van Wendel de Joode et al. 2005).

In a North-American epidemiological study (Sprince et al. 1996), no association was seen between dermatitis and skin exposure measured from patches attached to the mid-forearm of the machinists. This is possibly due to the non-typical location of the patch, as well as the limitations of the method: the surrogate skin techniques are generally thought to overestimate true exposure as the patches or other dosimeters may absorb more MWF than normal skin, and they may also become saturated with MWF (van Wendel de Joode et al. 2007).

Ordinary video-recording has been used to estimate overall exposure time and to identify risk phases in machining (Wassenius et al. 1998). According to the study by Wassenius and his co-workers, skin exposure, i.e. "wet time" of the skin, varied considerably among machinists, the relative wet time ranging from 0–100%.
2.1.6. Respiratory exposure

Methodology

A traditional method for assessing exposure to MWF is collection of oil mist on a filter followed by solvent extraction and infra red (IR) analysis as described in the NIOSH 5026 method (NIOSH 1996). The method is applicable especially for neat oils and for estimating the oil component in emulsifiable or semi-synthetic MWF, but it is not suitable for assessing exposure to all classes of water-miscible MWF. In the USA, NIOSH has recommended inhalable thoracic particulates, quantified by gravimetric analysis, as the measure of MWF exposure (NIOSH Method 0500) (NIOSH 1998). As NIOSH 0500 measures also particulates from other sources than MWF, more specific methods have been proposed. The ASTM method P-42-97 includes filter collection, gravimetric analysis and extraction with a ternary solvent blend. In the NIOSH 5524 method, an additional binary blend of methanol and water is used to enhance the removal of water-soluble components (NIOSH 2003). Also supercritical fluid extraction has been used for removal of MWF from filters (Brudin et al. 2006). Other methods include e.g. measurement of boron or potassium (HSE 2003) or ethanolamines (NIOSH 1994) as markers of MWF. Exposure to MWF has been assessed also with real-time aerosol photometers that collect all particles up to 10 μm in diameter, and give an estimate of short-time exposures to total aerosols (Sprince et al. 1997; O’Brien et al. 2001).

Microbial contaminants in machine shops have been assessed by measuring viable and total bacteria, fungi, and endotoxins in the air. For viable microbes, e.g. Andersen-impactors (Woskie et al. 1996; Laitinen et al. 1999) have been used followed by incubation and counting of colony forming units (CFU). Total bacteria have been collected on filters and counted by light microscopy after staining (Sprince et al. 1997; Abrams et al. 2000). Endotoxins can be monitored separately or together with other air contaminants from filters and quantified using enzyme based assays (Thorne and DeKoster 1996a; Sprince et al. 1997; Abrams et al. 2000; Linnainmaa et al. 2003). Similar analytical methods are used for quantifying microbial contaminants in bulk MWF.
Workplace measurements

Assessment of exposure to MWF has commonly included assessment of total or thoracic particulate mass or extractable oil mist collected on filters, and of microbial contaminants. Since the mid-1990s, total particulate mass concentrations have usually been small compared to occupational exposure limits (OEL), the mean concentration being below 1 mg/m³ in most reports from large or medium-sized machine shops (Thorne and DeKoster 1996a; Woskie et al. 1996; Greaves et al. 1997; Kriebel et al. 1997; Sprince et al. 1997; Kennedy et al. 1999; Abrams et al. 2000; Oudyk et al. 2003; Ross et al. 2004). However, occasional high concentrations, up to about 10 mg/m³, were reported from small metal companies in USA by Piacitelli et al. (2001). In European studies from the United Kingdom (Simpson 2003) and France (Ameille et al. 1995; Massin et al. 1996), the concentrations of total particulates or extractable oil mist have ranged from 0.65 to 2.2 mg/m³. Some studies have indicated that neat oil operations may produce more aerosols compared to operations using water-miscible MWFs (Woskie et al. 1996; Piacitelli et al. 2001; Simpson et al. 2003), but the findings are not fully consistent (Greaves et al. 1997). Summary of workplace measurements of particulates and microbial contaminants are presented in Table 2.
Table 2. Reported workplace measurements in machine shops with assessment of total or thoracic particulates

| Workplace and departments | Country       | Mean mass concentration of total or thoracic particulates or extractable mass (mg/m³)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Concentration of bacteria and endotoxins in the air (units/m³)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 machine shops</td>
<td>Canada</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 machine shops</td>
<td>UK</td>
<td>Mineral oil operations: 1.1 (0.060–4.4) Water-miscible MWF operations: 0.67 (0.04–23) 1.2 (extractable oil mist) 0.35 (&lt;0.01–13) (MWF mist)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A large automotive machining factory</td>
<td>Canada</td>
<td>0.02–0.84</td>
</tr>
<tr>
<td>79 small machine shops</td>
<td>USA</td>
<td>0.050–10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.010–6.8 (extractable mass)</td>
</tr>
<tr>
<td>23 small machine shops</td>
<td>USA</td>
<td>0.040–1.8</td>
</tr>
<tr>
<td>Automotive transmission factory (two machining and one assembly department)</td>
<td>USA</td>
<td>Valve body department: 0.32 Case department: 0.56 Assembly department: 0.13</td>
</tr>
<tr>
<td>13 machine shops</td>
<td>Canada</td>
<td>0.46</td>
</tr>
<tr>
<td>General Motors factories</td>
<td>USA</td>
<td>Neat MWF operations: 0.43 ± 0.26 Soluble oil MWF operations: 0.55 ± 0.17 Synthetic MWF operations 0.41 ± 0.08</td>
</tr>
</tbody>
</table>

continues...
<table>
<thead>
<tr>
<th>Workplace and departments</th>
<th>Country</th>
<th>Mean mass concentration of total or thoracic particulates or extractable mass (mg/m³)¹</th>
<th>Concentration of bacteria and endotoxins in the air (units/m³)¹</th>
<th>Comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large automobile transmission factory (machining and assembly departments)</td>
<td>USA</td>
<td>Median: Machinists: 0.33 (0.040–1.4) Asssemblers: 0.08 (0.020–0.20)</td>
<td>Endotoxins: Machinists: 31 (2.7–980) EU Assemblers: 3.1 (2.5–3.5) EU Bacteria: Machinists: 17 200 (740–150 000) CFU Assemblers: 320 (44–1800) CFU</td>
<td>In connection with a cross-sectional study</td>
<td>Sprince et al. 1997</td>
</tr>
<tr>
<td>Large automobile parts factory</td>
<td>USA</td>
<td>Median: Neat oil operations: 0.240 Soluble oil operations 0.22</td>
<td>Bacteria: Neat oil operations: 120 CFU Soluble oil MWF operations: 750 CFU Endotoxins: Neat oil operations: 13 EU Soluble oil MWF operations: 16 EU</td>
<td>In connection with a cross-sectional study</td>
<td>Woskie et al. 1996 Kriebel et al. 1997</td>
</tr>
<tr>
<td>Large engine factory (old line, new line and assembly)</td>
<td>USA</td>
<td>Old line: 1.2 New line: 0.74</td>
<td>Endotoxins: &lt;4–790 EU Bacteria: 81–550 CFU</td>
<td>- Large temporal variation in microbes - Correlation between endotoxins in MWF and air - Positive correlation between bacteria in bulk MWF and endotoxins in the air - Formaldehyde mean concentration: 0.22 mg/m³</td>
<td>Thorne and DeKoster 1996a</td>
</tr>
<tr>
<td>Ball bearings factory</td>
<td>France</td>
<td>0.65 – 2.2 (extractable oil mist)</td>
<td>NM</td>
<td>Samples collected in the factory over several years</td>
<td>Massin et al. 1996</td>
</tr>
<tr>
<td>Engine factory</td>
<td>France</td>
<td>2.6 ± 1.8 (extractable oil mist)</td>
<td>NM</td>
<td>In connection with a cross-sectional study</td>
<td>Ameille et al. 1995</td>
</tr>
<tr>
<td>Three transport manufacturing factories</td>
<td>USA</td>
<td>Neat oil operations: 0.85 Soluble oil MWF operations: 0.77 Synthetic MWF operations: 0.64</td>
<td>NM</td>
<td>In connection with a cross-sectional study</td>
<td>Woskie 1994</td>
</tr>
</tbody>
</table>

¹ Arithmetic mean if not otherwise indicated; NM = not measured; EU = endotoxin units (1 EU = 0.1 ng); CFU = colony forming unit
Several studies have shown that the microbial quality of the workplace air is dependent on the quality of the bulk MWF and there are great temporal variations in the microbial condition of the MWF in use (Thorne and DeKoster 1996a; Laitinen et al. 1999; Virji et al. 2000; Veillette et al. 2004). Therefore, short-term air measurements may represent exposure to microbial components poorly. Although the bacteria die, endotoxins remain in the fluid even when antimicrobial agents are used, and they have thus been proposed to indicate the microbial quality of bulk MWF better than microbes themselves (Linnainmaa et al. 2003). In some studies, airborne endotoxins have been found to be good indicators of respiratory exposure to microbial contaminants or total aerosols of MWF (Thorne and DeKoster 1996a; Laitinen et al. 1999; Abrams et al. 2000). In addition to careful maintenance of MWF, e.g. local ventilation systems, machine enclosures and increasing the workers' distance from the machine have been suggested as means to control exposure to microbial components (Virji et al. 2000; Linnainmaa et al. 2003; Simpson et al. 2003).

The need to assess certain harmful ingredients of MWF has been emphasized (Woskie et al. 2003; Gordon 2004) but so far, specific MWF ingredients in machining operations have seldom been reported. In one study from the USA, alkanolamines were analysed from particulate mass filter samples; monoethanolamine (MEA) or diethanolamine (DEA) were not detected, while triethanolamine (TEA) was discovered around large multiple operation machines in concentrations up to 0.244 mg/m$^3$ (Kenyon E. et al. 1993). TEA was quantified from particulate mass filters also in a Swedish study in concentrations ranging from 0.002 to 0.036 mg/m$^3$ (Lillienberg et al. 2008). Neither of these methods discovered MEA or DEA, probably because of their volatility and subsequent escape from the filter. Formaldehyde originating from formaldehyde-releasing antimicrobials has been assessed in some studies in mean concentrations varying generally from 0.003 mg/m$^3$ to 0.05 mg/m$^3$ (Cohen 1996; Thorne and DeKoster 1996a; Linnainmaa et al. 2003; Godderis et al. 2008; Lillienberg et al. 2008). The recent study by Lillienberg et al. (2008) reported a fairly high concentration, 0.13 mg/m$^3$, in one of the three assessed machining companies. The respective company used recirculation of air, which suggests that formaldehyde may become concentrated in machine shops air as it passes through the
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oil mist separators. Relatively high concentrations, up to 0.22 mg/m³ have been reported in two North American studies from the 1990’s (Cohen 1996; Thorne and DeKoster 1996a). The results might be due to somewhat poorer hygienic conditions in the respective plants at that time and also due to heavy use of formaldehyde liberators. The concentration of fatty acid components nonanic and neodecanic acid was 0.1–0.2 mg/m³ in machine shops according to White and Lucke (White and Lucke 2003). The loss of volatile compounds from oil mist filters has been assessed (Simpson 2003), but there are very few field reports of ambient volatile compounds in machine shops. The recent studies from Sweden (Lillienberg et al. 2008) and The Netherlands (Godderis et al. 2008) attempted to measure several MWF-borne contaminants. In the Swedish study, volatile compounds were found in two companies out of three, the mean total concentrations being 6.25 and 1.79 mg/m³, respectively. In the Dutch study, vapours of MWF were detected in two out of six departments, the total concentrations being 4.1 and 5.1 mg/m³; in some departments, solvents such as tetrachloroethylene and higher alkanes could be identified but not quantified.

2.1.7. Occupational exposure limits

The most commonly used OEL values in metalworking processes in Finland and in many other industrialized countries are those for oil mist, and for particulate mass such as inhalable dust or thoracic mass collected on filters. In Finland, the 8h OEL for extractable oil mist is 5 mg/m³, and for inorganic and organic dust 10 mg/m³ and 5 mg/m³, respectively (Sosiaali- ja terveysministeriö 2007). Other relevant exposures, for which Finnish OELs have been established, include alkanolamines (MEA; DEA and TEA) and formaldehyde. There are no official OELs for total volatile organic compounds (VOC), bacteria and fungi, and endotoxins in Finland, but recommended exposure limits based on either measurement data or foreign OELs are used. For the total VOC, the recommended limit for good industrial air is 5 mg/m³ (Niemelä et al. 1997). The 8h OELs for aliphatic (20 ppm; 72 mg/m³) or cyclic (100 ppm; 350 mg/m³) hydrocarbons can be applied as well, but the respective OELs are very high and therefore not useful in MWF operations. A reference value of 500 CFU/m³ is considered to indicate a microbial
source in homes and offices (Reponen et al. 1992; Sosiaali- ja terveysministeriö 2003). For industrial workplaces such a concentration is thought acceptable, but instead, atypical species may indicate a microbiological hazard. For endotoxins, a Dutch threshold limit value of 200 EU/m³ has been used in industrial and agricultural workplaces. Table 3 lists the most relevant chemical exposures in machine shops and their OELs in Finland and in some other countries.

Table 3. Current occupational exposure limits (OEL) or recommended exposure limits (REL) of selected chemical and microbial components of MWF, representing 8 h exposure.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Finnish OEL</th>
<th>North American OEL</th>
<th>European OEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil mist (extractable)</td>
<td>5 mg/m³</td>
<td>5 mg/m³ (OSHA, ACGIH)</td>
<td>1 mg/m³ (water-miscible MWF aerosol, Germany)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2 mg/m³ (REL, ACGIH)</td>
<td>5 mg/m³ (mineral oil MAK, Germany)</td>
</tr>
<tr>
<td>Inhalable dust or total</td>
<td>5 mg/m³</td>
<td>0.4 mg/m³ (thoracic particulate mass; NIOSH)</td>
<td>5 mg/m³ (respirable dust, UK)</td>
</tr>
<tr>
<td>particulates</td>
<td>(organic dust)</td>
<td>0.5 mg/m³ (total particulate mass; NIOSH)</td>
<td>10 mg/m³ (inhalable dust, UK)</td>
</tr>
<tr>
<td></td>
<td>10 mg/m³</td>
<td>5 mg/m³ (respirable dust, UK)</td>
<td></td>
</tr>
<tr>
<td>(inorganic dust)</td>
<td></td>
<td>10 mg/m³ (inhalable dust, UK)</td>
<td></td>
</tr>
<tr>
<td>MEA</td>
<td>2.5 mg/m³</td>
<td>8 mg/m³ (NIOSH)</td>
<td>2.5 mg/m³ (HSE, UK)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 mg/m³ (ACGIH)</td>
<td></td>
</tr>
<tr>
<td>DEA</td>
<td>2 mg/m³</td>
<td>15 mg/m³ (NIOSH)</td>
<td>2.5 mg/m³ (HSE, UK)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 mg/m³ (ACGIH)</td>
<td></td>
</tr>
<tr>
<td>TEA</td>
<td>5 mg/m³</td>
<td>5 mg/mm³ (ACGIH)</td>
<td>5 mg/m³ (Sweden)</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>0.37 mg/m³</td>
<td>0.016 ppm (NIOSH)</td>
<td>2.5 mg/m³ (HSE, UK)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.37 mg/m³ (ceiling value, ACGIH)</td>
<td></td>
</tr>
</tbody>
</table>

OSHA = Occupational Safety and Health Administration; ACGIC = American Conference of Governmental Industrial Hygienists; NIOSH = National Institute for Occupational Safety and Health; MAK = Maximale Arbeitsplatz Konzentration (maximum workplace concentration, Germany); HSE = Health and Safety Executive; UK = United Kingdom; MEA = monoethanolamine; DEA = diethanolamine; TEA = triethanolamine
2.2. Health effects associated with metalworking fluids

2.2.1. Dermatitis

2.2.1.1. Definitions

_Contact dermatitis_ is an eczematous skin reaction caused by direct and usually repeated contact of skin with harmful objects or chemicals (ESCD 2008). Occupational contact dermatitis (OCD) is contact dermatitis caused predominantly by exposures at work: it most often manifests as eczema of the hands. The most important types of OCD are irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD) (Diepgen and Coenraads 2000), and contact urticaria (CU).

_Irritant contact dermatitis_ is a non-immunologic local inflammatory reaction of the skin following single or repeated contact with a chemical substance or another irritant factor. Contactants are e.g., detergents and surfactants, acid and alkaline solutions, organic solvents, sometimes even water. Diagnostic tests have not been developed, and the diagnosis is clinical, arrived at by exclusion of other possible skin manifestations (ESCD 2008).

_Allergic contact dermatitis_ is a delayed-type immunological reaction resulting in an eczematous skin reaction in response to contact with an allergen in sensitized individuals. ACD arises as a result of two essential stages: an _induction phase_, which primes and sensitizes the immune system for an allergic response, and an _elicitation phase_, in which this response is triggered. The allergy-inducting agents or antigens are low-molecular weight organic compounds, ionized metals etc. Contact allergy is demonstrated through patch testing by a dermatologist, in which small amounts of suspected allergens are applied with an adhesive tape on the skin of the back for 48 hours. A positive test shows up as a miniature eczema during the following few days (ESCD 2008).

_Contact urticaria_ deviates from regular contact dermatitis in the type of clinical reaction, its time sequence, the causal agents, and the pathogenetic mechanism. The clinical reaction appears on the site of direct contact, usually the fingers, and it consists of small, itching wheals, emerging within 10–20 minutes after contact and rapidly disappear-
ing. Pertinent allergens are high-molecular, complete antigens such as proteins in natural rubber latex or food stuffs. Pathogenetically, this is a type 1 allergy based on specific IgE antibodies, and the patients usually have an atopic constitution (ESCD 2008).

*Atopic dermatitis* is caused by endogenous and not by external factors. It is a common chronic skin disease that mainly affects children and young adults, although in a considerable number of these persons the disease itself or the vulnerability of the skin persists into adult life. Other atopic diseases such as allergic rhinitis and atopic asthma are common in the patients. The range of clinical manifestations in both skin and mucosa is wide (Hanifin and Rajka 1980; Lammintausta *et al.* 1991).

### 2.2.1.2. Occurrence

**Skin symptoms and dermatoses**

In cross-sectional studies, the point or period prevalence of dermatitis in machinists and related workers has varied, depending on the screening methodology as well as on the disease and occupational definition (Smit *et al.* 1992). Hand dermatitis (HD) during the past year was reported by 7.4% of the engineering workers in an industrialized city in Sweden according to a mailed questionnaire (Meding and Swanbeck 1990). A questionnaire and clinical study of dermatoses in a Swedish metalworking plant was conducted because of frequent skin complaints: as many as 56% of all workers (metal workers and other workers) reported having suffered from "skin problems" at some point during their employment (Gruvberger *et al.* 2003). Clinical investigations including patch testing were performed to those with suspected work-related skin disease, and according to them, about 17% of the metal workers were found to have a work-related contact dermatitis on their hands or lower arms, representing about 7% of all metal workers in the plant.

In a recent Dutch evaluation of skin questionnaires, the prevalence of HD during the past 12 months was about 20% in machinists, and it was somewhat higher when based on symptoms as compared to a skin screening list that comprised pictures of dermatitis in the order of increasing severity (van Wendel de Joode *et al.* 2007). The screening list was suggested to be a better means for discovering severe dermatitis,
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and useful especially in investigations, where the workers are not seen by a dermatologist.

In two older studies, about 11% of the workers in the metal industry had HD in dermatological examination (Coenraads et al. 1983), whereas 27% of machinists in 10 metalworking factories had "major skin changes", as examined by a dermatologist (de Boer et al. 1989). In the latter study, hand eczema was associated with water-miscible MWF rather than with neat oils. About 19% of Italian metalworkers had "minor" and 7% had "major skin disorders" according to a dermatological examination, and the overall prevalence of skin lesions was about three-fold compared to office worker controls (Papa et al. 2000). Sprince and her co-workers reported about 13% prevalence of "definite hand dermatitis" and 27% prevalence of "combined (definite or possible) hand dermatitis" in North-American machinists, observed by a dermatologist: the dermatitis was more frequent in the workers who used semi-synthetic MWF than in those who used soluble oil MWFs, and the risk was about two-fold in machinists as compared to assemblers (Sprince et al. 1996).

The above listed studies suggest that up to about one fourth of the machinists or related metal workers may suffer from mild dermatoses, but that the prevalence of more serious skin disorders is generally around or below 10%. It is also possible that the workers with severe dermatitis have transferred to other jobs and have therefore not been discovered. In some general validation studies of skin questionnaires, self-report has been thought to underestimate the true prevalence of hand eczema (Smit et al. 1992; Meding and Barregard 2001). On the other hand, detailed clinical evaluations and reported sick leaves in some studies suggest that most of the skin problems discovered in cross-sectional questionnaire studies are mild (de Boer et al. 1989; Funke et al. 2001; van Wendel de Joode et al. 2007).

**Occupational skin diseases**

In European studies based on morbidity registers, the incidence of occupational skin disease (OSD), in machinists or related metal workers has varied between 0.46 to 3.8 cases per 1000 person years in the during 1990s and up to the present. Dickel and his co-workers reported an OSD incidence of 0.46 in metal processors during 1999–2001 in
Saarland (Dickel \textit{et al.} 2002) and an OSD incidence of 0.9 in machinists during 1990–1999 in North Bavaria (Dickel \textit{et al.} 2001). The studies were based on the official register of occupational skin diseases in the respective federal states in Germany. Most of the reported OSDs were contact dermatoses affecting the hands. An annual incidence of OCD in the metal and automotive product manufacturing industry, on the other hand, was estimated to be about 3.8 in the United Kingdom during 1996–2001 (McDonald \textit{et al.} 2006). The relatively high incidence of OCD in the United Kingdom may be due to the reporting system: the case definition appears to be less strict than in the German registers, and the majority of the notifications are done by occupational physicians and not by dermatologists. In a Danish study, incidences were not calculated, but machinists ranked among the commonest occupations diagnosed with occupational hand eczema in the beginning of the 2000s in the register of all notified and recognised occupational diseases in the country (Skoet \textit{et al.} 2004).

A high cumulative incidence of HD has been shown in prospective studies of metalworker trainees. In a German study, a three-year cumulative incidence of 15\% was found in apprentices including 58\% machinists, 33\% other blue collar workers and 9\% office workers in the automobile industry (Funke \textit{et al.} 2001). A later follow-up study of the same subjects revealed that the HD persisted after the end of apprenticeship in 40\% of those who had had it during the first study, and that 18\% of the originally non-symptomatic subjects had developed HD after the apprenticeship. The overall annual incidence of 28.2 cases per 1000 workers was calculated (Apfelbacher \textit{et al.} 2008). In a Swiss study, the six-month cumulative incidence of HD in metal worker trainees was 9\%, whereas the 2.5-year cumulative incidence was 23\% (Berndt \textit{et al.} 1999). In a study from Singapore, about half of 24 new machinists had HD after the follow-up period of 6 months (Goh and Gan 1994). Some of the HD in these studies might be atopic dermatitis worsened by irritants in metalwork. Nevertheless, the noticeable discrepancy between the follow-up studies and register studies suggest that some cases of OSD may be missed from the statistics due to the healthy worker effect, where the persons with symptoms change the work and thereby never get diagnosed with OSD.
According to the various epidemiological data, irritant contact dermatitis (ICD) is more common than allergic contact dermatitis (ACD), constituting about 60–90% of the cases of occupational contact dermatitis in machinists (de Boer et al. 1989; Pryce et al. 1989; Dickel et al. 2002; Diepgen 2003). It has been widely acknowledged that atopic dermatitis is a risk factor for ICD, and that ICD often develops in the early years of employment in the presence of irritating factors such as those in machining work (Lammintausta and Kalimo 1993; Coenraads and Diepgen 1998; Diepgen and Coenraads 1999; Berndt et al. 2000; Funke et al. 2001). ICD frequently precedes and accompanies ACD, because there is often parallel exposure to both irritants and allergens, and because the compromised skin condition induced by irritants facilitates the access of allergens into the skin (Diepgen and Coenraads 1999).

2.2.1.3. Metalworking fluids as causes of dermatitis

Irritant contact dermatitis

Wet work is suggested as an important cause of ICD in machinists, as well as in many other occupations (Diepgen 2003). However, the MWFs themselves are irritating to skin. The irritancy is thought to result mostly from the alkalinity of the fluids and to the emulsifiers and surface active agents that are able to effectively break down the protective skin barrier (Geier and Lessmann 2006), although also the mineral oil or other hydrocarbon lubricants of MWFs may dissolve the skin barrier and thereby enhance the skin irritation. The irritancy of MWFs has been suggested to increase along with increased water and emulsifier content (de Boer et al. 1989; Sprince et al. 1996), indicating that the order of increasing irritancy would be neat oils < emulsifiable oil MWFs < semi-synthetic MWFs < synthetic MWFs. Based on a study of soluble oil MWFs, there are also differences in irritancy within the different classes of MWF (Huner et al. 1994; Wigger-Alberti et al. 1997). The study by Huner et al. (1994) did not discover the components responsible for the irritancy. However, alkalinity was not the cause as the pHs of the there tested MWFs were very similar.

Other irritating factors in machining include e.g. abrasive or solvent-based hand cleansing agents, industrial detergents, degreasing agents
and solvents, occlusion caused by protective gloves, dirty work, metal particles and mechanical friction (Pryce et al. 1989; Berndt and Elsner 2000; Papa et al. 2000).

**Allergic contact dermatitis**

During the 2000s, formaldehyde, formaldehyde-releasing antimicrobial agents (formaldehyde liberators), alkanolamines, and colophony have ranked as the most common MWF ingredients that cause contact allergy (Geier et al. 2004a; Geier et al. 2004b; Aalto-Korte et al. 2008a), but also a number of other ingredients have been reported to sensitize the skin. Reported positive patch test reactions from formaldehyde liberators include those to 1) oxazolidines such as the mixture of 3,4-dimethyloxazolidine and 3,4,4-trimethyloxazolidine (Bioban CS 1135), 1-aza-3,7-dioxo-5-ethylbicyclo(3,3,0)octane (Bioban CS 1246) (Dahlquist 1984; Camarasa et al. 1993) and N,N-methylene-bis-5-methylloxazolidine (Madan and Beck 2006), 2) morpholines such as the mixture of 4-(2-nitrobutyl)morpholine and 4,4-(2-ethyl-2-nitrotrimethylene) dimorpholine (Bioban P 1487) and N, N-methylenebismorpholine (Dahlquist 1984) and 3) hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (Grotan BK) (Keczkes and Brown 1976). Concomitant reactions to formaldehyde and several formaldehyde liberators, are frequently seen (Gruvberger et al. 1996; Geier et al. 2004a; Herbert and Rietschel 2004; Anderson et al. 2007; Aalto-Korte et al. 2008a). The allergic reactions to formaldehyde liberators are usually due to formaldehyde allergy, but also specific sensitizations to formaldehyde liberators such oxazolidines, hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, benzylhemiformal and hexamethyleneteramine have been reported in machinists (Geier et al. 2004a; Aalto-Korte et al. 2008a).

Other than formaldehyde-releasing antimicrobials reported as contact allergens in machinists include e.g. benzisothiazolinone (Alomar et al. 1985; Gruvberger et al. 2003), octylisothiazolinone (Aalto-Korte et al. 2007), sodium pyrithione (Isaksson 2002), chloroacetamide (Lama et al. 1986), o-phenylphenol (Adams 1981a), and p-chloro-m-xylene (Adams 1981b). Iodopropynyl butylcarbamate (IPBC) (Majoie and van Ginkel 2000) and 1-2-(2,4-dichlorophenyl)-2-(2-propenyl)-1H-imidazol (Imazalil) (Piebenga and van der Walle 2003) are among reported sensitizing fungicides in water-miscible MWF.
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Alkanolamines, namely MEA, DEA and TEA used as corrosion inhibitors and pH adjusters in MWF are frequently reported skin allergens in machinists (Geier et al. 2004a; Geier et al. 2004b; Geier et al. 2006). Also their derivatives such as alkanolamineborates (Bruze et al. 1995) may cause contact allergy. Emulsifiers causing contact allergy include colophony (de Boer et al. 1989; Grattan et al. 1989; Geier et al. 2004b), fatty acid esters (Niklasson 1993) and ethers (Gruvberger et al. 2003; Jensen and Andersen 2003a), coconut DEA (Pinola et al. 1993) and diglykolamine (Geier et al. 2002).

Other allergens include extreme pressure agents such as tricresyl phosphate and zinc-dialkyl-dithiophosphate (Kanerva et al. 2001; Gruvberger et al. 2003) and odorants such as vanillal (Mitchell and Beck 1988) and balsam of Peru (Panconesi et al. 1980; de Boer et al. 1989). Also contact allergy to dissolved metal salts, such as those of nickel, chromium and cobalt, in MWF (Einarsson et al. 1975; Samitz and Katz 1975; Einarsson et al. 1979; Pryce et al. 1989; Papa et al. 2000), dyes suggested as originating from tramp oils (Geier et al. 2003), as well as glyoxal formed in the machining process (Aalto-Korte et al. 2005) have been reported. Contact allergens in neat oils include e.g. cycloaliphatic epoxy resin (Jensen and Andersen 2003b), mercaptobenzothiazole (Aalto-Korte et al. 2008b), epoxide 7 (Rycroft 1980), and stabilized chlorinated paraffin fraction (Scerri and Dalziel 1996).

ACD due to other exposures than MWF are occasionally reported in machinists. Some cases have been caused by components in other lubricants (Aalto-Korte 2000; Aalto-Korte et al. 2008b), and some by contact with barrier creams or emollients (Austad 1982), hand cleansing agents (Papa et al. 2000) and nickel dissolved from tools or work-pieces in direct skin contact (de Boer et al. 1989; Papa et al. 2000). ACD to protective gloves has been reported in various occupations including those related to machining (Skoet et al. 2004; Kuuliala et al. 2007).

2.2.2. Other skin diseases

Other skin diseases in machinists include various traumatic skin ulcers, pigmentation, folliculitis (oil acne) (Gruvberger et al. 2003) and paronychia (de Boer et al. 1989). Paronychia and oil acne are nowadays very rare due to improved hygiene and the diminished use of neat oils during the last couple of decades (Berndt and Elsner 2000).
2.2.3. Respiratory symptoms and asthma

2.2.3.1. Definitions

*Occupational asthma* is a disease characterized by variable air flow limitation and/or hyperresponsiveness and/or inflammation due to causes and conditions attributable to a particular occupational environment and not to stimuli encountered outside the workplace (Bernstein et al. 2006).

*Allergic occupational asthma* appears after a latency period, and it can be 1) caused by most high- molecular-weight and certain low-molecular-weight agents for which an allergic (IgE-mediated) mechanism is shown, or 2) induced by specific occupational substances but the allergenic mechanisms responsible have not been characterized (Bernstein et al. 2006). The principal diagnostic criteria of occupational asthma in Finland follow the international guidelines (Allergy practice forum 1992; Cartier and Malo 1999; Bernstein et al. 2006), and consist briefly of the following: 1) diagnosis of asthma, 2) onset of symptoms after entering the work, and 3) association between symptoms and work. In order to prove the causality between work and the disease, IgE-mediated allergy to an agent at work, and significant work-related changes in peak expiratory flow (PEF) recordings are needed. If one or both of these are lacking, a positive response in a specific bronchial provocation test (BPT) is required.

*Chronic bronchitis*, i.e., chronic inflammation of bronchial mucosa, is characterized by chronic phlegm production and cough lasting for several days at a time during a minimum of three months a year for at least two consecutive years (American Thoracic Society 1962). The diagnosis is usually based on symptoms and exclusion of other possible diseases.

*Allergic alveolitis*, or hypersensitivity pneumonitis, is an immunologically induced inflammation of the alveoli caused by biological dusts. Typical symptoms include cough, wheezing in physical exercise and chest tightness, and these are often accompanied by fever, chills, muscular or articular pain and headache. The symptoms appear usually after the work shift or at night and ease within a couple of days. The diagnostic criteria consist of, for instance, 1) findings of interstitial lung disease by history, physical examination, and pulmonary function testing, 2) a consistent chest radiograph, 3) exposure to a recognized cause of al-
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Allergic alveolitis and 4) demonstrable antibodies to the relevant antigen (Cormier et al. 1999).

Allergic rhinitis is clinically defined as a symptomatic disorder of the nose induced after allergen exposure by an IgE-mediated inflammation. Symptoms of allergic rhinitis include rhinorrhea, nasal obstruction, nasal itching and sneezing which are reversible spontaneously or with treatment (Bousquet et al. 2008).

2.2.3.2. Animal studies

A few attempts have been made to identify the harmful ingredients of MWF in inhalation tests with experimental animals. In mice, pulmonary and sensory irritation, followed by a decrease in respiratory frequency was caused by a synthetic MWF and its components; the main ingredients responsible for the effects were concluded to be fatty acid alkanolamine condensates and triazine antimicrobials (Detwiler-Okabayashi and Schaper 1996). In two similar studies, effects of semi-synthetic and soluble oil MWFs were evaluated: the most irritative components in a semi-synthetic MWF were alkanolamines, potassium soap, sodium sulphonate and the triazine antimicrobial (Krystofiak and Schaper 1996). In a soluble oil MWF, the pulmonary irritation was suggested to be mostly due to sodium sulphonate (Schaper and Detwiler-Okabayashi 1995). Lim and co-workers (Lim et al. 2005a) found that a soluble oil MWF caused respiratory inflammation at a fairly low concentration, while changes in immune cells took place especially in high MWF concentration. The fact that the used MWF did not contain alkanolamines or formaldehyde suggests that the tests did not represent exposure to some of the most typical MWF ingredients. Inhalation toxicity of DEA and TEA was recently investigated in rats; DEA caused laryngeal reversible metaplasia and signs of inflammation at or above 3 mg/m³, and TEA at or above 20 mg/m³ (Gamer et al. 2008).

The microbial changes in used MWF have been suggested to be the major contributors to the adverse pulmonary effects of MWF in animal models (Gordon 2004). Thorne and DeKoster studied the effects of used and unused, undiluted MWF on guinea-pigs, and found that used MWF was consistently more toxic than the unused MWF, causing significant lung inflammation according to the bronchoalveolar lavage
(BAL) test (Thorne and DeKoster 1996b). In another study on rats, the effects of MWF containing endotoxins were assessed: endotoxin-specific IgE increased dose-dependently, and immediate lung inflammation was observed after both acute and subacute exposure (Lim et al. 2005b).

2.2.3.3. Occurrence

Work-related respiratory symptoms

Symptoms of the upper respiratory tract and eyes, and chronic cough have been abundant also in fairly clean industrial environment in a number of plant surveys since the mid-1990s. In France, Ameille et al. (1995) discovered a significantly higher prevalence of chronic cough and/or phlegm in 179 machinists using neat oils as compared to 129 workers not exposed to neat oils, while Massin and his co-workers (Massin et al. 1996) reported an association between machining work and chronic cough, bronchitis-like symptoms, dyspnoea and bronchial hyper-responsiveness in a study of 114 machinists and 55 factory worker controls: the OR for chronic cough and phlegm was 4.6 and statistically significant as compared to the factory workers. However, the OR had not been adjusted for smoking and age. The study also suggested dose-dependent associations between cumulative exposure to MWF and dyspnoea, airway hyper-responsiveness and pulmonary function. The cumulative exposure was calculated from 92 measurements over altogether 14 years. While the measurements may actually represent cumulative exposure well enough, this is not a common approach, and the results are therefore not comparable to other dose-response studies. In a recent study from an aluminium fabrication plant in Belgium, upper respiratory tract symptoms, but not changes in pulmonary function, were found (Godderis et al. 2008). A very high prevalence of self-reported sinus irritation in both machinists (46%) and non-machinists (38%) was reported in a large North-American automobile plant by Kriebel and his co-workers (Kriebel et al. 1997). In the same study, self-reported chronic cough was significantly more prevalent in machinists than in non-machinists, and it was especially associated with the use of neat oils. The results are hampered by the fact that the non-machining control
group was not uniform, i.e., it consisted of assemblers who might be exposed to MWF and of subjects from a separate training centre of the plant; however, there was no description of the possible exposures of the subjects from the training centre.

Greaves and co-workers reported a spectrum of respiratory symptoms in a large questionnaire study with exposure assessment of 1811 workers in General Motors automobile factories (Greaves et al. 1997). The prevalence of cough, phlegm, wheezing and breathlessness was higher in machinists than in assemblers. Cough, phlegm, wheezing, signs of chronic bronchitis and chest tightness were statistically significantly associated with exposure to synthetic MWF; the adjusted ORs, indicating increasing prevalence per mg/m³, ranged from 3.5 to 7.2. Phlegm and wheezing were connected also with the use of neat oils, while soluble oil MWFs caused only slight increase in respiratory symptoms. As all of the assemblers had at least some exposure to MWF, the results may underestimate the true effects of MWF.

Rosenman et al. (1997) conducted follow-up inspections including a questionnaire and exposure measurements in 37 machine shops where at least one case of work-related asthma had been diagnosed during 1988–1994. A total of 755 co-workers of the persons with diagnosed asthma were interviewed, and 20% of them reported daily or weekly respiratory symptoms: those exposed to water-miscible MWF had more symptoms than those exposed to neat oils. Sprince et al. (1997) reported significantly more respiratory symptoms, except for lung function changes, in machinists (N=186) than in assemblers (N=66), and found an exposure response relationship between symptoms and total aerosol, viable bacteria and fungi in an automobile transmission plant. An extensive questionnaire study of Canadian machinists (N=2935) working in an automotive factory reported a high prevalence of respiratory symptoms (Oudyk et al. 2003). The machinist were found to have both upper and lower respiratory symptoms that were associated with the average aerosol concentration in the department. The associations were statistically significant for wheezing, sore throat, hoarseness and an upper respiratory symptom grouping.
Lung function changes

Kriebel and co-workers found a dose-response relationship in changes in pulmonary function over the work shift (Kriebel et al. 1997). A prevalence of a 5% drop in forced expiratory volume in one second (FEV1) was three-fold in workers exposed to more than 0.15 mg/m\(^3\) of total aerosol mass as compared to those exposed to less than 0.08 mg/m\(^3\) in both machinists and non-machinists. In a Canadian 2-year follow-up study (Kennedy et al. 1999), lung function changes were more prominent in 82 machining apprentices than in the 159 unexposed control apprentices: the average change in bronchial hyper-responsiveness during the follow-up was about two-fold compared to the controls, and a significant association was found between duration of exposure to synthetic fluids and bronchial hyper-responsiveness. Kennedy et al. (1989) also investigated 89 machinist apprentices and 42 assemblers during one work shift, and reported an OR for a 5% FEV1 decrement of 4.4 (confidence interval, CI 1.0–20) in the use of soluble oils, 5.8 (CI 1.1–29) in neat oils and 6.9 (CI 1.4–35) in synthetic MWFs, respectively. The confidence intervals were generally wide because of the small number of subjects. The FEV1 decrements were also associated with inhalable aerosol levels higher that 0.20 mg/m\(^3\), and with childhood asthma. In another similar study, a prevalence of 5% FEV1 drops over the work shift was 42% in machinists and 27% in assemblers (Robins et al. 1997). In a study of machinists maintaining hard metal saw tips, a statistically significant association was seen between FEV1 reduction and exposure to MWF containing soluble cobalt (Kennedy et al. 1995). Two French studies (Ameille et al. 1995; Massin et al. 1996) indicated some effects of metalworking on pulmonary functions and bronchial hyperreactivity, respectively.

It is noteworthy that in the study by Greaves and co-workers the assemblers with a history of machining work reported more physician diagnosed asthma than did the current machinists, suggesting that some machinists with asthmatic symptoms had transferred to jobs with less exposure (Greaves et al. 1997). In the same population, it was also shown that FEV1 or forced vital capacity (FVC) or post-hire asthma was not associated with current work as machinist but instead with past exposure to MWFs (Eisen et al. 1997; Eisen et al. 2001). In some studies, pulmonary
function has not been found to be associated with metal-working at all, or the association has been weak (Rosenman et al. 1997; Sprince et al. 1997; Godderis et al. 2008). It has been suggested that FEV1-recordings in connection with cross-sectional surveys may provide useful data on the over-shift irritant effects of occupational exposures, but that they are not good indicators of occupational asthma (Becklake et al. 2006).

**Occupational asthma**

According to a surveillance system for work-related or occupational respiratory diseases (SWORD) in the United Kingdom, workers engaged in the manufacture of metallic and automotive products had an estimated annual incidence of 0.45 cases of occupational asthma per 1000 workers during 1992–2001, compared to the overall incidence of 0.13 (McDonald et al. 2005). About 90% of the cases were reported by occupational physicians and the rest were reported by the chest physicians, suggesting that there are differences in the reporting of occupational asthma between the two specialities, and that some of the registered cases of asthma do not meet the principal criteria of occupational asthma. In another part of the United Kingdom, MWFs were the second commonest cause of occupational asthma. It was responsible for 11% of the cases during 1991–2005, based on the so-called SHIELD surveillance system, which is similar to SWORD (Bakerly et al. 2008). The rising trend in occupational asthma due to MWF was acknowledged, and it was suggested to be partly explained by known major outbreaks of occupational asthma in two metalworking factories in the respective geographical area (Fischwick et al. 2005; Robertsson et al. 2007).

A 5-year cohort morbidity study in Michigan, USA, showed an elevated annual incidence (6.7 vs. 4.6 cases per 1000 persons) of hospital admissions due to non-malignant respiratory diseases in machinists compared to non-machinists (Reeve et al. 2003). A study on medical insurance claims from eight machining plants in the USA showed a three-fold in incidence of occupational asthma in tool grinders in comparison to other work tasks in the same plants (Park 2001). In another study from the USA, incidences were not calculated, but metalworking fluids ranked the second most common cause (after diisocyanates) of work-related asthma in the state of Michigan in 1988–94, as reported
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to an obligatory surveillance system (Rosenman et al. 1997). The above-mentioned information sources were not similar, nor were any of the studies based on a uniform occupational or case definition. Therefore, the results can only be considered as rough estimates of occupational asthma in American machinists.

In Finland (Piipari and Keskinen 2005), France (Ameille et al. 2003), Spain (Orriols et al. 2006) and Canada (Contreras et al. 1994; Provencher et al. 1997), machining and related work have not been found to be high incidence occupations for occupational asthma in disease registers. All of these registers are based on physician-reported cases, and in all except the Finnish register, reporting is voluntary. Even though it is likely that systems based on physicians' reports cannot detect occupational respiratory diseases exclusively, the cases of occupational asthma in the reports have been found to exceed the insurance claims statistics serving as official registers in France, the United Kingdom and Spain (Ameille et al. 2003; McDonald et al. 2005; Orriols et al. 2006). Voluntary systems may therefore provide more realistic figures on the incidence of occupational asthma than the official records in these countries. The rarity of occupational asthma in the FROD was not reflected in a Finnish nationwide follow-up study on asthma incidence by occupation (Karjalainen et al. 2002). The follow-up study showed an elevated risk of adult-onset asthma in machinists and related workers as compared to administrative workers, the OR being 1.52 (CI 1.35–1.72). The study suggested that occupational asthma in many occupations including machinists may be under-diagnosed in Finland. However, even if an elevated risk is acknowledged in epidemiological studies, asthma related to a specific exposure is often difficult to diagnose in individuals.

2.2.3.4. Metalworking fluids as causes of occupational asthma

Reports of clinically investigated occupational asthma in machinists are rare, and the specific components of MWF capable of causing occupational asthma have not been well characterized (Gordon 2004). So far, the identified MWF ingredients, discovered by specific bronchial provocation tests, include alkanolamines (Savonius et al. 1994; Piipari et al. 1998), pine oil reodorant (Robertson et al. 1988), and colophony, pine oil and terpenes (Hendy et al. 1985). In another report, the chal-
challenge test was positive with the used rather than with an unused MWF in one out of four patients with positive BPT to MWF, suggesting that either microbial contaminants or other changes in the fluid chemistry are responsible for the respective patient's reaction (Robertson et al. 1988). A diagnosis of occupational asthma has in some cases been confirmed with a provocation test performed with the patient's MWF, but further tests to discover the specific causative ingredient have not succeeded (Robertson et al. 1988). IgE-mediated allergy was not demonstrated in any of the abovementioned reports, and the mechanisms behind the reactions remain unknown.

2.2.4. Other respiratory diseases

Chronic bronchitis and extrinsic allergic alveolitis are described in many industrial environments including machine shops (Zacharisen et al. 1998; Hodgson et al. 2001; Fishwick et al. 2005; Dawkins et al. 2006; Gupta and Rosenman 2006). Large outbreaks of respiratory diseases have occurred in machining plants even in relatively well controlled environment. In two recent European studies, worsened microbial quality of MWF was considered as the main cause of the numerous respiratory diseases, namely up to 19 cases of extrinsic allergic alveolitis and 74 cases of asthma (Fishwick et al. 2005; Dawkins et al. 2006; Robertson et al. 2007). In some of the allergic alveolitis patients, specific serum precipitins have been found to the used MWF or to bacteria identified in them (Dawkins et al. 2006).

There are solitary reports of lipid pneumonia in machining environment (Cullen et al. 1981), and a hard metal disease has been described in wet grinders exposed to soluble cobalt compounds in MWF (Sjogren et al. 1980; Cugell 1992). Endotoxins can cause various respiratory symptoms (Douwes and Heederik 1997; Douwes et al. 2003), but organic dust toxic syndrome (ODTS) due to endotoxins in MWF has not been reported. Likewise, IgE-mediated allergic rhinitis due to MWF has not been reported.
2.2.5. Cancer

Some studies have indicated that machinists may have an elevated risk of skin, esophageal, stomach, spleen, liver and laryngeal cancer as well as of cancers of the colon and rectum (Savitz 2003; Malloy et al. 2007). The investigations have been focused on machinists with a 20–30 years of exposure to MWF. Carcinogenic nitrosamines that are formed from secondary amines and nitrosating agents are found even in modern MWFs (Järvholm et al. 1991), while modern severely refined mineral oils in MWF contain only very small amounts of carcinogenic polyaromatic hydrocarbons (PAH) (Tolbert 1997). The cancer risk of modern MWFs, like that of many other occupational exposures, is difficult to recognise because of the long latency of cancer (Tolbert 1997; Vainio 1997).
III AIMS OF THE STUDY

Thorough investigations of the exposure and skin and respiratory diseases and symptoms in machinists have not been conducted in Finland. Worldwide, data are lacking on specific components of water-miscible metalworking fluids in the air of machine shops, as well as on skin exposure to metalworking fluids.

The aims of this study were to enhance knowledge on allergens, exposure, and skin and respiratory effects of water-miscible metalworking fluids. The detailed objectives were

- To analyse the statistics of occupational skin and respiratory diseases and their causative agents
- To study the frequency of work-related skin and respiratory symptoms in machinists
- To investigate the association between exposure to total aerosols and respiratory symptoms
- To assess respiratory exposure to irritating and sensitizing chemicals in machine shops
- To find means for quantifying skin exposure to metalworking fluids
- To assess skin allergens in metalworking fluids.
IV MATERIALS AND METHODS

4.1. Study design

The study consisted of five parts: 1) Analysis of the occupational skin and respiratory disease statistics of machinists in Finland during 1992–2001 (Study I); 2) Cross-sectional telephone interview study on the skin and respiratory symptoms of 757 machinists in 60 companies (Studies II and III); 3) Assessment of working conditions and their effect on respiratory symptoms in 60 companies participating in the cross-sectional study (Study III); 4) Detailed measurements of skin and respiratory exposure to MWFs in ten machine shops in nine of the participating companies (Studies IV and V), and 5) Chemical analysis of the skin sensitizing components in metalworking fluids acquired from nine machine shops (Study VI). The procedure of the cross-sectional study, workplace assessments and analysis of skin sensitizers (parts 2–5) is outlined in Figure 1.

This thesis is based on the results of the abovementioned studies. The overall study design was approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa, Finland.
IV MATERIALS AND METHODS

Figure 1. Procedure of the cross-sectional study and work-place assessments (Parts 2–5)
4.2. Subjects and workplaces

Analysis of statistics

Incidences, causative agents and trends of occupational skin and respiratory diseases in machinists were investigated based on data of the Finnish Register of Occupational Diseases (FROD) and the patient register of the Finnish Institute of Occupational Health (FIOH) during the 10-year period 1992–2001 (Study I). The main diagnoses, their main causative agents, and age and sex distributions were collected from 1992 to 1999 from the occupational category of turners, machinists and tool-makers (class no. 751) according to the Finnish classification of occupations (Statistics Finland 1987). Because of changes in the classification of occupations in 2000, the data from 2000–2001 were collected from machine-tool setters and setter-operators (class no. 7223), metal-wheel grinders, polishers and tool sharpeners (no. 7224), and machine-tool operators (no. 8211) (ISCO–88 (COM)). The total number of machinists was about 14 000–20 000 in 1992–2001, and about 4% of them were women (Statistics Finland). The total Finnish work force was about 2.2 million during 1992–2001. Allergic respiratory diseases (ARD) were classified into asthma, allergic rhinitis, allergic alveolitis and organic dust toxic syndrome (ODTS), whereas occupational skin diseases (OSD) were classified into allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), contact dermatitis of unknown mechanisms (ACD/ICD), contact urticaria (CU) or protein contact dermatitis, occupational acne, paronychia, skin infections, other skin diseases, and unspecified skin diseases. To get more detailed information on e.g. the exposure times and causative factors of the diseases, the cases investigated at FIOH were extracted from the FROD, and coupled with data from the patient register of FIOH. 45 cases of skin diseases and 15 cases of respiratory diseases were investigated at FIOH.

Cross-sectional study

The prevalence of skin and respiratory symptoms as well as exposure and working habits of machinists were studied using a cross-sectional telephone questionnaire (Studies II and III). The subjects consisted of machinists and machine maintenance workers in metal companies.
located in and around the cities of Helsinki, Tampere, and Turku, in southern Finland. The companies in which machining was one of the main activities were selected from the membership register of Mechanical Engineering Employers in Finland. The selection was based on the companies' products and other descriptions that indicated the use of machining operations. The number of companies in the register that appeared to use machining was 347, and they were contacted in random order. If a certain company did not answer the contact call at all, or if it turned out that the company did not have any machining workers, or it did not want to participate, the company in question was skipped and the next one on the list was contacted. The companies were grouped into three size categories according to the number of machinists or machine maintenance men inquired on the phone: the small enterprises had less than 15, the medium-sized enterprises had 15–50 and the large enterprises had more than 50 machinists. The contact calls were continued until there was a sufficient number of machinists from all company sizes. Altogether 82 companies were contacted and 64 companies agreed to participate. Contact information on all machinists and machine maintenance men (later referred to as machinists) were obtained from each company. Finally, in order to ensure that the study population was exposed to MWF, the machinists were asked about this at the beginning of the interview. In order to be included, the workers had to have a minimum exposure to MWF of one hour per week.

The exposed population consisted of a total of 961 machinists in 64 companies. Of these, 757 (79%) participated in the questionnaire study. 726 (96%) were men, and 34 (4%) were machine maintenance workers. As there were only 31 (4%) women, they were excluded. The population available for analysis thus numbered 726, consisting of 216 machinists from small companies, 212 from medium-sized companies and 329 from large companies. This represents about 4% of the total workforce of machinists in Finland at the time of the study. The control population consisted of the male office staff of the large companies, representing several occupations such as technical draftsmen, CAD draftsmen, engineers and clerks. The control subjects did not work with MWF for more than one hour/month and had not worked with MWF for more than one month ever during their life. 84 (99%) of the 85 contacted controls participated in the study.
IV MATERIALS AND METHODS

Assessment of exposure

The working conditions and their effects on the respiratory symptoms were assessed during visits to 60 of the 64 companies that participated in the cross-sectional study, and aerosols were measured in 57 of the visited companies (Study III). Of the 60 companies visited, 10 machine shops from nine companies representing different sizes, and the use of different MWFs and processes, were invited for detailed workplace measurements (Studies IV and V).

4.3. Clinical investigations

In the Study I, the patients investigated in the FIOH were extracted from the FROD. The patients had been diagnosed according to the normal procedure of FIOH. Delayed contact allergy was investigated with patch testing, which included a modified European standard series as well as series according to exposure, namely oils and cooling fluids, antimicrobials, ethanolamines, and coconut fatty acid derivatives. Most of the patients were also patch tested with their own materials, such as MWFs, protective gloves and hand cleansing agents, from the workplace. Immediate allergy, manifesting as CU, asthma or rhinitis, was investigated with skin prick tests including European standard series with common environmental allergens, and with additional series according to exposure, e.g. with diisocyanates or carboxylic acid anhydrides (Lachapelle and Maibach 2003). Also specific serum IgE antibody tests (radio allergy sorbent tests, RAST) were done according to exposure. Occupational asthma was investigated according to the recommendations (Allergy practice forum 1992; Cartier and Malo 1999), and they included specific bronchial provocation tests (BPT) in a test chamber of about 6 m³, and in one case a workplace challenge. BPTs were done with a workplace substance that was related to the patient’s symptoms or was associated with falls in peak expiratory flow (PEF) in the work place or to which the patient was sensitized, or that was otherwise known to be sensitizing. Test substances included e.g. acid anhydrides and the patient's own MWF. If rhinitis was suspected, the upper airways were examined by an otorhinolaryngologist before and after the BPT.
4.4. Telephone interview

The cross-sectional data were collected using a structured questionnaire in a computer-assisted telephone interview (CATI) during the winter 2002–2003. The questionnaire inquired about demographics, education and work history, working habits, handling of chemicals, protective measures, skin, respiratory and eye symptoms and their connection to the work, exacerbating factors, and consequences of symptoms on the quality of life and the working ability. The analysis focused on recurring and prolonged symptoms during the past 12 months.

Skin symptoms were required to have occurred at least once or lasted for at least two weeks in order to fulfil the criteria of recurring or prolonged, respectively. The skin-related questions focused on the hand dermatitis (HD), defined as dermatitis on the hands or forearms (Study II). The respiratory questions inquired about cough, phlegm, wheezing, dyspnoea, and nasal, laryngeal and eye symptoms (Study III). For respiratory symptoms, recurring or prolonged symptoms were defined as symptoms occurring at least weekly. Also asthma diagnosed by a doctor and current asthma medication was asked. In addition, atopic skin and respiratory symptoms and previously diagnosed occupational diseases were inquired.

The questions on atopic symptoms and skin symptoms were mainly based on the Nordic Occupational Skin Questionnaire (Flyvholm et al. 2002), and the questions on respiratory symptoms were modified from the Finnish Tuohilampi questionnaire (Susitaival et al. 1996) and from the Finnish Environment and Asthma Study Questionnaire (Jaakkola et al. 2003). The questions concerning work tasks, work habits, protective measures and exposure were designed specifically for the study. Also identification codes for the interviewees’ main machines and their department were asked in order to locate the machines for the workplace assessments.

Most of the questions had classified answer alternatives. Re-classification and classification of open answers were done after the data collection by the researchers, when needed.
4.5. Assessment of working conditions and total aerosols in machine shops

Work habits and measures to control exposure were assessed in 60 and total aerosol was measured in 57 of the workplaces that participated the cross-sectional telephone interview study. The workplace visits were started during the interviews, and were continued up to about eight months after the telephone interviews (Study III). Information on, for instance, ventilation systems, exposures, protective measures such as protective gloves, and work habits were recorded on a structured form specifically designed for the study. Total aerosol content was measured with a portable real-time aerosol photometer, personal DataRAM (MIE Inc., Bedford, Massachusetts, USA). DataRAM measured the mass concentration of all aerosols, dusts and fumes in the air falling in the size range of 0.1–10 μm. The aerosols were measured in the breathing zone of the machinists and in general ambient air of the workplace. A total of 674 machines were observed, and a total of 380 breathing zone measurements were conducted. The rest of the machines were not used at the time of the visit, so their aerosols were not measured. In addition, 57 measurements of workshops' general air were conducted. The results were recorded on the structured form and subsequently inserted to the cross-sectional telephone interview data chart. The total number of interviewed machinists that could be combined reliably to breathing zone measurements by using the machine and department codes asked in the interview was 290, and another 121 workers could be coupled to the department and thereby to the general air measurements, although their main machine was not identified or actively used during the workplace visits. The number of machinists available for the analysis of symptoms according to aerosol concentration in general air was therefore 411.

4.6. Air measurements

Detailed measurements of air contaminants were conducted in 10 machine shops in nine companies (Studies IV and V). Both breathing zone sampling and stationary sampling were performed. The samplers were located so that different parts and processes in the workshops were
evenly represented, and the machines producing the highest concentration of total aerosol, as measured with the DataRAM, were included. Personal air samples were collected from three to six workers at each workplace, depending on the total number of machinists and machines. Inhalable dust, oil mist, volatile organic compounds (VOC), aldehydes and microbes were collected and analysed with standardized methods (Table 4). A new method was developed for alkanolamines: they were collected on glass-fibre filters treated with sulphuric acid, desorbed from the filter by methanol and analysed by liquid chromatography and mass spectrometric detection (LC-MS) using an internal standard method. The air sampling and analysis methods are outlined in Table 4. The analyses were done in the laboratories of the regional offices of FIOH in Helsinki, Turku and Kuopio.
### IV MATERIALS AND METHODS

Table 4. Sampling and analysis methods of air measurements in ten metal workshops.

<table>
<thead>
<tr>
<th>Measured substance</th>
<th>Number of samples</th>
<th>Sampling time</th>
<th>Duration of sampling (hours)</th>
<th>Air flow (L/min)</th>
<th>Sampling method/collection medium</th>
<th>Analysis method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing zone samples</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volatile organic compounds (VOC)</td>
<td>42</td>
<td>A</td>
<td>1</td>
<td>0.1</td>
<td>Tenax sorbent tube</td>
<td>Thermodesorption, GC-MS (ISO 2004)</td>
</tr>
<tr>
<td>Aldehydes</td>
<td>42</td>
<td>M</td>
<td>2</td>
<td>1</td>
<td>SepPak collector</td>
<td>LC-MS (US Environmental Protection Agency 1999)</td>
</tr>
<tr>
<td>Alkanol-amines</td>
<td>42</td>
<td>M</td>
<td>2</td>
<td>2</td>
<td>Acid-treated glass fibre filter</td>
<td>Desorption with methanol, LC-MS</td>
</tr>
<tr>
<td>Endotoxins</td>
<td>42</td>
<td>A</td>
<td>2</td>
<td>2</td>
<td>IOM-cartridge/glass fibre filter</td>
<td>Enzyme-based spectrophotometry, (CEN 2002)</td>
</tr>
<tr>
<td>Stationary samples*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oil mist</td>
<td>21</td>
<td>A</td>
<td>4–6</td>
<td>2</td>
<td>IOM cartridge/teflon or glass fibre filter</td>
<td>Extraction to tetrachloroethylene, IR (NIOSH 1996)</td>
</tr>
<tr>
<td>Microbes</td>
<td>21</td>
<td>A</td>
<td>2</td>
<td>2</td>
<td>Cannea cartridge/polycarbonate filter</td>
<td>Cell culture, microscopy (Palmgren et al. 1986)</td>
</tr>
</tbody>
</table>

*Personal breathing zone samples from three machine shops and stationary samples from seven machine shops (21 samples)

M = morning; A = afternoon; GC-MS gas chromatography and mass spectrometry; LC-MS = liquid chromatography and mass spectrometry; IR = infrared spectroscopy.
4.7. Skin exposure measurements

Skin exposure to alkanolamines and MWF was assessed in 37 machinists in nine machine shops with a hand-rinsing method developed for the study (Study V). Three of the 37 machinists used MWF that did not contain monoethanolamine (MEA), diethanolamine (DEA) or triethanolamine (TEA) according to analysis, and thus the results were based on 34 measurements. Briefly, the dominant hand of the machinists was rinsed after about two hours of working in the morning between coffee break and lunch. The hand was rinsed in a plastic bag with 200 ml of 20% isopropanol-water mixture for 1 minute. Reference samples were obtained in the same way after lunch, when the machinists had washed their hands carefully with soap and warm water. The rinse-off samples were analysed for alkanolamines by LC-MS using an internal standard method. The recovery efficiency of the hand rinsing method was tested in the laboratory prior to workplace measurements with an MWF including MEA and TEA, and found to be 59% for MEA and about 65% for TEA; 65% was decided to be used also for DEA. Samples of the emulsified MWFs in use were collected and analysed for their alkanolamine content: with this information, the alkanolamines in the hand rinse-off samples could be used to calculate the amount of the MWF itself remained on the skin after two hours' work.

4.8. Assessment of total exposure to alkanolamines

The systemic exposure to alkanolamines (MEA, DEA and TEA) via skin and respiratory tract during two hours' work was assessed based on air measurements and skin exposure measurements of 34 machinists in nine machine shops (Study V). For breathing volume, an assumption of 30 litres per minute was used, and it was assumed that the amount absorbed through the skin was 20% of the total amount of alkanolamines on the skin. The latter assumption was based on the recovery efficiency studies where about 60–70% of alkanolamines could be recovered. Another 10–20% was assumed to be lost due to evaporation of alkanolamines from the skin. When calculating total exposures,
the amount of alkanolamines in the rinse-off samples was corrected for recovery efficiencies and for the sampling time.

4.9. Analysis of metalworking fluid concentrates

A total of 17 MWF concentrates from nine machine shops were analysed for alkanolamines, total formaldehyde, other antimicrobials and resin acids of colophony (Study VI). The results of the GC-MS analysis were also monitored in order to identify other possible skin sensitizing substances. Alkanolamines, formaldehyde, isothiazolinones, methyl dibromoglutaronitrile (MDBGN) and iodopropynyl butylcarbamate (IPBC) were analysed by LC-MS or liquid chromatography with ultraviolet detection (LC-UV). Resin acids of colophony, as well as other possible skin sensitizing substances, were analysed with GC-MS. The limits of detection (LOD) were 0.02–0.1% for alkanolamines, 0.01% for formaldehyde, 0.0005–0.001% for isothiazolinones and other antimicrobials, and 0.005% for resin acids. The analysis results were compared with the information in the safety data sheets (SDS).

4.10. Statistical methods

SAS and SPSS programs were used for the statistical analysis. In Studies II and III, cross-tabulations were used for monitoring symptoms according to e.g. work characteristics and skin or respiratory atopy. Crude and adjusted odds ratios (OR) and their 95% confidence intervals (CI) for skin and respiratory symptoms and their combinations were calculated using multivariate logistic regression and ordinal regression models. The OR for the respective reference group, i.e. the population with no exposure or smallest exposure, was 1.

In Study II, the outcomes of major interest were: 1) HD, and 2) work-related dermatitis elsewhere than on the hands or forearms (DE). The outcome symptoms had to have occurred during the past 12 months, repeatedly or prolonged. ORs for HD and DE were calculated in machinists vs. controls, and they were adjusted for atopic dermatitis, childhood
dermatitis, respiratory atopy, age, and sensitive skin symptoms (dry skin, symptoms of metal allergy, and itching when sweating).

In Study III, the outcomes of interest were: 1) various upper and lower respiratory tract symptoms, 2) a combination of upper respiratory symptoms (no symptoms, nasal, throat or eye symptoms) for which a specific symptom index consisting of 0–3 symptoms was used, 3) a combination of lower respiratory symptoms (no symptoms, cough, phlegm production, wheezing or breathlessness) for which a symptom index consisting of 0–4 symptoms was used and 4) current and ever asthma. The outcome symptoms had to have occurred during the past 12 months, repeatedly or prolonged. ORs for the respiratory symptoms, respiratory symptom indexes and current and ever asthma were calculated in machinists vs. controls, in machinists with high exposure vs. low exposure according to total aerosol concentrations in the breathing zone and general air, in machinists with increasing quartiles of aerosol concentration in the general air, and in machinists with long exposure history vs. short exposure history. Adjustments were made for age, smoking habits, and atopy in childhood, i.e., atopic skin or respiratory disorder during childhood or school age.

In the study IV, Spearman’s correlations were used for studying the associations between exposure variables in detailed exposure measurements. A p-value of < 0.05 indicated statistical significance.
V RESULTS

5.1. Occupational skin diseases

During 1992–2001, skin diseases formed 27% of all occupational diseases in machinists in the FROD (Study I). During the study period, a total of 279 cases of occupational skin disease (OSD) were reported. Of them, 90% were contact dermatitis: 144 (57%) were irritant contact dermatitis (ICD) and 107 (43%) were allergic contact dermatitis (ACD). The annual incidence of skin disease in machinists increased from 1.0 to 1.5 cases per 1000 employees, and the annual number of ACD diagnosis increased three-fold during the study period. The incidence of skin disease was about three times that in the total workforce. The incidence of ACD was highest in the age group of 55–59 years, and that of ICD was highest in the age of 45–49. The proportion of ICD was highest in young adult workers in 20–34 years of age, and again in the oldest age group, namely 60–64 years. The commonest inducers of ICD were MWF, oils and lubricants, organic solvents, wet and dirty work and washing agents. The commonest causes of ACD were MWF, their ingredients, such as formaldehyde, ethanolamines and colophony, and metals.

45 (17%) of the dermatitis cases were diagnosed in the FIOH. 27 (60%) patients had ACD: 15 (55%) of them had eczema only on their hands, and the rest had eczema also on the wrists, forearms, face or legs. The exposure time varied between 2 months and 44 years. In the skin prick tests, only one patient had IgE-mediated allergy to a workplace agent. The patient was sensitized, and he had CU and allergic rhinitis due to methylhexahydrophthalic acid anhydride (MHHPA) in a hardener of epoxy resins used in a nearby process. Details of the patients are presented in Table 2 (supplemental data) in Study I.
5.2. Skin symptoms

In the telephone interview study (Study II), both HD and DE were more common in machinists than in the controls. 21% of machinists had had HD in the past 12 months compared to 11% in the office workers. In 93% of the machinists with HD in the past 12 months, the HD was recurring or prolonged. 68% of those with recurring or prolonged HD thought that HD was related to their work, and 40% could identify a worsening factor or factors at work. Currently, 5% percent of the machinists reported severe and 25% reported moderate HD; 16% had visited a doctor during their adulthood because of HD, and 6 (0.8%) had a diagnosis of OSD. Reporting of HD was highest in those who had suffered from HD in childhood and in those who reported symptoms of metal allergy. About 10% reported recurring, DE during the last 12 months. The skin symptoms according to occupation and atopic symptoms are presented in Table 5.

<table>
<thead>
<tr>
<th>Skin symptoms in the past 12 months N (%)</th>
<th>According to occupation</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>DE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Machinists (N=726)</td>
<td>153 (21)</td>
<td>71 (10)</td>
<td></td>
</tr>
<tr>
<td>Maintenance men alone (N=34)</td>
<td>7 (20)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Office workers (Controls, N= 84)</td>
<td>10 (11)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>According to atopic symptoms (Machinists and office workers; N=810)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HD in childhood (N= 29)</td>
<td>17 (59)</td>
<td>3 (10)</td>
<td></td>
</tr>
<tr>
<td>Symptoms of metal allergy (N=42)</td>
<td>19 (45)</td>
<td>6 (14)</td>
<td></td>
</tr>
<tr>
<td>Any sensitive skin symptom(s)(^1) (N=412)</td>
<td>115 (28)</td>
<td>50 (12)</td>
<td></td>
</tr>
<tr>
<td>Atopic dermatitis (N=168)</td>
<td>53 (32)</td>
<td>29 (17)</td>
<td></td>
</tr>
<tr>
<td>Respiratory atopy (N=163)</td>
<td>37 (23)</td>
<td>9 (6)</td>
<td></td>
</tr>
</tbody>
</table>

HD= hand or forearm dermatitis
DE= recurring work-related dermatitis elsewhere than on hands or forearms
\(^1\) Sensitive skin symptoms were dry skin, itching during sweating, and symptoms of metal allergy
V RESULTS

Machinists had about a two-fold risk of recurring, prolonged HD in the past 12 months as compared to the controls, the OR being 1.7 (0.8 –3.5). The risk of DE was more than four-fold compared to the controls with an OR 4.4 (1.0 –8.8). The strongest risk factor for HD was not metalworking but HD in childhood, with an OR of 4.1 (1.8 –9.3). Atopic dermatitis and sensitive skin symptoms were statistically significant risk factors of both HD and DE (Table 3 in Study II). One fourth of those reporting HD in the past 12 months told that the dermatitis had affected their mood. HD had also influenced the activities at work, and affected on sleeping as well as free time activities.

5.3. Occupational respiratory diseases

Respiratory allergies formed 3% of all occupational diseases in machinists in the FROD during 1992–2001 (Study I). Altogether 34 cases of allergic respiratory diseases (ARD) were reported. Most of the allergic respiratory diseases (29 cases, 85%) were asthma. There was no clear trend in ARD in machinists, and the number of cases per year varied from one to seven. The incidence of asthma was about the same, whereas the incidence of allergic rhinitis was only one fifth of that in the total work force. The most common causes of asthma were metals or plastic chemicals such as carboxylic acid anhydrides or diisocyanates. MWFs or alkanolamines in them caused three cases of asthma. The incidence of asthma was highest in the age group of 55–59.

15 (50%) of the ARD cases were reported from the FIOH: 13 cases of asthma and two cases of rhinitis. The exposure times ranged from one day to 34 years. Occupational asthma was confirmed by specific challenge tests in 12 cases, and by a workplace challenge in one case. In addition to the one case of concomitant CU and allergic rhinitis, IgE-mediated sensitization to workplace compounds was shown in one asthma patient and one rhinitis patient, both of whom were sensitized to carboxylic anhydrides used in nearby processes. Details of the patients are presented in Table 3 (supplemental data) in Study I.
5.4. Respiratory symptoms and their connection with exposure

All respiratory symptoms except asthma were more common in machinists than in the office workers. The most common recurring or prolonged symptoms (occurring weekly) during the past 12 months were nasal symptoms in 19%, phlegm production in 12% and cough in 9% of the machinists compared to 4%, 8% and 4% in the controls, respectively. The occurrence of any respiratory symptom was 31%. The occurrence of any respiratory symptoms was a little higher in the medium size companies (37%) as compared to the small (32%) and large companies (28%), respectively.

Especially the risk of upper airways and eye symptoms was higher in machinists than in the controls. The adjusted OR for nasal symptoms was 6.2 (1.9–20.0), and the OR for upper respiratory symptom index was 4.1 (1.8–9.3). In addition to upper respiratory tract symptoms, the risk of any respiratory symptom was elevated, the OR being 2.5 (1.3–4.6) (Table 2 in Study III).

The median total aerosol concentration measured in 57 machine shops' general air was 0.17 mg/m³ (range 0.007–0.67), and the median aerosol in breathing zone was 0.12 mg/m³ (range 0.001–3.0). When the machinists were divided into high and low exposure groups according to the total aerosol measurements in general air of the machine shops, an association was seen between exposure and both upper and lower respiratory symptoms, and many of the OR's were statistically significant. The risk was highest for breathlessness with an OR 7.1 (2.0–24.9). For upper and lower respiratory symptom indexes, the ORs were 2.1 and 2.8, respectively, and statistically significant. When the machinists were compared according to the breathing zone measurements, the highest ORs were calculated for breathlessness, with an OR 7.0 (1.6–31.9), wheezing with OR 4.8 (1.6–14.8) and nasal symptoms with OR 1.8 (1.0–3.3).

When the machinists were grouped according to increasing quartiles of aerosol concentration in the general air, a dose-response was seen in many upper and lower symptoms, and the respective risks were increased especially above the median aerosol concentration, i.e. in the third (0.17
RESULTS

<0.28 mg/m³) and fourth (0.28–0.67 mg/m³) quartile. Significant association was shown already in the second quartile for cough with OR 12.8 (1.6–101.6), while in the third quartile, significant increase was seen for nasal symptoms with OR 2.3 (CI 1.1–4.8), cough with OR 22.0 (2.8–171.3), wheezing with OR 4.0 (1.0–15.4), any symptoms with OR 2.6 (1.4–4.8), upper respiratory symptoms index with OR 1.9 (1.0–3.6) and lower respiratory symptom index with OR 3.3 (1.5–7.6). Significant changes were not seen for phlegm and breathlessness until in the fourth quartile, the ORs being 2.5 (1.1–5.7) and 6.7 (1.4–31.5), respectively.

The risks of throat symptoms, cough and chronic bronchitis were increased and statistically significant in metalworkers who had worked at least 15 years, compared to those with less than 15 years' work history.

5.5. Work tasks, use of chemicals and control of exposure

In the telephone interview, 96% reported machining as their main work task, and the remaining 4% were machine maintenance men. 81% had a vocational training in machining; the most common jobs were CNC (computer numerical control) or NC (numerical control) machinist, turner and grinder. Multiple operation machining centres were commonly used: about 60% of the metalworkers reported operating several machines, and 76% did some maintenance work on their own machine. 90% handled freshly machined metal pieces numerous times every day, 78% got splashes of MWF on their skin daily, 85% used compressed air in cleaning the fabricated pieces, and 36% reported visible mist in the workshop frequently. Protective gloves were used by 92% of the interviewees. The most common glove materials were leather/textile, plastic- or rubber-coated textile, and plastic-pimpled textile.

In the workplace assessments carried out in the 60 companies, a total of 674 machines were monitored. 50% of the machines were manual, 49% were NC machines, and 1% were fully automated machining centres. The most common techniques were turning, milling and drilling. The most frequent materials were various steels such as alloyed or non-alloyed steel and cast iron, but also other metals as well as plastic and graphite were fabricated. Water-miscible MWF was used in 87% of the
machines, while neat oils, alcohol or unknown lubricants were used in the remaining machines. According to the SDSs, a total of 62 MWFs were used, most workplaces using several MWFs. Of the monitored machines, only 26% had local ventilation and were enclosed, and one third of the machines had neither. The rest had various equipment. Contrary to the telephone interview, 12% of the workers reported never using protective gloves when machining, and many thought that it was difficult to choose suitable gloves. Based on visual observation, the gloves used seemed to be quite clean and undamaged, but the manner and frequency of using the gloves varied. Furthermore, the glove materials were generally not optimal for MWFs, as plastic pimpled gloves and gloves made of leather and textile were common.

5.6. Respiratory exposure to components of metalworking fluids

In all of the 10 machine shops in which detailed air measurements were conducted, altogether 17 different water-miscible MWFs were used. The mean concentrations of oil mist (0.14 mg/m³) and inhalable dust (0.78 mg/m³) were clearly below the occupational exposure limits (OEL), and also the concentration of microbial contaminants was low (Study IV). Several aldehydes, of which formaldehyde formed about 50%, were identified with a mean total concentration of 0.095 mg/m³. The mean concentration of VOC was 1.9 mg/m³. The most common VOCs were high boiling aliphatic hydrocarbons and aromatic hydrocarbons, but also several MWF ingredients with possible sensitizing or irritant effects were identified in most of the machine shops in small concentrations (Table 3 in Study IV). Such ingredients included e.g. terpenes, of which 3-carene, limonene, α-pinene and β-pinene were identified. Of the nitrogen compounds, skin sensitizing oxazolidines, morpholines and triethanolamineborate were identified. MEA, DEA, TEA and methyl diethanolamine (MDEA) were found in most of the workplaces; the mean total concentration of alkanolamines was 0.11 mg/m³, and MEA was the most commonly found compound (Studies IV and V). The mean concentrations of the measured contaminants in each of the 10 machine shops are presented in Table 6.
Table 6. Mean concentration of air contaminants in ten machine shops (A – J) in the breathing zone samples (42 samples) and in stationary samples (21 samples). The concentrations below the LOD have been replaced by a value of 50% of the LOD.

<table>
<thead>
<tr>
<th>Impurity</th>
<th>Inhalable dust (mg/m³)</th>
<th>Oil mist (mg/m³)</th>
<th>Aldehydes (mg/m³)</th>
<th>Total VOC (mg/m³)</th>
<th>Alkanolamines (mg/m³)</th>
<th>Endotoxins (EU/m³)</th>
<th>Bacteria (CFU/m³)</th>
<th>Fungi (CFU/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>42</td>
<td>21</td>
<td>42</td>
<td>42</td>
<td>42</td>
<td>21</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Sampling site</td>
<td>BZ</td>
<td>S</td>
<td>BZ</td>
<td>BZ</td>
<td>BZ</td>
<td>S</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.43</td>
<td>0.07</td>
<td>0.06</td>
<td>0.62</td>
<td>0.09</td>
<td>7</td>
<td>122</td>
<td>84</td>
</tr>
<tr>
<td>B</td>
<td>0.57</td>
<td>0.08</td>
<td>0.07</td>
<td>1.45</td>
<td>0.08</td>
<td>8</td>
<td>68</td>
<td>107</td>
</tr>
<tr>
<td>C</td>
<td>0.59</td>
<td>0.05</td>
<td>0.12</td>
<td>2.15</td>
<td>0.30</td>
<td>1</td>
<td>99</td>
<td>197</td>
</tr>
<tr>
<td>D</td>
<td>1.49</td>
<td>0.08</td>
<td>0.03</td>
<td>0.68</td>
<td>0.02</td>
<td>5</td>
<td>158</td>
<td>1027</td>
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<tr>
<td>E</td>
<td>0.41</td>
<td>0.10</td>
<td>0.05</td>
<td>2.08</td>
<td>0.15</td>
<td>3</td>
<td>71</td>
<td>213</td>
</tr>
<tr>
<td>F</td>
<td>0.87</td>
<td>0.06</td>
<td>0.03</td>
<td>0.76</td>
<td>0.02</td>
<td>13</td>
<td>33</td>
<td>594</td>
</tr>
<tr>
<td>G</td>
<td>0.76</td>
<td>0.03</td>
<td>0.06</td>
<td>2.37</td>
<td>0.06</td>
<td>3</td>
<td>72</td>
<td>576</td>
</tr>
<tr>
<td>H</td>
<td>0.66</td>
<td>0.01</td>
<td>0.05</td>
<td>3.15</td>
<td>0.02</td>
<td>2</td>
<td>67</td>
<td>1608</td>
</tr>
<tr>
<td>I</td>
<td>1.47</td>
<td>0.60</td>
<td>0.16</td>
<td>2.50</td>
<td>0.18</td>
<td>10</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>J</td>
<td>0.71</td>
<td>0.02</td>
<td>0.38</td>
<td>2.66</td>
<td>0.03</td>
<td>95</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Mean</td>
<td>0.78</td>
<td>0.14</td>
<td>0.095</td>
<td>1.9</td>
<td>0.11</td>
<td>18</td>
<td>120</td>
<td>550</td>
</tr>
</tbody>
</table>

N = total number of samples in 10 companies; BZ = breathing zone; S = stationary site; VOC = volatile organic compounds, EU = endotoxin units; CFU = colony-forming units

5.7. Skin exposure to alkanolamines and metalworking fluids

The median amount of alkanolamines in the rinse-off samples from the dominant hand of machinists varied between 0.1 and 76 μg/hand (Study V). Of the 37 workers from whom rinse-off samples were obtained, 34 had used MWFs that contained MEA, DEA or TEA: 10 used MWF which contained MEA, five used MWF containing DEA and 19 used MWF containing both MEA and TEA. The median amounts of alkanolamines were 7.4 mg/hand for MEA (10 samples), 12 mg/hand
for DEA (five samples), and 0.30 and 0.42 mg/hand for MEA and TEA (19 samples), respectively. The amounts of alkanolamines in the samples corresponded to a remainder of 1–2 ml of diluted MWF during two hours of work.

5.8. Total exposure to alkanolamines

The workers were exposed to MWF predominantly through the skin (Study V). The distribution of alkanolamines between skin and respiratory tract varied depending on the alkanolamine which was present in the workers’ MWF. The median amount of MEA on the hands after two hours of work was 10 mg, which was 43 times the amount inhaled. For DEA, the median amount on the skin, 10 mg, was 100 times higher than the amount inhaled. In those who used MWF containing both MEA and TEA, the median amounts on the skin were 1.9 for MEA and 3.4 for TEA, which were about nine-fold and 170-fold compared to the estimated inhaled amounts, respectively (Table 6 in Study V).

5.9. Skin sensitizers in metalworking fluids

All of the 17 analysed MWF concentrates contained formaldehyde (Study VI). The concentration of total formaldehyde ranged from 0.002–1.3%. Fifteen of the 17 MWFs contained alkanolamines in up to 39% concentration. In the LC-analysis of alkanolamines, also oxazolinine, 3-oxazolidine-ethanol, methylidethanolamine, triethanolamine borate, 2-amino-2-ethyl-1,3-propanediol, amino-2-propanol and morpholine were detected in some products. Other than formaldehyde-releasing preservatives were identified in 11 MWFs, the most common one being IPBC -fungicide. Benzisothiazolinone was detected in one, and octylisothiazolinone in one MWF each. Resin acids of colophony were detected in seven MWFs. There were defects in the SDS of all MWFs. The concentration of the analysed compounds and the correspondence of the results with SDSs are presented in Table 1 of Study I.
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6.1. The main findings

This study showed that occupational skin diseases (OSD) are common in machinists, and that MWFs and their ingredients are the main causes of both irritant and allergic contact dermatitis. An increase was also shown in the number of allergic contact dermatitis cases during the 1990's. The abundance of OSD in machinists was reflected by the high frequency of reported skin symptoms in the telephone interview study. The telephone interview also revealed that dermatitis elsewhere than on the hands or forearms was related to the machining work. Skin atopy was found to be an important risk factor of skin symptoms both on the hands and forearms, and elsewhere.

Occupational allergic respiratory diseases were among the least reported occupational diseases in machinists. MWFs were only rarely found to be the cause of occupational asthma, whereas plastic chemicals originating from other processes than metalworking caused several cases of occupational asthma. Contrary to the registered occupational diseases, various respiratory symptoms were frequently reported in the telephone interview. The risk of upper respiratory tract symptoms was clearly increased in machinists compared to the office workers. Furthermore, the risk of both upper and lower respiratory symptoms was elevated in machinists with high exposure vs. machinists with low exposure in an overall clean machine shop environment.

The workplace assessments and exposure measurements revealed that the hygienic conditions were reasonably good in the machine shops visited. However, exposure control measures were found to vary, as
many of the machines were not equipped with proper local ventilation and enclosure, and the use of gloves was not systematic. The mean concentration of most of the measured air contaminants was well below the current OELs, but several chemical and microbiological substances capable of causing respiratory irritation or sensitization were nevertheless found in the air of machine shops. VOCs were the main impurity, and they exceeded the concentration of oil mist by more than ten-fold. Aldehydes were detected in concentrations close to that of oil mist. According to skin exposure measurements about 1–2 ml of diluted MWF remained on the skin of the machinists after two hours of work. Exposure to alkanolamines was shown to occur mainly through the hands. Skin sensitizers were identified in all of the 17 MWFs analysed. The information on the SDSs concerning skin sensitizers was found to be deficient.

6.2. Skin diseases and symptoms

6.2.1. Occurrence

Occupational skin diseases, especially hand dermatitis, are among the most common work-related diseases, and they affect a number of workers in many occupations (Diepgen and Coenraads 1999). The present result revealing about three-fold risk of OSD in machinists compared to the total population during 1992–2001, are in agreement with previous studies in which machinists have been acknowledged as a high-risk occupation (Coenraads and Diepgen 1998; Dickel et al. 2001; Diepgen 2003; Skoet et al. 2004). The incidence of 1.62 cases per 1000 persons per year in the FROD fell within the range of other European studies reporting annual incidences ranging from 0.46 to 3.8 per 1000 workers (Dickel et al. 2003; McDonald et al. 2006). The differences between the studies may be due to different notification procedures, inclusion criteria, and definition of the occupational group. However, the present study and those of others based on disease registers have shown much lower incidences than the ones recently shown in a German long-term follow-up study on apprentices including 58% machinists, 33% other blue collar workers and 9% office workers in the automobile industry.
The workers were followed up for about 13 years after beginning of their apprenticeship. The overall cumulative incidence of HD, of which part was probably atopic dermatitis, was 30%. An annual incidence of 28.2 cases per 1000 workers was calculated (Apfelbacher et al. 2008). The discrepancy between the register studies and the German follow-up study results largely from the healthy worker effect, meaning that the machinists with skin symptoms have left the work without seeing a doctor and their dermatitis is therefore not discovered or reported. Also, even if machinists stayed in the profession, their skin diseases might not be recognized in occupational health units, or the reporting of diseases may be neglected.

The present findings on irritant contact dermatitis (ICD) being the most common diagnosis is in line with previous studies (de Boer et al. 1989a; Dickel et al. 2002). Unlike discussed in the Study I, the incidence of ICD was not highest in the age of 20–34 years, but rather its relative amount compared to ACD was high, as presented in Figure 2 (Study I). The high proportion of ICD in young adults may be due to skin atopy, as atopic dermatitis often manifests in the early years of work life when there is exposure to irritants (Lammintausta and Kalimo 1993). The number of cases of allergic contact dermatitis (ACD) per year increased three-fold during the study period. One reason for this is that the knowledge of skin sensitizing chemicals such as alkanolamines, colophony and coconut-DEA in MWFs, increased during the 1990's.

Although ICD was on the whole more common than ACD, ACD was more common among the patients diagnosed at the FIOH, probably because the most complicated cases are usually referred to the FIOH and mild cases of ICD are diagnosed elsewhere, such as in occupational health care units or local hospitals. Also specific causative agents are usually identified at FIOH in more detail because of extensive patch testing protocols and testing with the patients' own MWFs from work. It is thus also possible that some cases of ACD have been diagnosed and notified as ICD in the FROD, because occupational allergens have not been identified.

In the present telephone interview study, the 1-year prevalence of HD in machinists was higher than in the controls. It was also higher than in a Swedish study with a 1-year prevalence of 7.4% in engineering work (Meding and Swanbeck 1990). On the other hand, current HD
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was reported less than in some other studies (Coenraads et al. 1983; de Boer et al. 1989a; de Boer et al. 1989b; Sprince et al. 1996; Gruvberger et al. 2003). Almost all of the machinists in the present study reporting symptoms in the past 12 months had had symptoms more than once or prolonged, suggesting that mild dermatoses were not reported. Also severe and moderate current eczema was reported by 5% and 25%, respectively, suggesting that some machinists' ability to work is impaired due to dermatitis. Also other aspects of life, such as mood or sleeping, were affected by the dermatitis. The association of dermatitis with quality of life has been shown also in other studies (Agner et al. 2008). Based on the frequent reports of OSD in machinists in the FROD, the dermatoses of machinists usually seem to be well recognised. However, some cases were found to be missing from the statistics. This information was based on the clinical investigations that were done afterwards for those who reported recurring or prolonged symptoms in the past 12 months in the telephone interview (Suuronen et al. 2005). In the clinical investigations, seven new occupational skin diseases were discovered, consisting of four cases of ACD and three cases of ICD.

When adjusted for atopic symptoms and age, machinists were found to have a 1.7-fold risk of HD compared to the controls, but the result was not statistically significant. The fairly small OR and the wide confidence interval could have been due to too small control group or to more allergic subjects in the control group. On the other hand, symptoms related to skin atopy such as atopic dermatitis, HD in childhood, and sensitive skin symptoms, were shown to be more important risk factors than metalworking as such. It is therefore likely that a part of the reported HD is atopic dermatitis, possibly worsened by irritants at work. HD was also very common among subjects who reported symptoms of metal allergy, which usually indicates nickel or cobalt allergy (Flyvholm et al. 2002). Symptoms of metal allergy may well represent non-occupational nickel allergy (Liden 1994), and the frequently reported HD in these subjects may have resulted from elicitation of the pre-existing allergy when the worker is in contact with metallic tools or MWFs containing dissolved nickel or cobalt (Einarsson et al. 1975; Einarsson et al. 1979; Liden et al. 1998).

People work predominantly with their hands, and thus HD constitutes the majority of occupational skin diseases (Coenraads and
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Diepgen 1998). DE was not very frequent in the present study either, but it nevertheless proved to be much more common in machinists than in the controls. When adjusted for atopic symptoms and age, the risk of DE was found to be about four-fold and statistically significant. In addition, metalworking was a clearly stronger risk factor than atopic symptoms. The results suggest that MWFs may cause contact dermatitis also in other body parts than the hands when the fluids evaporate, spray or are splashed to the surroundings. This assumption is supported by the cases investigated at FIOH during 1992–2001 (Study I), as 12 of the 27 investigated machinists with ACD had eczema also elsewhere than in their hands, such as on the face, forearms or legs. Exposure of other skin areas than the hands has also been observed in dermal exposure assessment studies (Roff et al. 2004).

6.2.2. Causative agents of allergic contact dermatitis according to the statistics

During the study period of 1992–2001, the most common causative agents of ACD were antimicrobials and especially formaldehyde and formaldehyde liberators; this finding is in line with other studies (de Boer et al. 1989b; Geier et al. 2004a; Geier et al. 2006). Concomitant patch test reactions to formaldehyde and formaldehyde liberators are common in machinists (Camarasa et al. 1993; Geier et al. 2004a). In most cases the primary allergen has been the formaldehyde released from the formaldehyde liberating antimicrobial agent (Aalto-Korte et al. 2008a).

Chromium, nickel and cobalt caused ACD in total of 12 cases. It is likely that the contact allergies to chromium represent mainly exposure to chromium released from chromium tanned leather gloves (Hansen et al. 2006) while contact allergy to nickel may be due to, e.g., direct skin contacts with tools containing nickel (Liden et al. 1998). However, nickel is a frequent allergen in the general population, and its occupational relevance is often controversial (Liden 1994; Shah et al. 1998; Skoet et al. 2004). Nickel, chromium and cobalt may also dissolve into MWFs from tooling edges and machined pieces, but the concentrations reported thus far have been low, suggesting that induction of contact allergy is possible only in rare cases (Einarsson et al. 1975; Alomar et al. 1985; Papa et al. 1985).
2000; Skoet et al. 2004). However, it is possible that the concentration of dissolved cobalt in MWF is high enough to induce contact allergy when hard metal alloys containing cobalt are machined (Sjogren et al. 1980; Linnainmaa et al. 1996). The concentration of metals was found small also in the samples of used MWFs acquired from the ten machine shops in the present study: the mean concentration of total cobalt, nickel and chromium was 0.16, 0.26 and 0.17 μg/ml, respectively (Suuronen et al. 2005).

Alkanolamines were reported as causative agents less frequently than in some other recent studies (Geier et al. 2004a; Geier et al. 2006). The lower frequency is probably due to the fact that alkanolamines were tested relatively seldom in Finland during the study period of 1992–2001.

Occasional cases of ACDs were caused by rubber or plastic chemicals during 1992–2001 in machinists. Rubber and plastic chemicals are common occupational contact allergens, but they are not often reported in machinists (Halkier-Sorensen 1996; Riihimäki et al. 2004; Skoet et al. 2004). Based on the FIOH cases, in addition to MWFs themselves, coconut fatty acid derivatives in liquid hand soaps seem to be noteworthy causes of ACD in machinists.

6.3. Respiratory diseases and symptoms

6.3.1. Occurrence

Based on the present study, machinists are seldom diagnosed with occupational asthma. During 1992–2001, occupational asthma constituted only about 3% of the occupational diseases of machinists, the annual incidence being 0.17 cases per 1000 workers. The incidence was about the same as that in the total working population. There are only few studies on occupational asthma in machinists, but the incidence was lower than in a study from the same time period from the United Kingdom, with an annual incidence of about 0.45 per 1000 workers in metallic and automotive parts manufacture (McDonald et al. 2005). However, comparison between the registers is hampered by differences in data collection, and by apparent differences in the criteria of occupational asthma. For example, about 90% of the cases in the United Kingdom
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are reported by occupational physicians often in the early state of the disease, when thorough investigations have not yet been conducted.

The rarity of notified occupational asthma and rhinitis in machinists is largely explained by the fact that the chemicals encountered in machine shops usually do not cause respiratory diseases with a known mechanism such as IgE-mediated allergy. Also, a part of the respiratory effects of MWF are likely to be due to non-specific irritancy of the components and bacterial contaminants (Gordon 2004). A diagnosis of IgE-mediated, allergic asthma and rhinitis is supported by well standardized allergy tests such as skin prick tests and serum IgE-tests (RAST) (Lachapelle and Maibach 2003). The diagnosis of occupational asthma in machinists, however, is usually based on BPTs according to exposure, in addition to other clinical findings consistent with occupational asthma (Allergy practice forum 1992; Cartier and Malo 1999; Bernstein et al. 2006). The few exceptions in the present study were carboxylic anhydrides and diisocyanates which may cause IgE-mediated allergy (Baur and Czuppon 1995; Piirila et al. 2000). Machinists are not typically exposed to either of these substances, but instead, the cases reported from FIOH were due to other than machining processes in the surroundings.

The telephone inquiry revealed that despite the rarity of notified ORDs, respiratory symptoms were very common in machinists even in overall clean work environment according to total aerosol concentration. The result reflects the general discrepancy between epidemiological studies and clinical diagnoses, and supports the idea that even if asthma is seen to relate to the work in large populations, the causality is often difficult to show at an individual level (Karjalainen et al. 2001). The results showed an elevated risk of upper respiratory symptoms in machinists compared to office workers, and the result was statistically significant. A statistically significantly increased risk of upper as well as lower respiratory symptoms was found in machinists with high exposure vs. machinists with low exposure according to the median aerosol concentration in general air. Furthermore, when the symptoms were studied according to increasing quartiles of aerosol concentration in general air, many of them displayed a dose response pattern: the level related to increased symptoms seemed to be at the median concentration of 0.17 mg/m³, suggesting that improvements in workplace hygiene should be
targeted to achieve this level. The risk of current and ever asthma was increased in machinists with high exposure vs. machinists with low exposure according to general air measurements, the ORs being 3.6 and 1.7, respectively. However, the result was not statistically significant. The wide confidence intervals probably result from the small number of subjects with asthma. The findings are in line with the literature, as abundance of upper respiratory symptoms has been reported in many studies (Oudyk et al. 2003; Ameille et al. 1995; Kriebel et al. 1997; Sprince et al. 1997; Godderis et al. 2008). There is also some evidence that machining has an effect on pulmonary function and asthma (Massin et al. 1996; Eisen et al. 1997; Robins et al. 1997; Kennedy et al. 1999). The study by Oudyk et al. (2003) even showed a dose-response pattern consistent with our results in fairly similar aerosol concentrations (Oudyk et al. 2003). The above-mentioned studies indicate that irritant factors such as dusts, alkaline pH of the MWF aerosol, and microbial contaminants of MWF in the workplace air play an important role in the development of many symptoms, whereas some of the substances may cause more specific, hypersensitivity-type symptoms of the lower respiratory tract. The frequency of symptoms varied to some extent in companies where detailed workplace measurements were done (unpublished results). However, the overall number of workers in the 10 machine shops was too small for drawing conclusions regarding the effect of individual air contaminants on respiratory symptoms.

It is possible that all ARDs are, in general, not recognized, as the allergic respiratory diseases were very rarely registered even if respiratory symptoms were reported frequently in the telephone interview. As with the skin symptoms, the persons reporting repeated or prolonged respiratory symptoms in the telephone interview were invited for clinical investigations at the FIOH. Only one case of occupational asthma caused by MWF was diagnosed among them (Suuronen et al. 2005). These results support the notion that many of the respiratory symptoms reported in the telephone interview have been caused by unspecific irritation. They also emphasize the general difficulties in showing the causality between work exposures and a disease at individual level, especially when the causative agent is not an established respiratory sensitizer (Karjalainen et al. 2001; Karjalainen et al. 2002). Nevertheless, they show that occu-
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Occupational asthma may occur as well. Based on the presented facts, more attention should be paid to respiratory symptoms of machinists, and occupational heath physicians should be encouraged to refer machinists to detailed clinical investigations whenever work-related respiratory symptoms are suspected.

6.3.2. Bronchial provocation tests with metalworking fluids

The use of BPTs in diagnosing occupational asthma is in accordance with international recommendations (Allergy practice forum 1992; Cartier and Malo 1999). There are nevertheless some deficiencies in the protocol, especially concerning chemical exposures such as MWF. For instance, BPTs are meant to be done below irritant concentrations to avoid unspecific reactions, indicating that the protocol is not comparable to work environment. On the other hand, unwanted and unspecific irritant reactions may not always be identified. A noteworthy fault is that some cases of occupational asthma may be missed as all possible causative agents at the work can seldom be tested. Generally, BPTs might are not optimal for showing the causality of diseases that are caused by non-sensitizing exposures work (Karjalainen et al. 2001).

During 1992–2001, three cases of asthma due to MWF were diagnosed with BPT at the FIOH. One BPT was done with MWF but the asthma was recorded in the patient files as having been caused by DEA, although DEA had not been tested separately. When the test is done with a preparation such as MWF, it is not known which of the ingredients is responsible for the reaction. Assumptions on the specific causative agent(s) should not be made based on BPT done with an MWF, unless the ingredients are tested individually. So far, this has been done in only a few cases (Hendy et al. 1985; Robertson et al. 1988; Savonius et al. 1994; Piipari et al. 1998). In some of the reported cases, the reactions may even have been irritant rather that specific due to a too high test concentration. During 2002–2007, a total of 44 BPTs were done at FIOH with MWF, four of which were positive (unpublished data). 43 of the BPTs, and all of the positive BPTs, were done using a clean, diluted MWF at a low (air) concentration, suggesting that MWFs can indeed induce specific, hypersensitivity-type reactions, although with an
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unknown mechanism. It has been suggested that microbial contaminants are the main cause of the adverse health effects of the fluids (Robertson et al. 1988; Gordon 2004; Stear 2005; Robertson et al. 2007). The findings from the FIOH nevertheless indicate that also pure MWFs and their components may cause asthma. Based on the above-mentioned facts, careful detection of exposures is needed in order to optimize the BPTs and to avoid unnecessary testing. In order to learn more about MWFs as a cause of asthma, BPTs with ingredients and with used MWFs should be considered when the patient's condition allows it.

6.4. Occupational exposures in machine shops

6.4.1. Respiratory exposure to chemical components of metalworking fluids

The quality of the air was generally good in 60 of the companies where the working conditions were assessed, as the concentrations of total aerosol were low, mean concentration in the general air being 0.17 mg/m³. Also, in the 10 machine shops where detailed workplace measurements were conducted, the mean concentrations of extractable oil mist and inhalable dust were low compared to OEL’s or other reference values. The results are comparable to those in a recent Swedish study showing mean total aerosols varying from 0.19 and 0.25 mg/m³ in three metal companies (Lillienberg et al. 2008). Total aerosol and inhalable dust were also comparable to a number of North American studies, in which the concentrations have been generally below 1 mg/m³ (Sprince et al. 1997; Kennedy et al. 1999; Abrams et al. 2000; Oudyk et al. 2003; Ross et al. 2004). On the other hand, also very high total aerosol concentrations, up to about 10 mg/m³, have been reported occasionally (Piacitelli et al. 2001; Simpson et al. 2003). The DataRAM aerosol photometer has been shown to overestimate aerosol concentration as compared to gravimetric methods (O'Brien et al. 2001). It nevertheless indicates overall air contaminants well enough, and it has proved to be useful and easy to apply in the present and other studies from machine shops (Sprince et al. 1997; Lillienberg et al. 2008). Taking into account the overestima-
tion, total aerosols measured with a real-time aerosol photometers can be compared to the NIOSH recommended exposure limit of total 0.5 mg/m$^3$ particulates that are collected on filter and quantified with a gravimetric method (NIOSH 1994).

Although the concentration of the total VOCs was below the recommended industrial level of 5 mg/m$^3$ in all of the samples, VOCs proved to be the biggest class of contaminants, and their concentration was more than 10-fold as compared to oil mist which has traditionally been measured in machine shops. Although the need to measure volatile components in machine shops has been addressed (Woskie et al. 2003), reports of such measurements are very rare. In a Dutch study, oil mist was not found at all, but total concentration of 4.1 mg/m$^3$ and 5.5 mg/m$^3$ of volatile compounds was found in two out of six departments (Godderis et al. 2008). Some solvents such as tetrachloroethylene, alkanes and aromatic solvents could be identified but not quantified. The methodology they used appears to be less sensitive than the present method. Total volatile compounds were also measured in the recent Swedish study, the mean concentrations being 6.25 mg/m$^3$ and 1.79 mg/m$^3$ in two metal companies, respectively.

Alkanolamines were found in all machine shops. MEA was found in all machine shops, and DEA and TEA were found in concentration near or below the detection limit in nearly all machine shops. The small concentration of DEA is due to its presence in only five of the 37 analysed MWFs in use, whereas the absence of TEA is likely to result from its poor volatility. A moderate concentration of TEA was found in only one machine shop where also the concentration of oil mist was relatively high, and thus the TEA was probably retained in the mist and not in vapour phase. The acid treated filter method, which was developed for the present study, is suitable for measuring alkanolamines both in vapour and in mist. All alkanolamines can therefore be quantified with it. Earlier, TEA has been measured from total aerosol samples at concentration up to 0.244 mg/m$^3$ when using synthetic MWF containing 40% TEA, and up to 0.019 mg/m$^3$ when using semi-synthetic MWF containing 3% TEA (Kenyon E., et al. 1993). In the same study, MEA and DEA were found in the analysis of MWF but not in the air, which is explained by their volatility and their consequent escape from the sampling filter. In another study from Sweden, TEA was measured from
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total aerosol samples in concentrations up to 0.063 mg/m³ (Lillienberg et al. 2008). Based on the abovementioned studies, total particulate mass filters are not applicable to MEA and DEA. Alkanolamines are common in modern MWFs and the present method showed to be sensitive and easy to apply. Therefore, alkanolamines could be used as indicators of exposure to all classes of water-miscible MWFs.

Although aldehydes may be formed as a result of oxidative decomposition of hydrocarbons (Aalto-Korte et al. 2005), formaldehyde is likely to originate mainly from formaldehyde-releasing antimicrobials in MWF (Thorne and DeKoster 1996a). Also formaldehyde was found in all machine shops, the mean concentration (0.040 mg/m³) being about 11% of the 8-hour OEL and about the same as the oil mist concentration. This finding is in line with previous studies from Finland (Linnainmaa et al. 2003), Sweden (Lillienberg et al. 2008) and Belgium (Godderis et al. 2008), whereas in a North American study from the 1990s, the concentration was higher, 0.22 mg/m³ (Thorne and DeKoster 1996a).

Of all the contaminants identified in the workplace measurements, terpenes (Hendy et al. 1985; Norback et al. 1995), formaldehyde (Piipari and Keskinen 2005), and alkanolamines (Savonius et al. 1994; Piipari et al. 1998) have been reported to cause occupational asthma or asthma-like symptoms. Some of these compounds have been shown to associate with asthma even at low concentrations (Norback et al. 1995). However, it has been suggested that a low level of total VOC has little effect on the development of asthma (Nielsen et al. 2007). All small molecules including formaldehyde, alkanolamines and many of the VOCs may increase their concentration in machine shops air, as they are not well retained by oil mist separators.

The results from the workplace measurements suggest that many of the current OELs are too high for machine shops. The OELs for oil mist, inhalable dust, alkanolamines and formaldehyde should be lowered to comply better with current exposures. For example, the OEL for oil mist should be lowered to 0.2 mg/m³, which is recommended by the American Conference of Governmental Industrial Hygienists (ACGIH 2005), and the OEL for alkanolamines should be revised to take into account the mixed exposure to several alkanolamines. Another possibility is to establish new target values clearly below current OELs.
6.4.2. Microbial contaminants in workplace air

High concentrations of microbial contaminants were not discovered in workplace air in the present study: the concentrations of bacteria and endotoxins were generally below 10% of those reported in some North American studies (Sprince et al. 1997; Virji et al. 2000). Concentrations of bacteria and fungi exceeded the recommended levels for homes and offices in only a few samples, and they were generally at a level considered normal for industrial workplaces (Reponen et al. 1992). The only machine shop where the Dutch exposure limit for endotoxins (200 EU/m³) was exceeded was the only one using MWF without any preservatives. Microbial contaminants have been suggested to be likely contributors to outbreaks of occupational asthma and especially allergic alveolitis (Hodgson et al. 2001; Dawkins et al. 2006; Robertson et al. 2007). In some of the cases, the patients have been shown to have serum antibody precipitins to MWF or bacterial species in it, even in cases where the concentration of microbes has been very small (Dawkins et al. 2006; Robertson et al. 2007). The amount of microbial contaminants in the air is not only dependent on their amount in the fluid but also on the ventilation and enclosure systems (Virji et al. 2000; Linnainmaa et al. 2003; Veillette et al. 2004; Stear 2005). Thus, both careful maintenance of MWF and other control measures to avoid respiratory exposure are important in controlling health risks of microbial contaminants in MWF.

6.4.3. Skin exposure

The present dermal exposure measurement was among the first attempts to quantify skin exposure to MWFs. Skin proved to be the primary exposure route of alkanolamines. The calculated amount of MWF retained on the hands was about the same as in the previous study by Roff et al. (2004), in which approximately 0.5–1.4 ml of fluid was retained in the glove samples. However, the present rinse-off and LC analysis method seems to be easier to use and more sensitive. The method closely resembles the draft of a CEN standard method for measuring dermal exposure (CEN/TS 15279), published shortly after the present experiments. The present method can be used e.g. for assessing the efficacy of protective gloves, and monitoring practices in glove usage. In
addition, alkanolamines can be used as markers of not only total MWF but also of other allergens or toxic substances in MWF, as they can be assessed from the known relative amounts in the MWF, taking into account differences in volatility. Total exposure to alkanolamines as well as skin problems due to MWF can be markedly reduced by avoiding skin exposure, i.e. by using protective gloves fitted for MWFs. Both thick, chemically protective nitrile gloves (NIOSH 1998) and disposable nitrile gloves (Xu and Que Hee 2008) have been reported as suitable for MWFs. On the other hand, textile gloves coated partly with nitrile rubber are likely to protect skin well in normal machining work without being too warm or sweaty.

6.4.4. Skin sensitizers in metalworking fluids

All of the analysed MWFs were shown to contain several skin sensitizers. Thus, simultaneous exposure to many skin sensitizers is very likely to occur in machinists. Formaldehyde releasing antimicrobials, alkanolamines and IPBC were found frequently in MWFs, suggesting that if allergy to these substances has been discovered, it is difficult to avoid exposure to them just by changing to another MWF. Formaldehyde liberators could not be quantified in the MWF due to their instability, but instead, several formaldehyde liberators based on oxazolidine and morpholine derivatives were identified as formaldehyde and alkanolamines specific for the respective antimicrobial. The rarity of DEA, compared to MEA and TEA, is probably due to the fact that their use has been diminished by some manufacturers of MWF, because DEA may form carcinogenic nitrosamines (Järvholm et al. 1991). For example, in Germany, the use of DEA is limited to 0.2% in the MWF concentrates (Anonymous 1993). Isothiazolinones, such as benzisothiazolinone and octylisothizolinone may be present in the original MWF formulation, or they may be added as separate biocides into the MWF in use. Thus, they should be analysed in the used MWF if occupational contact allergy to them is suspected.

The present results suggest that exposure and thereby occupational relevance of contact allergies to specific ingredients in MWF may be difficult to reveal because of the deficient information on the skin sensitizers given in SDS. The deficiencies in the SDS concerning the skin sensitizers have been reported earlier, too (Henriks-Eckerman et al.
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The results pointed out that chemical analysis and careful exposure assessment are important in diagnostics of occupational dermatitis. The current Finnish recommendation for the patch test series used for machinists, namely the "oils series", compiled by the Finnish Contact Dermatitis Research Group, does not contain MEA, DEA or IPBC. Based on the present and other related studies (Majoie and van Ginkel 2000; Geier et al. 2004a), the recommendation should be revised, and at least MEA, DEA and IPBC should be added to it.

6.5. Validity issues

6.5.1. Finnish Register of Occupational Diseases

Although the coverage of the FROD is not totally comprehensive, it nevertheless provides a basis for estimating incidences and trends of occupational diseases. According to law, physicians are obligated to report all diagnosed occupational diseases to the authorities, which should in theory add to the coverage of the register. However, the data are affected by shortcomings common in occupational disease registers, such as neglects in notifying cases, and lack of detailed information on exposures (Halkier-Sorensen 1998; Diepgen 2003; McDonald et al. 2005). It is also evident that some cases are missed because the occupational background of the diseases may not be recognised. Although false positive diagnoses may occur, the FROD is probably more prone to underestimate occupational diseases than to overestimate them.

6.5.2. Telephone interview

The study population represented the workforce adequately, as it covered about 4% of the machinists in Finland, and the participation rate was reasonably good, 79%. In addition, the population was distributed over a fairly large geographical area, and different machining techniques, products, and company sizes were included. The present computer-assisted telephone interview method, as well as the structured questionnaire on skin and respiratory symptoms and atopy, are well established and they have been used in occupational health studies also earlier (Leino et al. 1997; Kaukiainen et al. 2005; Jaakkola et al. 2007).
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It is possible that self-report underestimates hand eczema (Meding and Barregard 2001). It was also shown recently that a telephone interview underestimates skin symptoms as compared to a mailed questionnaire, probably because there is not enough time for the respondent to consider some of the more difficult questions on the phone (Olsen et al. 2008). Despite the reported underestimation, self-report is considered to bring out skin symptoms of concern to the respondent (Smit et al. 1992; Susitaival et al. 1995). These features are likely to apply also to inquiries on respiratory symptoms.

The most important shortcoming in the present cross-sectional telephone interview was the small size of the control group. This made the confidence intervals of the OR's wide, especially as regards rare symptoms. By dividing the metal workers into high and low exposure groups according to the total aerosol measurements, respiratory symptoms could be compared between larger populations, and indeed, statistical significance was then shown also for some rare symptoms. A dose-response pattern for several respiratory symptoms was detected when comparing risks across increasing quartiles of aerosol concentration. However, some of the ORs were very close to the limit of statistical significance and should therefore be considered as suggestive.

The general shortcoming of the cross-sectional studies, namely the healthy workers effect, according to which subjects with symptoms have left their work prior to the study, cannot be ruled out (Eisen et al. 1997). Male office workers were chosen as controls both for practical reasons and because they were expected to have a similar age distribution and e.g. smoking habits, but no occupational exposure to skin or respiratory allergens or irritants. Naturally, the different socio-economic status of the office workers compared to the machinists, might affect the results.

Assemblers working in the metal companies were not used because they may be exposed to aerosols of MWF or they may handle newly machined pieces contaminated with MWF. It is possible that also the present control group had been occasionally exposed to MWFs; however, persons reporting more than one hour of exposure to MWF per month were excluded. It is also possible that the machinists with more symptoms had transferred to office work or that more allergic persons generally look for clean jobs such as office work (Eisen et al. 1997). However, the office workers were required not to have worked with MWF
for more than one month ever during their life, indicating that there were no former machinists among the controls. If either an exposed or a more allergic control group had been used, the present results would have underestimated the true effects of MWF exposure.

The study on respiratory symptoms according to exposure was limited by the following facts: 1) due to the large number of participating companies, the workplace measurements were not done in parallel with the telephone interview; instead, they were conducted up to about eight months after the interview, 2) some interviewed workers could not be observed in the workplace assessments because they were not working at the time of the visit, 3) some of the interviewed machinists could not be coupled to the workplace measurements because they were not identified on the basis of the machine coding given in the interview or because their machine was not used at the time of the visit and 4) the short term aerosol measurements can only be considered to be rough estimates of the true exposure.

Concerning the detailed exposure measurements conducted in 10 machine shops, only 42 workers were observed, and the population was too small for drawing any conclusion on respiratory symptoms associated with specific components of MWFs in the air.

6.5.3. Air measurements

The DataRAM aerosol photometer has been shown to overestimate exposure as compared to aerosols quantified with gravimetric methods, meaning that the aerosol concentrations in the presently studied companies would have been lower if measured with gravimetric methods. Obviously, the present measurements are only rough estimates of the long-term exposure. It should also be borne in mind that the DataRAM measures all aerosols and it is therefore not specific for MWF-borne contaminants is the air.

In the detailed workplace measurements, the protocol and the sampling locations were carefully planned with experienced occupational hygienists. Measurements of total aerosol, oil mist, inhalable dust, VOC, aldehydes and microbial contaminants were carried out with well-established and validated sampling and analysis methods. The new hand-rinsing method was tested, and the recovery efficiency
of alkanolamines was determined prior to the field experiments. The analysis of alkanolamines was validated prior to the field experiments. Several machining techniques and MWFs from companies of different sizes were chosen for the measurements in order to obtain samples representative of the industry as a whole. The worst locations, according to total aerosol measurements, were chosen as sampling sites. Consequently, the particle contaminants, namely oil mist, dust and microbial results may overestimate the true exposure.

6.6. Practical implications

6.6.1. Recommendations to workplaces and occupational health services

In order to promote the health of machinists, more attention should be paid on both skin and respiratory exposure to MWF, and to mild dermatoses and respiratory symptoms. Skin exposure should be taken into account in workplace risk assessments. The best way of preventing skin problems of machinists is to use protective gloves fitted for MWFs: these include e.g., textile gloves coated partly with nitrile rubber. Protective creams are not recommended, as their effectiveness varies, and they may even irritate skin (Schlieman 2007). In addition, they may contain skin sensitizers such as formaldehyde liberators and alkanolamines. Protection is important especially in patients with known contact allergy to water-miscible MWF ingredients such as formaldehyde, alkanolamines or iodopropynyl-butylcarbamate, as these are common in modern MWFs and are therefore not easily avoided simply by changing to another MWF formulation. In general, it should be borne in mind that the water-miscible MWFs are largely composed of similar or related ingredients, and that all formulations are very likely to contain some skin sensitizing components.

If an enclosed and ventilated machine is used, the operator is advised to wait a moment before opening the machine enclosures after a machining phase to avoid inhaling the aerosols. Also, the use of compressed air in cleaning up the newly machined pieces should be reduced to a minimum, as it has recently been shown to increase respiratory expo-
sure substantially (Lillienberg et al. 2008). Regular control measures are naturally needed to avoid extensive microbial growth in the MWF sump; practical help for this can be obtained from the MWF suppliers. Current oil mist separators seem not to be suitable for small-molecular-weight chemicals such as formaldehyde and alkanolamines. Therefore, in order to diminish respiratory exposure, new air cleaning methods should be introduced, or the machine shop's air should be lead out and replaced with fresh air instead of circulating it. If there is exposure to other chemicals than MWFs in the machine shop, for instance to paints, glues or welding fumes, they should also be considered as possible causes of respiratory symptoms.

6.6.2. Diagnostic implications

To improve the diagnostics of skin diseases in machinists, testing with the patients' own materials from work is highly recommended provided that patch test concentrations are planned carefully. It is also important to update patch test series in order to keep up with MWF formulations. The current Finnish recommendation for the patch test series used for machinists, namely the "oils series" should be revised, and at least MEA, DEA and IPBC should be added to it. Analysis of the patient's own MWFs is needed if allergy to MWF ingredients is shown, even though the respective allergens are not listed in the safety data sheet of the patient's MWFs. If the patient is allergic to isothiazolinones, they should be analysed from the used MWFs as they may be added to the bulk MWFs in use. In investigations of asthma, careful detection of exposure to both MWF and other chemicals provides means to optimize bronchial provocation tests and to avoid unnecessary testing. As there is very little knowledge on the specific asthma-causing agents in MWFs, it would be very informative to test the MWF ingredients separately, if a positive reaction has been found in BPTs with MWF, and if the patient's clinical condition allows it. Also, BPTs with the used MWFs could be taken into consideration in cases where there is a strong suspicion of occupational asthma related to machining, and if other BPTs, such as those with unused MWF, have not provoked a positive reaction.
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6.6.3. Recommendations for workplace assessments

When monitoring the workplace air, it is recommended to measure at least total aerosol, the concentration of which should remain near or below the NIOSH recommended exposure limit of 0.5 mg/m³, which is used for MWF operations. As it was shown that machinists' respiratory symptoms increased at about 0.17 mg/m³ total aerosol concentration, it is even recommended to aim at that concentration. Other chemicals that should be monitored include alkanolamines, which are common in modern MWFs, and which are easily quantified in the air with the new method. The OEL for diethanolamine of 2 mg/m³ can be used for the total alkanolamines, although it is recommended to aim at clearly lower concentrations, namely to about 0.2 mg/m³. This level was achieved in most of the measurements in the present study. Oil mist should be measured if the total aerosol concentration is near or above 1 mg/m³ or if neat oils are used, and it should not exceed the ACGIH recommended limit of 0.2 mg/m³. If the total aerosol is below 1 mg/m³, the concentration of oil mist is probably very low and thus not informative. Formaldehyde is likely to be present in the air of machine shops; according to the present results, a concentration below 0.2 mg/m³ is achievable. Measurement of VOCs is usually not needed, but as they provide plenty of information on small-molecular-weight compounds, they might be useful for diagnostic purposes, i.e., if occupational asthma is suspected. In addition to air measurements, occupational hygienists should pay much more attention to the skin exposure of machinists, and they should be prepared to advise the workers in selecting gloves suitable for MWFs.
VII CONCLUSIONS

The present study showed a high incidence of occupational skin diseases in machinists, and it also showed that most of the dermatoses were caused by MWFs. In addition, skin symptoms were frequently reported by machinists in the cross-sectional interview study. Based on the above-mentioned observations, much more attention should be paid to the skin protection of machinists.

It was shown that occupational asthma and rhinitis are very seldom notified in machinists, and that chemicals from surrounding processes, i.e., paints and metal fumes, were more common inducers of asthma than the MWFs. The small incidence of occupational respiratory diseases was not reflected in the cross-sectional study according to which various respiratory symptoms were frequent in workers exposed to MWF. The results emphasize the difficulties in showing the causal relationship between work and respiratory diseases especially when the causative agent is not a respiratory sensitizer. The present study provided new information on the association between exposure and respiratory symptoms, as the symptoms were shown to increase at and above the median aerosol concentration of 0.17 mg/m³ in the workshops' general air. It was also shown that a long history of exposure to MWF aggravated symptoms related to chronic bronchitis suggesting the effect of cumulative exposure on these symptoms. The results suggest that regardless of the overall satisfactory control measures, improvements in occupational hygiene are still needed, and that they should be targeted to achieve total aerosol concentration of about 0.17 mg/m³.

The measurements of several MWF-borne, small-molecular-weight chemicals in the workshops' air provided new information on substances that may affect the development of respiratory symptoms. It seems
worthwhile to continue to investigate in detail the chemicals in the workplace air, as such information may eventually lead to a better understanding of the respiratory effects of MWF. The study also provided tools for revising workplace measurement practices. For example, most of the concentrations were clearly below the respective OELs, indicating that current exposure limits are not applicable to MWF-operations. Thus, many of the OELs should be lowered. Also, changing the practice towards reaching clearly smaller yet achievable target values, such as 10% of the respective OELs, would serve as a useful guideline for improving working conditions. The new method for assessing skin exposure to alkanolamines and thereby to MWF was proven sensitive and easy to apply. According to it the skin proved to be the primary exposure route of alkanolamines. The present study on skin sensitizers in MWF provided useful information for diagnosing skin diseases, and it also showed that all water-miscible MWFs tend to contain skin sensitizers even if they are not listed in the safety data sheets.
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Occupational dermatitis and allergic respiratory diseases in Finnish metal working machinists

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Occupational dermatitis and allergic respiratory diseases in Finnish metalworking machinists

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Aim
To investigate the incidences and trends of occupational skin diseases (OSDs) and allergic respiratory diseases (ARDs) in machinists working in the fabrication of metal products.

Methods
Data from the Finnish Register of Occupational Diseases during 1992–2001 were analysed. Incidence rates for skin and respiratory diseases of machinists were calculated and compared to the total working population. The patients investigated at the Finnish Institute of Occupational Health in the same period were described in detail.

Results
A total of 279 dermatoses and 34 ARDs were reported. Skin diseases accounted for 27% of all occupational diseases. The incidences of the skin and respiratory diseases were 1.6 and 0.2 cases per 1000 person-years, respectively. This represents a 3-fold risk for getting an OSD compared to the total working population. The number of allergic contact dermatitis (ACD) increased 3-fold during the study period. The most common causes of ACD were metalworking fluids (MWFs) and their ingredients such as formaldehyde, ethanolamines and colophony. Eighty-five per cent of ARDs were asthmatics. The commonest causes of asthma were metal dusts and fumes, epoxy resins and hardeners and MWFs and their components.

Conclusions
Contact dermatitis is a common occupational health problem in metalworking machinists, whereas occupational respiratory disease is rare. Only a few specific chemicals in the metalworking have thus far been identified as respiratory allergens. Specific skin tests and inhalation challenge tests with MWFs and their ingredients are recommended if an OSD or a respiratory disease is suspected.

Key words
Contact allergy; machinists; metalworking fluids; occupational asthma; occupational respiratory disease; occupational rhinitis; occupational skin disease.

Introduction
Metalworking machinists are exposed to diverse skin and respiratory irritants and sensitizers at work. Metalworking fluids (MWFs), mainly used as 2–10% emulsions in water, are among the commonest chemical exposures. Most MWFs are mixtures of a base oil and auxiliary substances such as emulsifiers, antimicrobial agents, corrosion inhibitors, extreme pressure additives, etc. In addition, machinists can be exposed to lubricating oils, assembling chemicals and to chemicals originating from surrounding processes such as welding and painting.

Contact dermatitis among machinists has often been reported, mostly due to the components in MWFs [1–3]. Machinists’ dermatitis has also been observed in epidemiological studies based on the national morbidity statistics and the statistics from dermatology clinics [3–5]. Clinically investigated asthma and rhinitis in machinists have rarely been reported [6–9]. Most of the epidemiological studies have been cross-sectional questionnaire studies or plant surveys, some connected with epidemic outbreaks of respiratory symptoms in a specific plant or process [10,11].

We report here Finnish statistics on occupational skin diseases (OSDs) and allergic respiratory diseases (ARDs) of machinists.

Methods
The data in the Finnish Register of Occupational Diseases (FROD) and in the patient register of the Finnish
Institute of Occupational Health (FIOH) during 1992–2001 were analysed.

FROD is a national morbidity record where the cases of occupational disease diagnosed in Finland are recorded. Notification is made by the diagnosing physician who may be a private practitioner or work in any health care unit. In the FROD, each case of OSD and ARD is recorded with a maximum of three diagnoses and three causative agents. In the case of simultaneous allergic and irritant skin disease, the allergic disease is recorded as the main diagnosis, and in case of simultaneous asthma and rhinitis, the one that is more clinically pronounced is recorded as the main diagnosis. OSDs are classified into allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), contact dermatitis of unknown mechanism (ACD/ICD), contact urticaria (CU) or protein contact dermatitis, occupational acne, paronychia, skin infections, other skin diseases and unspecified skin diseases. ARDs are classified into asthma, rhinitis, allergic alveolitis and organic dust toxic syndrome (ODTS). The collection and reporting scheme of the data have been described earlier [5,12].

Up to 1999, data were collected from the occupational category of turners, machinists and toolmakers (class no. 751) according to the Finnish classification of occupations [13]. Thereafter, machinists were classified in the FROD as machine-tool setters and setter operators (class no. 7223), metal-wheel grinders, polishers and tool sharpeners (class no. 7224) and machine-tool operators (class no. 8211) [ISCO-88 (COM)]. The number of machinists was ~14 000–20 000 in 1992–2001, and ~4% of them were women (Statistics Finland). In order to get more specific information on clinical and causative factors of occupational allergic diseases of machinists, the cases investigated at FIOH were extracted from the FROD, and coupled with data from the patient register of FIOH. One case was removed because he had not been investigated at FIOH (wrong coding) and two cases because of wrongly coded occupation.

During 1992–2001, 17% of OSDs and 50% of ARDs were investigated at FIOH. All patients with a suspicion of occupational contact dermatitis were patch tested with the Finn Chamber method according to the recommendations of the International contact dermatitis research group, with modified European standard series and series according to exposure. The additional series included oils and cooling fluids, antimicrobials, ethanamines and coconut fatty acid derivatives. Most of the patients were also patch tested with products from their workplace. Standard skin prick tests including common environmental allergens were also used in all patients suspected of having occupational dermatitis. Additional skin prick tests, e.g. carboxylic anhydrides, were performed according to exposure when it was clinically relevant [14]. The patients were followed up for 6 months after the diagnosis either with a mailed questionnaire or with a visit to FIOH.

The investigations for occupational asthma or rhinitis at FIOH were performed according to the international guidelines [15,16]. Before the challenge tests, the stability of the lower airways was assessed with spirometry and by following FEV1 and peak expiratory flow (PEF) for 24 h. Skin prick tests were performed using the standard series. Additional skin prick tests with metal compounds and carboxylic anhydrides, and specific serum IgE antibody tests (radio allergy sorbent test) with isocyanates, were performed according to the exposure.

When occupational asthma was suspected, the inhalation challenge tests were performed using the substance to which the patient connected his symptoms, was sensitized to or was associated with falls in PEF in the workplace. Among the chemicals used in the challenge tests were MWFs (diluted, unused), diethanolamine (DEA), disocyanates and epoxy resin compounds. The inhalation challenge tests were carried out in an exposure chamber for 15–30 min. For diisocyanates and metal salts, a standard protocol was applied, whereas with the other agents, the patients handled the chemical as at work [17,18]. MWFs were either warmed to 40°C in an open dish or aerosolized to the chamber by compressed air. Epoxy resins and hardeners containing carboxylic anhydrides were heated to ~60°C. The air concentrations of the substances were kept below the occupational exposure limit values to avoid irritant reactions. A control challenge without the active chemical was performed in each patient. A PEF drop of ≥15% during the first hour, or a drop of ≥20% thereafter for 24 h, was regarded as significant. Lung function was followed up with a microspirometer (One Flow; STI Medical, St Romans, France or Micro Plus Spirometer, Micro Medical, UK).

If occupational rhinitis was suspected, the upper airways were examined and followed by an otorhinolaryngologist before and, for 1 h, after the challenge. The diagnosis was based on the amount of nasal secretion, nasal blockage and acoustic rhinometry measurements [19]. This study design was approved by the Ethics Committee on occupational health issues of the hospital district of Helsinki and Uusimaa.

Results

During 1992–2001, a total of 1027 occupational diseases were diagnosed in machinists. The incidence was 5.9 cases per 1000 person-years among machinists and 2.7 cases per 1000 person-years in the total workforce. The most important occupational diseases were hearing loss (31%), skin diseases (27%) and strain injuries (26%). Asbestos-related diseases constituted 9%, other diseases 4% and ARDs 3% of the occupational diseases.

During the study period, a total of 279 cases of OSDs in 262 patients (91% men) were reported. Ninety-seven
per cent of the dermatoses were contact dermatitis of which 144 (53%) were ICD and 107 (39%) ACD. The rest were unspecified ACD/ICD (21 cases), CU (one case), occupational oil acne (one case) and other or unspecified skin diseases (five cases). Fifteen people had two and one had three notified skin diseases (combinations of ACD and/or ICD). The number of ACD cases per year increased during the study period from four to 13, while the number of ICD increased from 10 to 19 cases. A total of 34 cases (32 in men) of ARDs in machinists were reported, one to seven cases yearly. The commonest diagnosis was asthma, numbering 29 cases. There were four cases of allergic rhinitis and one case of allergic alveolitis.

The 10-year incidences of OSD and respiratory disease are shown in Figure 1. Incidences of ACD, ICD and asthma according to age are shown in Figure 2. The annual incidence of skin disease in machinists increased from 1.0 to 1.5 cases per 1000 employees while in the total working population it decreased from 0.5 to 0.4. Twenty-four cases (9%) of the skin diseases were in women. The incidence of all skin diseases among women was 3.3 cases per 1000 person-years compared to 1.6 among men. Only two cases of asthma were reported in women.

Cases of ACD and asthma and the main causes are listed in Table 1. A total of 121 (89%) of the patients were men. Their mean age was 43 years. The average exposure time was 15 years (2 months to 44 years). The most common causes of ACD were MWFs, their ingredients, such as formaldehyde, ethanolamines and colophony, and metals. Twenty-five per cent of the cases were investigated at the FIOH, most of them due to specific MWF ingredients. The commonest inducers of ICD were MWFs, oils and lubricants, organic solvents, wet and dirty work and washing agents. The most important causes of asthma were metals and synthetic resins. In two persons, both an OSD and ARD were notified. Both of the cases were investigated at the FIOH. One had ACD caused by formaldehyde and asthma caused by DEA (patient no. 12 in Table 2 and patient no. 3 in Table 3; note that Tables 2 and 3 are available as Supplementary data at Occupational Medicine Online). The other had ACD, CU and rhinitis caused by methylhexahydrophthalic anhydride (MHHPA) (patient no. 22 in Table 2). This case has been reported in detail [20].

Forty-five (17%) of the cases of dermatitis in the FROD were reported from the FIOH. Twenty-seven (60%) of them were of a main diagnosis of ACD and 18 (40%) that of ICD. In skin prick tests, 12 (27%) of the patients had positive reactions to environmental allergens in the standard series. In skin prick tests, only one patient had a positive reaction to occupationally relevant allergens, namely to MHHPA. Details of the patients with occupational ACD are shown in Table 2. All diagnoses of ACD required occupationally relevant contact allergies discovered on patch testing. Fifteen patients had eczema only on the hands. The rest had eczema also on the wrists, forearms, face or legs. Seventeen of the 18 patients with ICD as the main diagnosis had hand eczema. One patient had ICD on his arms, face, neck and legs due to heat and sweating. MWF was the main cause in 15 cases of ICD. Other main causes of ICD were soldering fluid and dirty work. After a 6-month follow-up, 24 (53%) of the patients with ACD still had skin symptoms. Eventually, 21 (47%) patients had to change their work tasks or job, or retire mainly because of skin problems.

Fifteen (50%) of the cases of ARDs recorded in the FROD were reported from the FIOH: 13 cases of asthma and two cases of rhinitis. The details of the asthma patients at FIOH are in Table 3. Seven of the patients
were ex-smokers and two were current smokers. Six of the patients had positive reactions on the standard skin prick test series. Exposure times ranged from 1 day to 34 years. Dyspnoea, cough and wheezing were the commonest symptoms. Eight of the patients had started regular asthma medication, but in the challenge tests, only one patient was on regular medication (patient no. 12, Table 3). Workplace PEF monitoring was carried out in eight cases. IgE-mediated sensitization to workplace compounds was shown in one asthma and two rhinitis patients, all of whom were sensitized to carboxylic anhydrides.

Occupational asthma was confirmed by specific challenge tests in 12 cases and by a workplace challenge in one case. The FEV1 drops varied between 16 and 37% and the PEF drops between 17 and 30%. Seven asthmatic reactions were late, four were immediate and two were dual. Asthma medication was started or continued in 12 cases. Occupational rehabilitation was recommended in four, and avoidance of exposure in the other cases.

The rhinitis cases were caused by carboxylic anhydrides. One diagnosis was based on work-related symptoms, exposure, IgE-mediated sensitization to MHHPA and other cases from the same workplace. The other patient did not get a positive nasal or lower airway reaction in MHHPA challenge, but developed a skin reaction. The final diagnosis was based on symptoms, IgE-mediated sensitization to carboxylic anhydrides and occupational CU from MHHPA (patient no. 22, Table 2).

**Discussion**

The present study confirms that among machinists chemically induced OSD is common, whereas occupational respiratory disease is very rare. During the study period, OSD increased and risk was higher in women and young age groups. The causative factors of OSD were mainly the ingredients of MWF whereas respiratory diseases were mainly caused by other exposures.

Skin diseases are common occupational diseases in modern industrialized countries, and machinists have been found to be among high-risk occupations for occupational contact dermatitis [3,4,5,21]. The incidence of OSD in machinists (1.62 per 1000 person-years) in the present study was quite high compared to previous register-based studies with incidences ranging from ~0.46 to 1.62 per 1000 persons per year [4,22,23]. However, international comparisons are difficult to make due to differences in notification procedures and reporting and definition of occupational group. Nevertheless, the prevalence of clinically assessed minor or major skin disorders in populations of machinists has been >25% in cross-sectional studies, suggesting that the morbidity records highly underestimate the incidence of OSD [4,24–26]. The finding that ICD was more common than ACD is in accordance with results of earlier studies [27]. The increase in incidences of OSD during the study period is probably due to the poor employment situation at the beginning of 1990s and to improvements in diagnostics such as increase in knowledge about the
skin-sensitizing chemicals of metalworkers during the 1990s [1,2,14,28–30].

The results indicate that female machinists are at higher risk of getting OSD than men. Our results are in line with previous studies in which the higher risk for hand eczema in women has been associated with wet work such as household work [31]. The higher rates of ICD in the young age groups may be due to skin atopy and irritative factors in machining. It has been shown that childhood atopic dermatitis is a risk factor for ICD and that atopic dermatitis manifests itself especially in the early years of working life [32].

The commonest inducers of ACD among machinists were antimicrobials, especially formaldehyde released from formaldehyde liberators in MWFs [3]. The MWF formulations constantly change, and it is important for clinicians to keep up with new ingredients used in MWF. An example of a new preservative in MWF is iodopropynyl butyl carbamate (IPBC) [33]. Recently, we had a case of occupational ACD to IPBC at FIOH. Contact allergy to ethanolamines may be under-diagnosed in Finland, as usually only triethanolamine (TEA) is included in test series. At FIOH, TEA has been tested since 1991 and DEA and MEA since 1997. Plastic or rubber chemicals are not typical contact allergens in machinists. The cases caused by rubber chemicals are mostly due to wearing of protective rubber gloves, although MWFs and other lubricating oils may contain the same chemicals [2,34,35].

Our results showing a low risk of occupational asthma in machinists differ from observations in the UK where the incidence of asthma within some machining-related occupations was 2-fold higher compared to our results, and where MWF ranked 13th of the asthma-causing agents reported by chest physicians [36]. The difference is largely due to the different notification systems and criteria of occupational asthma. It was recently reported

<table>
<thead>
<tr>
<th>Causative agent</th>
<th>No. of ACDs (FIOH cases)</th>
<th>No. of asthmas (FIOH cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial agents</td>
<td>34 (10)</td>
<td>0 (0)</td>
</tr>
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<td>Formaldehyde and formaldehyde releasers</td>
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</tr>
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<td>Isothiazolinones</td>
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</tr>
<tr>
<td>Methylenebromogluaronitrile</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>Other or non-specified antimicrobials</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>MWFs (ingredient not specified)</td>
<td>18 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Metals and metal compounds</td>
<td>12 (1)</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Cobalt and its compounds</td>
<td>6 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Nickel and its compounds</td>
<td>4 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Chromium and its compounds</td>
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<td>3 (1)</td>
</tr>
<tr>
<td>Welding fumes</td>
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<tr>
<td>Hard metal dust</td>
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<td>Plastic chemicals</td>
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<td>7 (5)</td>
</tr>
<tr>
<td>Epoxy resins</td>
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</tr>
<tr>
<td>2,4,6-Tris-(dimethylaminomethyl) phenol</td>
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</tr>
<tr>
<td>Polyamines (epoxy hardeners)</td>
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<tr>
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<td>Resins and plastics not specified</td>
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<tr>
<td>Alkanolamines</td>
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</tr>
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<td>Monoethanolamine</td>
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</tr>
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<td>DEA</td>
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<tr>
<td>Causative agent not reported</td>
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<td>2 (0)</td>
</tr>
</tbody>
</table>

Cases investigated at FIOH are in parenthesis.
that occupational asthmas account for only 5% of all adult-onset asthmatics in Finland suggesting that, in general, occupational asthmas are difficult to diagnose [37]. In Finland, chemically induced occupational asthmas are usually diagnosed at FIOH with specific inhalation challenge tests. It is unusual for all suspected causative agents to be tested, as the test protocol is burdensome for the patients. Another drawback in specific challenge tests is that the cumulative effect of several irritants is missed. Thus, it is possible that the present results underestimate machinists’ asthma and rhinitis.

Causative agents of ARD in machinists differ from the ones of ACD due to different immunological mechanisms in the skin and lungs, and differences in exposure factors, such as accessibility of the agent to the upper airways or the lungs. As shown in the present study, the typical respiratory exposures in machining rarely cause IgE-mediated diseases. ARD induced by diisocyanate and carboxylic anhydride may be IgE mediated, whereas to our knowledge, IgE sensitization to epoxy amine hardeners has not been reported [17,38]. In the FIOH patients, exposure to plastic chemicals originated mostly from processes other than machining. Some asthmas induced by metal compounds have been connected with IgE sensitization, but none of the present FIOH patients were sensitized to metals [39]. Although irritating to the airways, MWF ingredients are not common causes of occupational asthma. Endotoxins in MWFs may cause various respiratory symptoms, but the mechanism behind symptoms other than those in ODTS is unclear [40]. In Finland, allergic alveolitis in machinists is quite unknown possibly because their occupational exposure is not considered as a typical inducer of alveolitis or because of generally high microbiological quality of workplace air.

According to Finnish legislation, physicians are required to report every case of occupational disease to the FROD. A case is recorded in the FROD regardless of whether the disease is finally accepted and compensated by the insurance company. Also some non-occupational diseases or symptoms may be notified. Nonetheless, in our opinion, a more serious drawback is incompleteness of the data due to under-reporting and under-diagnosis [5]. Only the main diagnoses in the FROD data were analysed in this study because information obtainable from the additional diagnoses of non-FIOH patients is limited. In part of the cases investigated elsewhere, the specific causative agents are not investigated, but the occupational origin of the diseases is recognized according to common national principles. All new notifications are checked by the researchers at FIOH prior to data recording in order to correct the most obvious mistakes in coding of the diagnosis or causing factors. The general shortcomings of morbidity statistics have been discussed previously by other researchers [4,5,21,36,37].

In conclusion, the chemicals used in metalworking may cause both skin and respiratory allergies. The causative agents, immunologic mechanisms and cumulative effect of several irritants and sensitizing chemicals regarding the onset of occupational asthma and rhinitis need further investigation. In order to validate the present results, epidemiological studies coupled together with clinical investigations are needed.

Acknowledgements

We thank Anja Saalo for providing the data from the FROD used in this analysis. The study was funded by the FIOH and the Finnish Work Environmental Fund. Statement of the roles of the authors—R.J.: experimental design, data analysis and critical revision of the manuscript; K.S.: experimental design, data analysis and writing of the manuscript; K.A.-K.: patient register analysis and writing of the cases of FIOH skin patients; R.P.: patient register analysis and writing of the cases of FIOH respiratory patients and T.T.: experimental design and critical revision of the manuscript. Statement of ethical standards: relevant ethical standards and current best practice have been adhered to this study. Statement of approval of the writers: all authors have read and approved the manuscript.

Conflicts of interest

None declared.

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21. Halkier-Sorensen L. Occupational skin diseases: reliability and utility of the data in the various registers; the course from notification to compensation and the costs. A case study from Denmark. *Contact Dermatitis* 1998;39:71–78.


Table 2. Details of the patients with occupational allergic contact dermatitis or contact urticaria investigated at the Finnish Institute of Occupational Health (occupationally non-relevant reactions to neomycin, bacitracin, balsam of Peru, fragrances, merthiolate (thiomersal), Compositae mix, captan, chloracetamide, 4-phenylenediamine (PPD) and benzoylperoxide are excluded).

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, sex, occupation</th>
<th>Occupationally relevant contact allergies on patch testing</th>
<th>Exposure</th>
<th>Causatives of occupational ACD</th>
<th>Other diagnosis</th>
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<tbody>
<tr>
<td>1</td>
<td>38, M, turner</td>
<td>DEA ++, nickel sulfate ++, MWF1 ++</td>
<td>MWF1: DEA 3% *</td>
<td>DEA in a MWF</td>
<td>Exacerbation of ACD from nickel at work</td>
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<td>DEA +</td>
<td>MWF1: 14% DEA *</td>
<td>DEA in MWFs</td>
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<tr>
<td>3</td>
<td>50, M, grinder</td>
<td>MEA +, DEA ++, cyclohexylthiophthalimide ++, MWF2 ++</td>
<td>MWF1: MEA 8.1%, DEA 2.1% *</td>
<td>MEA, DEA in MWF and cyclohexylthiophthalimide in rubber seals;</td>
<td>OICD from MWFs</td>
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<td>4</td>
<td>40, M, grinder-sharpener</td>
<td>MEA +, DEA ++</td>
<td>MWF1: MEA 9.4%, MWF2: DEA 1.9% *</td>
<td>MEA in a MWF;</td>
<td>OICD from MWFs</td>
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<td>5</td>
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<td>formaldehyde ++, abietic acid +, MEA ++, DEA ++</td>
<td>MWF: MEA 0.024%, DEA 14% *, resin acids of colophony 1% *, formaldehyde &lt; 0.001%,</td>
<td>DEA, MEA and abietic acid in a MWF</td>
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<td>colophony ++, abietic acid +</td>
<td>MWF: resin acids of colophony 1.6% *</td>
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<td>OICD from metal dust</td>
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<td>22, M,</td>
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<td>MWF: tall oil 15-30% *, colophony in a MWF</td>
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http://www.occmed.oupjournals.org
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<tr>
<th>Machinist</th>
<th>Formaldehyde</th>
<th>Benzylhemiformal</th>
<th>Bioban CS 1135</th>
<th>Grotan BK</th>
<th>MWF</th>
<th>Formaldehyde</th>
<th>Hand cleansing jelly</th>
<th>Occupational asthma</th>
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<td>++,</td>
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<td>++,</td>
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<td>MWF2: formaldehyde 0.004%, colophony</td>
<td>Guideroy oil: formaldehyde 0.001%</td>
<td>Hand cleansing jelly: resin acids of colophony 15.5%</td>
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<td>MWF: formaldehyde in a MWF</td>
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<td>Machinist</td>
<td>MWF: Grotan BK 1-5%, formaldehyde 0.61%</td>
<td>MWF: formaldehyde in a MWF</td>
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<tr>
<td>36, F,</td>
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<td>Machinist</td>
<td>Additive for MWF: Grotan BK 70%, formaldehyde 16.6%</td>
<td>Formaldehyde in MWFs and antimicrobials</td>
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<td>48, M,</td>
<td>++,</td>
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<td>Sparkler</td>
<td>MWF: Grotan BK 1-5%, formaldehyde 0.99%</td>
<td>Formaldehyde in a MWF; occupational asthma from DEA (patient no. 3, Table 3)</td>
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<tr>
<td>55, N,</td>
<td>+,</td>
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<tr>
<td>CNC-</td>
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<td>44, M, machinist</td>
<td>formaldehyde ++, Bioban CS 1135 ++, benzylhemiformal ++, Grotan BK ++, (ethylendiamine +)</td>
<td>Machine cleansing agent: Grotan BK 5–15% †</td>
<td>MWF: formaldehyde 27 ppm *</td>
<td>formaldehyde in a MWF and a guideway oil; blepharoconjunctivitis allergica from formaldehyde in a MWF and a guideway oil; OICD from MWFs</td>
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<td>15</td>
<td>44, M, machinist</td>
<td>formaldehyde +, benzylhemiformal +, Bioban CS 1135 +, Grotan BK +, chloro/methyl-isotiazolinone +</td>
<td>MWF1: Grotan BK †</td>
<td>MWF2: formaldehyde 1.2% †</td>
<td>formaldehyde releasing Grotan BK in a MWF and from chloro/methyl-isothiazolinone in an additive for MWF</td>
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<td>formaldehyde ++, Quaternium 15 ++, benzylhemiformal ++, Grotan BK ++, Bioban CS 1135 ++, coconut diethanolamide ++, epoxy resin ++</td>
<td>Liquid soap: coconut diethanolamide †</td>
<td>Cream soap: coconut diethanolamide †</td>
<td>coconut diethanolamide and formaldehyde in hand-cleansers</td>
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<td>17</td>
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<td>formaldehyde ++, Quaternium 15 +, benzylhemiformal +, Bioban CS 1246 +, Bioban CS 1135 ++, Grotan BK ++,</td>
<td>MWF1: formaldehyde 0.76% *</td>
<td>MWF2: formaldehyde 0.0026% *</td>
<td>coconut diethanolamide in hand-cleansers and formaldehyde in a MWF</td>
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<td>Hand-cleansing jelly: coconut diethanolamide, formaldehyde 4 ppm *</td>
<td>Liquid soap: coconut diethanolamide †, formaldehyde &lt; 1 ppm *</td>
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<td>Sex</td>
<td>Occupation</td>
<td>Chemicals/Ingredients</td>
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</tr>
<tr>
<td>-----</td>
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<td>-------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>37</td>
<td>M</td>
<td>Machinist</td>
<td>Hexamethylenetetramine++, Coconut diethanolamide +, MWF1 ++, MWF2 +, Hand-cleansing jelly ++, Liquid soap ++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>50</td>
<td>M</td>
<td>Machinist</td>
<td>Cocamidopropyl betaine +, Liquid soap +, MWF ++, Boramine ingredient of the MWF ++</td>
<td>Liquid soap: cocamidopropyl betaine + cocamidopropyl betaine in a liquid soap, MWF containing alkanolamineborates alkanolamineborate in a MWF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>48</td>
<td>M</td>
<td>Machinist</td>
<td>Benzothiazolone +++</td>
<td>MWF: benzothiazolone 0.1% in a MWF, OICD from MWFs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>42</td>
<td>M,</td>
<td>Tool-maker</td>
<td>Euxyl K 400 +, Disperse Orange 3 ++++, Disperse Orange 1 ++++, Aminoaazobenzene +++</td>
<td>Euxyl K 400 in hand-cleansers and azo dyes in working clothes, Phosphating liquid: pH &lt; 2, Machine cleansing agent: pH 1.5, OICD from MWFs, grinding dust and acidic products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>45</td>
<td>M,</td>
<td>Driller</td>
<td>Epoxy hardener (1%) +, Positive skin prick tests: MHHPA, HHPA and MTHPA</td>
<td>Epoxy hardener (used nearby): MHHPA 98%, MHHPA in an epoxy hardener, Occupational CU and rhinitis from MHHPA; OICD from industrial oils, greases and MWFs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>45</td>
<td>M,</td>
<td>Machinist</td>
<td>Dimetoxydalbergione ++, Mansonone A ++, Palisander wood dust ++, Walnut wood dust ++</td>
<td>Sawed palisander and walnut wood dust, Palisander and walnut wood dust, OICD from organic solvents (not diagnosed at the FIOH)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
24 31, M, machinist-assembler
Epoxy glue: epoxy resin 80-100%†
epoxy resin and
methacrylates in glues and
anaerobic sealants
2-HPMA +++, EGDMA +++,
TEGDMA +++
A sealant: 2-HPMA 5-15% †
25 47, F, painter, sharpener
An epoxy paint hardener used nearby: tris-DMP 4% †
tris-DMP in an epoxy paint
hardener
tris-DMP ++
26 50, M, filer phenyl-α-napthylamine ++,
gunpowder ++
Grease: a small amount (< 0.01%) of phenyl-α-napthylamine*
phenyl-α-napthylamine in a
grease and ethylene glycol
dinitrate in gunpowder
27 49, M, tool assembler
Worked with nickel-coated steal objects
Exacerbation of ACD from
nickel at work
nickel sulfate +++

* Analysed at the FIOH
† Information in the safety data sheet or package label
‡ Additional information from the manufacturer
§ Formaldehyde liberator

M = male, F = female, MWF = metal working fluid, ACD = allergic contact dermatitis, OICD = occupational irritant contact dermatitis, MEA = (mono)ethanolamine, DEA = diethanolamine, MHHPA = methylhexahydrophthalic anhydride, HHPA = hexahydrophthalic anhydride, MTHPA = methyltetrahydrophthalic anhydride, HPMA = hydroxypropyl methacrylate, EGDMA = ethyleneglycol dimethacrylate, TEGDMA = triethyleneglycol dimethacrylate, tris-DMP = 2,4,6-tris-(dimethylaminomethyl) phenol
Table 3. Details of the patients with occupational asthma investigated at the Finnish Institute of Occupational Health

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, sex, occupation</th>
<th>Tasks</th>
<th>Work related symptoms</th>
<th>Suspected causative agents and exposure details</th>
<th>Prick tests with common environmental allergens (+/−/ND)</th>
<th>Specific IgE with workplace agents* (+/−/ND)</th>
<th>Workplace PEF (+/−/ND)</th>
<th>Positive inhalation challenge test's</th>
<th>Causatives of Occupational asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44, M, tool maker</td>
<td>grinding, machining, milling, turn-milling</td>
<td>sneezing, dyspnoea, chest tightness, itching of eyes</td>
<td>MWF, metals</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>MWF containing TEA</td>
<td>DEA and TEA</td>
</tr>
<tr>
<td>2</td>
<td>30, M, machinist</td>
<td>machining, grinding</td>
<td>sneezing, dyspnoea, wheezing</td>
<td>MWF</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>used MWF containing formaldehyde and ethanalamines</td>
<td>MWF</td>
</tr>
<tr>
<td>3</td>
<td>48, M, machinist (patient no. 12 in Table 2)</td>
<td>machining, welding, milling, grinding</td>
<td>cough, phlegm, dyspnoea, wheezing, night awakenings, nose stiffness, dermatitis</td>
<td>welding fumes (stainless steel, iron); MWF</td>
<td>−</td>
<td>−</td>
<td>ND</td>
<td>1. MWF containing DEA</td>
<td>DEA</td>
</tr>
<tr>
<td>4</td>
<td>30, M, machinist</td>
<td>machining</td>
<td>itching of eyes</td>
<td>epoxy paint and amine</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>mixture of</td>
<td></td>
</tr>
</tbody>
</table>

http://www.occmed.oupjournals.org
<p>| 5  | 56, M, turner | machining stainless steel and pieces painted with epoxy paints and amine hardeners; di-isocyanates (polyurethane insulation manufacturing in the same hall) | -- | -- | + | epoxy paint and trimethylhexamethylenedia mine hardener mixture of epoxy paint and trimethylhexamethylenedia mine hardener |
| 6  | 23, M, tester | cleaning, dyspnoea, wheezing | epoxy resin and anhydride hardener in a nearby process | + | + | + | MTHPA, PA and MHHPA containing hardener handling of carboxylic anhydrides containing epoxy resin in a workplace |
| 7  | 43, M, machinist | milling, drilling, grinding, turn-milling | sneezing, cough, dyspnoea, wheezing, dermatitis, itching of eyes | epoxy resins and anhydride hardeners used in the same hall; welding fumes and grinding dust (stainless | + | -- | ND | epoxy resin and trimethylhexamethylenedia mine hardener mixture of epoxy paint and trimethylhexamethylenedia mine hardener |</p>
<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Occupation</th>
<th>Symptoms</th>
<th>Allergen Details</th>
<th>Challenge</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>59, M</td>
<td>cast manufacturer</td>
<td>machining, gluing</td>
<td>dyspnöea, cough, phlegm</td>
<td>MDI containing polyurethane glue used in cast manufacturing</td>
<td>MDI (with inhaled steroid)</td>
<td>ND</td>
</tr>
<tr>
<td>9</td>
<td>53, M</td>
<td>balancer</td>
<td>balancing, welding</td>
<td>cough, dyspnöea, wheezing, night awakenings, respiratory infections</td>
<td>epoxy resins and anhydride hardeners (in moulding in the same hall); welding fumes (stainless steel and painted iron), soldering fumes, metals</td>
<td>six-valent chromium</td>
<td>chromium</td>
</tr>
<tr>
<td>10</td>
<td>21, M</td>
<td>grinder/machinist</td>
<td>grinding, milling, turn-milling</td>
<td>dyspnöea</td>
<td>grinding dust (hard metal, stainless steel and mild steel)</td>
<td>CoCl 0.1-110 mg/ml</td>
<td>cobalt</td>
</tr>
<tr>
<td>11</td>
<td>31, M</td>
<td>machinist</td>
<td>machining, grinding</td>
<td>cough, fever</td>
<td>MWF; welding fumes (stainless steel, mild steel, aluminium), metal dust; di-isocyanates (polyurethane insulation in the same hall)</td>
<td>grinding dust from stainless steel</td>
<td>metal dust</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>Gender</td>
<td>Occupation</td>
<td>Symptoms</td>
<td>Work Environment</td>
<td>Result</td>
<td>Location</td>
</tr>
<tr>
<td>---</td>
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<td>------------------</td>
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<td>----------</td>
</tr>
<tr>
<td>12</td>
<td>53, M</td>
<td>welding, phlegm, cough</td>
<td>welding fumes</td>
<td>-</td>
<td>ND</td>
<td>welding fumes</td>
<td>welding of stainless steel</td>
</tr>
<tr>
<td></td>
<td>work inspection</td>
<td>(stainless steel, mild steel)</td>
<td></td>
<td></td>
<td></td>
<td>of stainless steel</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>42, M</td>
<td>machining, hoarseness</td>
<td>welding fumes</td>
<td>+</td>
<td>+</td>
<td>welding fimes</td>
<td>welding of hard metal</td>
</tr>
<tr>
<td></td>
<td>driller milling, turn-milling</td>
<td>(stainless steel, hard metal)</td>
<td></td>
<td></td>
<td></td>
<td>of hard metal</td>
<td></td>
</tr>
</tbody>
</table>

*Skin prick tests or RAST (radio allergy sorbent test) according to exposure, e.g. metals, ethanolamines, formaldehyde, carboxylic anhydrides, amines, colophony, isocyanates, polyesters

M = male, ND = not done, MWF = metal working fluid, DEA = diethanolamine, TEA = triethanolamine, MTHPA = methyltetrahydrophthalic anhydride, MHHPA = methylhexahydrophthalic anhydride, PA = phthalic anhydride, MDI = diphenylmethanedi-isocyanate
II

Self-reported skin symptoms in metal workers

by


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Self-reported skin symptoms in metal workers

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Machinists and machine maintenance men working in the metal industry use metal-working fluids capable of causing irritant and allergic contact dermatitis. The objectives of this study were to find out the frequency of skin symptoms in machinists and machine maintenance men (metal workers) and to compare the risk of their skin symptoms to that in office workers (controls). A total of 726 male metal workers and 84 controls answered a structured telephone questionnaire enquiring about work, atopy, skin symptoms, their impact on life, etc. The risk of skin symptoms compared with that in the controls was estimated using a logistic regression analysis. Of the metal workers, 20% reported recurring or prolonged dermatitis on their hands or forearms during the past 12 months. The hand or forearm dermatitis (HD) affected mostly the metal workers’ mood and their activities at work. Recurring dermatitis elsewhere (DE) than in the hands and in connection with work was reported by 10%. The risk of HD was about twofold and the risk of DE was about fourfold compared with that in the controls. The HD of machinists may be severe and affect their ability to work. DE may have clinical significance in machinists.

Key words: allergic contact dermatitis; epidemiology; irritant contact dermatitis; metals; occupational.

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The machinists working in the metal industry are mainly exposed to water-soluble metal-working fluids (MWF) containing both irritant and sensitizing ingredients. MWFs are used as coolants and lubricants and in removing metal chippings from the machining site, e.g. in tooling, grinding, and drilling. Also other lubricating oils, glues, degreasers, and cleaning agents etc., are commonly used. Machinists have a high risk for dermatosis according to several publications, many of which are case reports or reports of clinical studies on populations of patch-tested machinists (1–5) or studies based on disease registers (6, 7). The incidence of skin disease in metal workers has varied between 0.46 and 3.7 cases/1000 persons per year, but definitions of occupations and the criteria for reporting vary (8–11). In two prospective studies from Germany, the 2.5- and 3-year cumulative incidence of HD in metal worker trainees was about 23% and 15%, respectively, whereas in cross-sectional studies, the prevalence of HD in metal workers or machinists has varied between 10% and 27% (12–16). In a recent study based on the Finnish Register of Occupational Diseases, the incidence of a skin disease in machinists (1.62 per 1000 person years) was about threefold compared with that in the total working population (17). There are no cross-sectional studies on dermatitis among machinists in Finland. Thus, it has been unknown whether cases are missing from the statistics or whether the frequency of skin symptoms in the Finnish machinists is similar to that in machinists elsewhere.

In the present survey, the frequency and causes of self-reported skin symptoms in machinists and machine maintenance workers were studied using data collected by a structured telephone interview. The risk of skin symptoms was compared with that among office workers not exposed to MWF, and the role of skin and respiratory atopy was estimated. This survey is part of a large machinist study in Finland that includes a prevalence study and a clinical study of skin and respiratory symptoms and diseases, an assessment of exposure to chemicals and a study of consequences of a diagnosis of occupational skin and respiratory disease in machinists. Other parts of the study have been and will be reported elsewhere (17–19).
Materials and Methods

Subjects

The study subjects consisted of machinists and machine maintenance men working in metal companies located in the cities of Helsinki, Tampere, and Turku and their surrounding areas in the southern part of Finland. The subjects worked in companies where machining was one of the main activities, and which were listed in the membership register of Mechanical Engineering Employers in Finland. The work included manufacturing of tools, metal packages, and bodies and parts of vehicles and machines. Contact information of all machinists and machine maintenance workers who were regularly exposed to MWF were obtained from the personnel manager or the safety officer of each company. The worker was included as a subject if he was exposed to MWF at least 1 hr per week. The companies were divided into 3 categories according to the number of machinists: the small enterprises had less than 15, the medium-sized enterprises had 15–50, and the large enterprises had more than 50 machinists. The exposed population consisted of a total of 961 machinists and maintenance men (referred to as metal workers in this article) in 64 companies: 28% of the subjects worked in small companies, 27% in medium-sized companies, and 46% in large companies. Of the total of 961 metal workers, 757 (79%) participated and 726 (95%) were men. 34 (4%) were machine maintenance men. The 85 controls consisted of male office staff of the large companies, representing several occupations such as technical draftsmen, CAD draftsmen, engineers, documenters, and clerks. 84 (99%) controls participated in the study. The controls did not work with MWF more than 1 hr per month, and they had not worked with MWF for more than 1 month ever during their lifetime. The mean age of the metal workers was 40.1 years (SD 10.9) and that of the controls 41.6 (SD 9.6). The mean duration of employment was 15.3 years for the metal workers and 10.1 years for the controls. The atopic symptoms of the metal workers and controls are listed in Table 1.

Questionnaire

The data were collected with a computer-assisted telephone interview during the winter 2002–2003. The structured telephone interview form was tested by the researchers prior to study. The interviewers were experienced, and they were familiarized with the questionnaire by the researchers. The questionnaire enquired about demographics, education and work history, working habits, handling of chemicals, protective measures, skin symptoms and their connection to the work, exacerbating factors, and consequences of symptoms, etc. The analysis focused mainly on skin symptoms on the hands and forearms during the past 12 months. The questions were based on questions D1–D10 and F1–F4 in the Nordic Occupational Skin Questionnaire NOSQ-2002 (20). Questions concerning atopy, life impact of dermatoses and occupational skin or respiratory diseases diagnosed by a physician were modified from questions G1–G8, A2–A4, C1–C2, D12, S2–S5, T1, E1–E5 and E7–E8, and H1–H2 in the NOSQ-2002 and from the Finnish Tuohilampi questionnaire (21). Dermatitis elsewhere (DE) than in the hands or forearms were enquired with the question: have you had recurring eczema elsewhere than in your hands or forearms during the past 12 months and related to work? The questions concerning work and exposure were specifically designed for this study.

Statistical methods

Only men were included in the analysis as there were very few women (4%) among the subjects. There were less than 1% of ‘don’t know’ answers and missing data for each question: these were excluded from the analysis. SAS and SPSS statistical software programs were used: odds ratios (OR) for the risk of hand or forearm dermatitis (HD) more than once or lasting for more than 2 weeks

### Table 1. Atopic symptoms of male metal workers and office workers

<table>
<thead>
<tr>
<th>Atopic symptoms</th>
<th>Metal workers (n = 726), n (%)</th>
<th>Office workers (n = 84), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No atopy</td>
<td>423 (58)</td>
<td>48 (57)</td>
</tr>
<tr>
<td>Atopic symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>303 (42)</td>
<td>35 (42)</td>
</tr>
<tr>
<td>Asthma diagnosed by a doctor</td>
<td>191 (26)</td>
<td>29 (35)</td>
</tr>
<tr>
<td>AD</td>
<td>36 (5)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>ADc</td>
<td>151 (21)</td>
<td>17 (20)</td>
</tr>
<tr>
<td>HD in childhood</td>
<td>25 (3)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Respiratory atopy and AD</td>
<td>52 (7)</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Only respiratory atopy (AD)</td>
<td>144 (20)</td>
<td>19 (23)</td>
</tr>
<tr>
<td>At least one sensitive skin symptom</td>
<td>384 (53)</td>
<td>26 (31)</td>
</tr>
</tbody>
</table>

AD, atopic dermatitis; HD, hand or forearm dermatitis.  
*a*Yes’ answer to question no. A2 in NOSQ-2002.  
*b*Yes’ answer to question no. A4 in NOSQ-2002.  
*c*Yes’ answer to question no. S5 in NOSQ-2002 (a subject may also have respiratory atopy or asthma).  
*d*HD in the age of 0–14; question no. D6 in NOSQ-2002.  
*e*Subjects who answered ‘don’t know’ to at least 1 question were removed from the data.  
*f*Sensitive skin symptoms were dry skin, symptoms of metal allergy, and itching when sweating, questions S2–S4 in NOSQ-2002.
during the past 12 months, and of recurring DE than in hands during the past 12 months and related to work were calculated in a multivariate logistic regression model including age, smoking, skin atopy, respiratory atopy, HD in childhood, and sensitive skin symptoms (symptoms of metal allergy, dry skin, and itching when sweating).

Results

Work tasks and exposure to chemicals

Of the male metal workers, 96% were machinists and 4% were maintenance workers, and 81% had completed vocational training in machining. The most common jobs were CNC (computer numerical control) or NC (numerical control) machinist, turner, and metal grinder. The work tasks were drilling, grinding, and tooling. More than 1 machine was used by 59% of the machinists, and 76% did some maintenance work on their own machines. 90% of the metal workers handled freshly machined metal pieces numerous times every day, and 78% got MWF splashes on their skin daily. 90% of the metal workers used protective gloves at least sometimes during the work. The most frequently used glove types were leather or leather/textile gloves, plastic- or rubber-coated textile gloves, and rubber-pimpled textile gloves.

Dermatosis

The prevalence of dermatosis and its connection to work among metal workers and controls is given in Table 2. Dermatoses were reported more frequently by metal workers than by the controls. The prevalence of HD in metal workers ever and during the past 12 months was 37% and 21% compared with 25% and 12% in the controls. Current HD was reported by 9% of the metal workers and by 5% of the controls. 16% of the metal workers had visited a doctor during their adulthood because of HD, and 6 metal workers (0.8%) had a diagnosis of occupational skin disease.

Almost all (93%) the metal workers reporting HD in the past 12 months had had it more than once or for at least 2 weeks. Of the metal workers with HD in the past 12 months, 5% reported severe and 25% reported moderate HD currently. 40% of the same respondents reported severe and 40% moderate HD at worst; 27% believed that HD had affected their mood, 20% reported that HD had affected their activities at work, and 15% reported difficulties in sleeping because of itching or pain. HD had affected also their daily activities, hobbies, and social activities.

Reporting of HD in the past 12 months was highest by those (metal workers and controls) with HD in childhood (59%) and by those with symptoms of metal allergy (45%). A high prevalence of HD was reported also by those with a history of atopic dermatitis (AD) (32%) and by those who had at least one sensitive skin symptom (28%).

More than a half of the metal workers with HD (118, 54%) believed that their dermatitis was initially caused by MWF. 68% of the HD in the past 12 months was reported to be work related. Most (82%) of those who reported work-related HD believed that it improved during times off work.

Work-related recurring eczema elsewhere than in the hands during the past 12 months (DE) was reported by 10% of the metal workers compared with 2% of the controls (Table 2). The most common locations were the face or neck and thighs or legs. Eczema both in the hands/forearms and elsewhere was reported by 4%, whereas eczema only elsewhere was reported by 6% of the metal workers.

Table 2. Dermatoses reported by male metal workers and controls according to their atopic history. Subjects answering ‘don’t know’ to questions on atopy were removed from the data

<table>
<thead>
<tr>
<th>Dermatitis</th>
<th>Metal workers</th>
<th>Office workers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No atopy (n = 423), n (%)</td>
<td>Respiratory atopya (n = 144), n (%)</td>
</tr>
<tr>
<td>HD more than once or at least for 2 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>103 (24)</td>
<td>56 (39)</td>
</tr>
<tr>
<td>In the past 12 months</td>
<td>58 (14)</td>
<td>33 (23)</td>
</tr>
<tr>
<td>and related to work</td>
<td>28 (7)</td>
<td>23 (16)</td>
</tr>
<tr>
<td>Recurring DE than on the hands in the past 12 months and related to workd</td>
<td>28 (7)</td>
<td>9 (6)</td>
</tr>
</tbody>
</table>

AD, atopic dermatitis; HD, hand or forearm dermatitis; DE, dermatitis elsewhere.

aAllergic rhinitis or asthma but no AD.
bAD (may also have respiratory atopy).
cSubjects with no atopy (57%), respiratory atopy (23%), or AD (20%).
dMay also have dermatitis on the hands.
The adjusted prevalence ORs for recurring and prolonged HD during the past 12 months and DE were higher among the metal workers than among the controls (Table 3). In the logistic regression model, the strongest risk factor for the respective HD was HD in childhood. For DE, the strongest risk factor was metal working. There were no significant differences between the machinists and the machine maintenance workers or according to the usage of gloves, as regards dermatitis.

**Dermatitis**

Our study comprised a large group of machinists and machine maintenance men working in a variety of metal companies. The prevalence of HD and DE was clearly higher in the metal workers than in the control group. It is possible that some of those with severe symptoms had already left their work prior to the present study. The 1-year prevalence of HD among metal workers in this study was higher than in machine-tool operators in a Swedish cross-sectional study (15), whereas current eczema was reported less frequently than what was found in 2 other cross-sectional studies on machinists (16, 22). In the report by Sprince et al. (16), the risk of dermatitis was associated with the use of semisynthetic MWF versus the use of soluble oil MWF. In the present study, differences in HD were not seen between machine maintenance men and machinists or according to the company size. This may be because of either rather uniform exposure of the metal workers or flawed question design. In addition, information concerning the type of MWF or the use of gloves was not specific enough to allow comparisons. In cross-sectional studies, it is difficult to see improvement in skin condition with glove use as those with skin problems usually use more gloves. Another reason for not seeing differences may be that gloves are wrongly used or of wrong type. For example, leather or textile gloves are not suitable for protecting skin from MWF, and they may even increase the exposure as they get contaminated.

In the present study, many subjects reported that their symptoms improved during times off work, and these were often regarded as being work related. However, not all symptoms reported as work related improved during absence from work. This could reflect the tendency of HD to become chronic. According to the reports of severity of the symptoms and effects of HD on different aspects of life, HD might have serious consequences to a machinist’s ability to work.

The vast majority of the occupational dermatitis cases are hand eczema (23). In the present study, also DE than in the hands in connection with work was asked. DE was much more often reported by the metal workers than by the controls, and the risk of DE in metal workers was about fourfold compared with that in the controls (Tables 2 and 3). Although these results have to be interpreted with caution, the skin symptoms on the face, neck, and thighs may be because of exposure to MWF, as machinists often get splashes of MWF on the respective skin areas. It was recently reported that 12 of 27 machinist patients at the Finnish Institute of Occupational Health with occupational allergic contact dermatitis on hands also had dermatitis, e.g. on their wrists, face or legs (17).

The risk of HD in metal workers was about twofold compared with that in the controls, but the confidence interval was wide because of too few subjects in the control group. Atopic constitution, especially AD, is a known factor in the development of HD (12, 24, 25). Also in this study, the metal workers with AD or HD in childhood had a higher risk of HD (Tables 2 and 3). The frequency of HD was high also in subjects with symptoms of metal allergy, which often means allergy to both nickel and cobalt. In these subjects, the reporting of HD may be high because of metal allergy primarily caused by non-occupational exposure. Subsequently, an elicitation of allergy may result from exposure to dissolved nickel and cobalt in MWF (5, 26). In the logistic regression model, strong positive association was found between recurring or prolonged

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**Table 3.** Prevalence odds ratios for hand or forearm dermatitis (HD) (more than once or for at least 2 weeks during the past 12 months) and for DE (recurring, related to work, and during the past 12 months) among male metal workers and office workers in a logistic regression model (sas) including the following risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No metal working</td>
<td>1.0</td>
</tr>
<tr>
<td>Metal working</td>
<td>1.7 (0.8–3.5)</td>
</tr>
<tr>
<td>No HD in childhood</td>
<td>1.0</td>
</tr>
<tr>
<td>HD in childhood</td>
<td>4.1 (1.8–9.3)</td>
</tr>
<tr>
<td>No AD</td>
<td>1.0</td>
</tr>
<tr>
<td>AD</td>
<td>1.9 (1.2–3.0)</td>
</tr>
<tr>
<td>No sensitive skin symptoms</td>
<td>1.0</td>
</tr>
<tr>
<td>Sensitive skin symptoms</td>
<td>1.0</td>
</tr>
<tr>
<td>(1–3, linear)</td>
<td>1.7 (1.4–2.2)</td>
</tr>
<tr>
<td>No respiratory atopy</td>
<td>1.0</td>
</tr>
<tr>
<td>Respiratory atopy</td>
<td>1.7 (1.1–2.7)</td>
</tr>
<tr>
<td>Age &lt;35 years</td>
<td>1.0</td>
</tr>
<tr>
<td>Age 35–46 years</td>
<td>1.5 (0.9–2.4)</td>
</tr>
<tr>
<td>Age &gt;46 years</td>
<td>1.4 (0.8–2.2)</td>
</tr>
</tbody>
</table>

AD, Atopic dermatitis; HD, hand or forearm dermatitis; DE, dermatitis elsewhere.
HD during the past 12 months and HD in childhood and between DE and AD. Part of the reported HD and DE are symptoms of AD. The concept of atopic skin diathesis (ASD) has also been used to estimate individual personal susceptibility to dermatitis (24). In the NOSQ, there are 3 questions probing for ASD: S2, S3, and S4 enquiring about symptoms of metal allergy, dry skin, and itching when sweating (20). These questions were used as a linear ‘sensitive skin symptom score’ in the regression model. The addition of 1 symptom elevated the risk of HD by OR of 1.7, meaning that the OR for HD with all 3 symptoms is 5.1.

Methodological aspects

The study population covered about 4% of the machinists in Finland, and it represented the respective workforce well. The small size of the control group is a limitation of this study. A general shortcoming of cross-sectional studies is the healthy worker effect, which may have affected also this study. It has been shown that self-report underestimates the true prevalence of skin diseases but that it is probably a good estimate of the skin diseases that are of concern to the respondent (27, 28).

In conclusion, the metal workers in this study had a higher risk for HD and DE compared with the office workers. Dermatitis on other body parts than on the hands may have clinical significance in machinists. The importance of atopy in the development of HD and DE was seen. In order to avoid disability to work as a result of severe dermatitis, those with symptoms should be identified as early as possible by the occupational health service system. The need for improving the skin care and protection of workers in metal workshops is evident.

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Respiratory symptoms and conditions related to occupational exposures in machine shops

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RESPIRATORY SYMPTOMS AND CONDITIONS RELATED TO OCCUPATIONAL EXPOSURES IN MACHINE SHOPS

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RESPIRATORY SYMPTOMS AND CONDITIONS RELATED TO
OCCUPATIONAL EXPOSURES IN MACHINE SHOPS
ABSTRACT

Objectives: Metalworking in automobile industries has been linked to respiratory symptoms and diseases, but there is little data on effects in populations representing a variety of metal companies or on dose-response relations. The aim of this study was to investigate the relations between occupational exposures in machine shops and occurrence of upper and lower respiratory symptoms, asthma and chronic bronchitis.

Methods: A cross-sectional study of 726 male machining workers and 84 male office workers from 64 companies in South Finland was conducted. All participants answered a questionnaire and aerosol measurements were performed in 57 companies.

Results: Exposure to metalworking fluids (MWF) was related to increased risk (OR ≥ 2) of upper airways symptoms, cough, breathlessness and current asthma compared to office work. Exposure to aerosol levels above median (≥0.17mg/m³ in the general workshop air) was related to increased risk (OR ≥ 2) of nasal and throat symptoms, cough, wheezing, breathlessness, chronic bronchitis and current asthma. Machining workers with ≥15-years job history experienced increased throat symptoms, cough and chronic bronchitis.

Conclusions: This large study representing machine shops in Southern Finland showed that machining workers experience increased nasal and throat symptoms, cough, wheezing, breathlessness and asthma even in environments judged as relatively clean by current exposure limits applied in Finland and elsewhere. The study suggests that improving machine shop environment could benefit the health of this workforce. It also suggests that it is time to consider reducing the current Finnish occupational exposure limit for oil mist or use of other more relevant indicators of exposure.

Key words: asthma, chronic bronchitis, machinists, metal working fluids, respiratory symptoms
INTRODUCTION

Machining workers in manufacturing fabricated metal products are exposed to several agents that could affect adversely respiratory health. The most common exposures are metalworking fluid emulsions (MWFs) and lubricating oils, but machinists may also inhale aerosols from surrounding processes, such as welding or painting. The MWFs are used for cooling, lubricating, and removing metal chippings from the machining site. They are mixtures of base oil (mineral, vegetable or synthetic oil) and various additives, including preservatives, biocides, emulsifiers and corrosion inhibitors.

Case reports have identified occupational asthma in relation to exposure to oil mists (1), metals (2-3), including chromium, nickel, and cobalt, and ethanolamines (4). Registry-based studies have suggested an increased risk of asthma, or more specifically occupational asthma, among machining workers (5-7). A recent Finnish population-based case-control study on new cases of adult asthma showed an increased OR of 4.52 (95% CI 2.35-8.70) among metal working men compared to administrative personnel and professionals (8). However, this has not been reflected in the Finnish Registry of Occupational Diseases, in which occupational asthma was reported in machinists less than in total working population (9). As a consequence of these studies, there has been concern in Finland and elsewhere that work-related asthma or at least milder forms of respiratory disease are under-diagnosed in machining workers.

Previous studies focusing on specific workplaces, mainly in automobile industry, have linked exposure to MWF with respiratory symptoms, lung function changes, and occupational asthma, bronchitis and/or allergic alveolitis (10-20). Majority of these have been conducted in North America. Our literature search did not identify any
previous study that had addressed respiratory effects of metal working in a population representing a wide variety of machining work. In addition, there is relatively little data on exposure-response relations between machining work and respiratory symptoms and diseases.

The aim of this study was to investigate the relations between occupational exposures in machine shops in South Finland and occurrence of upper and lower respiratory symptoms, chronic bronchitis and asthma. First, occurrence of these symptoms/diseases among machining workers was compared to that of office workers. Then, the occurrence of these symptoms/diseases was compared among machining workers with higher vs. lower exposure to aerosols and longer vs. shorter duration of metalworking job history.
METHODS

Study design and population

This study was a cross-sectional study of machining workers and office workers in metal industries located in and around the cities of Helsinki, Tampere and Turku in Southern Finland. Data collection took place in winter 2002-2003. The companies were selected from the membership list of the Mechanical Engineering Employers in Finland to represent machine shops in South Finland. Companies who had machining as one of their main activities were invited to participate in the study. Our aim was to recruit approximately similar amount of machining workers \((n= 250-300)\) from small enterprises (with <15 machining workers), medium-size enterprises (with 15-50 machining workers) and large enterprises (with >50 machining workers) to ensure that small enterprises would not be underrepresented in our sample, as we thought that small enterprises might have worse working conditions, so could have more health problems. Altogether 82 companies were contacted and 64 companies participated in the study (78%). The participating companies did different types of machining, including manufacturing of bodies and parts of machines, vehicles and weapons, making tools, metal packages, pipes and valves, and manufacturing metal structures for construction. Contact information of all machinists or machine maintenance men (later referred as machining workers) with regular exposure to MWF was obtained from the personnel manager or the safety officer. Information letter was sent to all of potential participants approximately one week before the planned interview, and the consent was asked in the beginning of the interview. This study was approved by the ethics committee of the Hospital District of Helsinki and Uusimaa.

A total of 961 machining workers with regular exposure to MWF were invited to the study. 757 machining workers (response rate 79%) participated: 216 from small
companies, 212 from medium-sized companies and 329 from large companies. Machining workers had to have a minimum exposure to MWF of 1 hour/week to be included. 86% of them worked with MWF daily and all of them had work periods with daily use of MWF. Only 4% of the machining workers were women (n=31), so they were too few for statistical analyses and were excluded. The final study population included 692 machinists (95%) and 34 maintenance workers (5%), altogether 726 men.

The control population consisted of male clerks and professional staff, such as technical draftsmen, CAD draftsmen, and engineers, working in the offices of the companies. The controls did not work with MWF more than 1 hour per month and had not worked with MWF for more than 1 month ever during lifetime. Of a total of 85 such office workers, 84 (99%) participated. The final study population consisted of 810 men.

**Questionnaire**

A computer-assisted telephone interview (CATI) was carried out by a trained interviewer with plenty of experience with it. CATI is an interactive computer system that aids interviewer to ask questions over the telephone and enter the answers into the database immediately. The program controls the interview logic, branching to or skipping questions as needed according to answers, and validates the logic of the data as it is entered. Exposure part of the questionnaire was designed specifically for this study, while the part on respiratory symptoms and diseases was modified from the Finnish Environment and Asthma Study questionnaire that was originally designed for studying general population samples (8, 21-23). The questionnaire inquired about personal characteristics, occupational history, use of chemicals and other agents, job
tasks, preventive measures, smoking, and occurrence of upper and lower respiratory symptoms, asthma, skin symptoms, and some general symptoms. Atopy questions were based mainly on the Nordic occupational skin questionnaire (24). According to requirements by the ethics committee, the names of interviewees were removed from the data prior to analysis. In order to be able to combine the workplace measurements to the corresponding questionnaire data, identification codes of the machining workers' main machine as well as the department were asked.

**Air measurements**

Worksite visits were performed in 60 companies to assess work habits and ventilation and other exposure control systems, and to measure aerosol concentrations at the machines (in the breathing zone of the operating machinist) and in the general air of the machining departments. Four of the 64 companies were not visited, two of these had only 1-2 machinists and two had their machining workshop located far from the study area, although their main building was in the area. Aerosol measurements were conducted in 57 companies using a hand-held real-time aerosol photometer, personal DataRAM (MIE Inc., Massachusetts, USA) (25-26). DataRAM measured the mass concentration of aerosols in size range 0.1-10 μm by measuring the amount of light scattered by the airborne particles of the materials. The measured aerosol consisted of a mixture of MWF mist and particles in the workplace air from dusts and fumes generated by the processes. Measurements were carried out in the operating area of all machines that were used during the worksite visit: the aerosol photometer was held in the breathing zone of each observed worker for 1-5 minutes during an active machining period and the average value was recorded. A total of 674 machines were observed, and a total of 380 breathing zone measurements were conducted. The rest of the machines were not in use at the time of the visit, so their aerosols were not
measured. In addition, general work air, i.e. the air in the passage areas and between the machines but not close to the machine openings, was monitored for 30 minutes to 2 hours in each machine shop and the average value over the monitoring period was recorded (a total of 57 measurements). The measurements took place at varying times between 8 a.m. and 4 p.m.

**Statistical methods**

*Outcome assessment*

Respiratory outcomes of interest were upper and lower respiratory symptoms and fever (as a marker for potential humidifier fever/allergic alveolitis) that the study subjects had experienced repeatedly or for a prolonged period during the past 12 months, at times other than in connection with a cold. Upper respiratory symptoms included nasal, throat and eye symptoms and had to occur at least weekly to fulfill our outcome criteria. Lower respiratory symptoms included cough, phlegm production, wheezing and breathlessness. Cough and phlegm had to occur at least weekly to fulfill the outcome criteria, while for wheezing and breathlessness at least monthly occurrence was applied. Chronic bronchitis was defined as occurrence of both chronic cough and phlegm production during the last year. In addition, occurrence of asthma currently and ever were investigated. Ever asthma was defined based on report of physician-diagnosed asthma ever during lifetime. Current asthma was defined based on report of physician-diagnosed asthma and current use of asthma medication.

*Exposure assessment*

First, occupational exposures in machine shops were assessed based on current job as a machining worker (i.e. machinist or machine maintenance worker) and the unexposed control group was formed of clerks or professionals working in the offices. Almost all machining workers reported exposure to MWFs (99%) and lubricating oils
(96%). As practically all workplaces used several types of MWFs, it was not possible to classify machining workers into different categories of MWFs.

Second, machinists were divided into higher and lower exposure groups by the median aerosol concentration a) in the breathing zone and b) in the general air of the workshop. The total number of machinists that could be combined to breathing zone measurements by using the machine and department codes asked in the interview was 290. Another 121 workers could be coupled to the department and thereby to the general air measurements, although their main machine was not identified or actively used during the workplace visit, so they could not be coupled to the breathing zone measurements. The total number of machinist workers in the analysis of the general work air measurements was therefore 411.

Third, machining workers were divided according to a longer occupational history of metalworking and a shorter history by the median duration.

Data analysis

Odds ratio (OR) was used as the measure of effect. Models included the symptom/disease of interest as the outcome (coded 1: symptom/disease present, 0: symptom/disease absent). In addition, any respiratory symptom (coded 1 when any of the upper or lower respiratory symptoms were reported to be present) was compared to no symptoms (coded 0). We also formed 2 symptom indices, one for upper respiratory symptoms (no symptoms, nasal, throat or eye symptoms) (scale 0-3) and one for lower respiratory symptoms (no symptoms, cough, phlegm production, wheezing or breathlessness) (scale 0-4) by giving value 1 for each symptom present and 0 if not present and summing these. Ordinal regression was used to assess the
relations between these symptom indices and exposures. Ordinal regression model assumes that more symptoms mean more ‘severe condition’. The model used was the proportional odds model. In the proportional odds model, which is a direct generalization of the binary logistic regression model, the odds ratios between each pair of levels is assumed to be the same regardless of which two adjacent levels are chosen. Thus, the odds ratio reported as output from this model for a four level ordinal regression is actually a weighted average of the three individual odds ratios as we increase from one level to the next. The three individual odds ratios are assumed to be the same by the model and thus the odds ratio in this model is fairly robust.

Four sets of models were analyzed with four exposure variables. 1) Exposure based on being currently a machining worker (coded 1) vs. clerk or professional working in office (coded 0, the reference category); 2) exposure represented by relatively high aerosol level in the breathing zone (≥ median concentration 0.12 mg/m³ coded 1), and 3) in the workshop general air (≥ median concentration 0.17 mg/m³ coded 1) vs. low aerosol level (<median concentration coded 0; the reference category); and 4) exposure based on long occupational metalworking history (≥ median of 15 years coded 1) vs. shorter history (coded 0, the reference category). We also analyzed OR of symptoms/conditions according to increasing quartiles of aerosol concentration in the workshop general air to explore potential dose-response relations. In multivariate regression analyses, adjustment was made for age (continuous variable), smoking (current, ex, never smoker), and atopy in childhood (atopic skin or respiratory disorders during childhood and/or school age vs. no such atopic diseases) as potential confounders.
RESULTS

Characteristics of the study population

Characteristics of the study population are presented in Table 1. These factors were adjusted for as potential confounders in the multivariate analyses.

Work tasks and exposures

The vast majority of the study population consisted of full-time machining workers with a traditional, mixed metalworking exposure. 99% of the machining workers reported working with MWFs daily, 86% on regular basis and the rest during work periods lasting at least one week at a time. The most common jobs were CNC (computer numerical control) or NC (numerical control) machinist, turner and grinder, and the most common processes were turning and milling. Multiple operation machining centers were commonly used. About 60% of the machining workers reported operating several machines, and 76% did some maintenance work on their own machine. 90% handled freshly machined metal pieces numerous times every day, 78% got splashes of MWF on their skin daily, and 85% used compressed air in cleaning the fabricated pieces.

87% of the MWFs were water-miscible, i.e. emulsifiable oils, semi-synthetic and synthetic MWFs. According to the safety data sheets, altogether 62 MWF products were used, and in most of the workplaces several types of MWFs were used simultaneously. The most common materials included stainless and non-alloyed steels, cast iron and aluminum. Although variation was observed in machine enclosures and ventilation, most of the workplaces paid adequate attention to exposure control and no serious defaults were observed. The median aerosol concentration in the breathing zone of machinists was 0.12 mg/m$^3$ (range 0.001-3.00)
and the geometric mean was 0.12 mg/m$^3$ (SD 4.07). The median concentration in the machine workshops' general air was 0.17 mg/m$^3$ (range 0.007-0.67), being 0.15 mg/m$^3$ (range 0.007-0.67) in the small, 0.28 mg/m$^3$ (range 0.03-0.6) in the medium-size and 0.13 mg/m$^3$ (range 0.05-0.27) in the large companies. The corresponding geometric means were 0.15 mg/m$^3$ (SD 2.41), 0.13 mg/m$^3$ (SD 2.84), 0.19 mg/m$^3$ (SD 2.39), and 0.14 mg/m$^3$ (SD 1.76, respectively.

**Occurrence of respiratory symptoms and diseases**

Occurrence of respiratory symptoms and conditions among machining and office workers are presented in Table 2. In general, all these symptoms and asthma, apart from wheezing, were more common among machining workers compared to office workers. The occurrence of many symptoms was over 2-fold in machining workers. The occurrence of any respiratory symptom was 31.5% in the small, 36.5% in the medium-size and 27.9% in the large companies.

**Effects of machining work**

Table 2 also shows crude and adjusted ORs of respiratory symptoms, fever and respiratory diseases in relation to machining work as compared to office work. The risk of upper airways and eye symptoms were consistently increased among machining workers, nasal symptoms showing statistical significance (adjusted OR 6.2, 95% confidence interval (95% CI) 1.9-20.0). ORs for cough, breathlessness and current asthma were 2 or more in relation to machining work. Confidence intervals were generally rather wide because of the small control group (office workers). The OR of any respiratory symptom was significantly increased in relation to machining work (2.5, 1.3-4.6), as was also the risk of upper respiratory symptom index (OR 4.2, 1.8-9.9).
Effects related to aerosol level and duration of metalworking

Table 3 shows adjusted ORs for respiratory symptoms/conditions and fever in machining workers exposed to relatively high compared to low aerosol concentrations, using the median concentration as the cut-off point. OR of nasal and throat symptoms, cough, wheezing, breathlessness and asthma were increased in relation to high aerosol levels, especially in the workshops' general air. These increased risks were statistically significant, apart from asthma that did not reach statistical significance, probably because of smaller number of subjects with this disease. However, the OR of ever asthma was high (4.1) in relation to high aerosol concentration in the breathing zone and the OR of current asthma was high (3.6) in relation to high average aerosol exposure in the workshop. Also the risk of chronic bronchitis was increased in relation to high aerosol exposure in the workshop. The risks of both upper respiratory symptom and lower respiratory symptom indices were significantly increased in relation to high aerosol exposure levels.

Table 4 shows adjusted ORs for increasing quartiles of workshops’ general air aerosol concentrations. A dose-response relation was indicated for nasal and throat symptoms, cough and phlegm production, breathlessness, chronic bronchitis, ever asthma, and lower respiratory symptom index. For most of the outcomes median concentration seemed to be the level above which the risk increased.

Table 5 presents crude and adjusted ORs of symptoms/conditions in relation to working for ≥15 years in metal industry compared to <15 years. The group with long metalworking history had significantly increased risk of throat symptoms, cough and chronic bronchitis.
DISCUSSION

This rather large study of metal industries in South Finland found that exposure to machining work was related to increased risk of upper airways symptoms, cough, breathlessness and current asthma compared to office work, although the hygienic conditions were in general good in the workshops. The median aerosol concentration in the breathing zone of machinists was 0.12 mg/m³ and the median aerosol concentration in the general air of the workshops 0.17 mg/m³, the former being measured during machine operation for 1-5 minutes and the latter in the general air of the workshops for 0.5-2 hours. The medium-size workplaces had slightly higher median air aerosol concentration than small and large companies, which was reflected in slightly higher prevalence of respiratory symptoms, but the differences between these were not statistically significant. Increased risk of upper airways symptoms and cough suggests importance of irritant mechanisms, while hypersensitivity-type mechanisms are likely to be important for breathlessness, asthma, and rhinitis-type of symptoms. Naturally there is a lot of overlap in the symptoms related to these two mechanisms, and both mechanisms could be of significance in metalworking environment. Long-term exposure to metalworking seemed to increase the risk of mainly irritant-type symptoms, namely throat symptoms, cough and chronic bronchitis.

Among machining workers, exposure to aerosol levels higher than median was related to increased risk of nasal and throat symptoms, cough, wheezing, breathlessness and asthma, and there was a trend of increasing risk with increasing level of aerosols for many of these symptoms when analyzed according to quartiles of exposure. This finding is interesting in the light that the aerosol concentrations measured were generally well below the recommended exposure level (REL) set by the National
Institute of Occupational Safety and Health (NIOSH) for total particulates (0.5 mg/m$^3$) and thoracic particulates (0.4 mg/m$^3$), quantified with gravimetric methods and applicable for machining operations (27, 28).

In Finland, extractable oil mist has traditionally been measured in machine shops, its occupational exposure limit (OEL) being 5 mg/m$^3$ (8-hour time-weighted average). Extractable oil mist forms only a minor part of the total aerosols of modern water-miscible MWFs, and thus its concentration in the present machine shops would be clearly smaller than that of the aerosol. Due to this and the fact that even the total aerosol concentrations were low, it is evident that current Finnish OEL for oil mist should be lowered substantially, at least to comply with the current recommendation of the American Conference of Governmental Industrial Hygienists: 0.2 mg/m$^3$ (29). In addition, other more relevant indicators of exposure to MWFs, such as total aerosols, should be applied. This suggestion is supported by our detailed exposure assessment study in ten of the present project’s companies (30).

Validity issues
Participation rate in this study was good among both machining workers (79%) and office workers (99%). The small sample size of office workers is a limitation of this study. It is explained by the fact that as machining workers were mainly men, we limited our control group to male office workers. On the other hand, the relatively large sample of machining workers allowed us to use an internal comparison group of workers exposed to low aerosol levels to explore potential exposure-response relations by comparing increasing exposure groups to low exposure according to measured aerosol concentrations and by comparing according to the duration of metalworking.
Cross-sectional study design is another limitation. Some influence of a selection phenomenon called the health worker effect cannot be excluded, i.e. if machining workers have quit working because of symptoms or diseases prior to our study, our effect estimates would underestimate the true effects. Indeed, the finding that long-term exposure to metalworking increased mainly the risk of irritant-type symptoms, while high current aerosol levels increased also the risk of hypersensitivity-type symptoms, suggests that some selection from the workforce due to hypersensitivity-diseases, such as asthma, is likely to occur on long-term. Another possible selection is that individuals with diseases, for example respiratory allergies, are more likely to take up office work, which again would lead to underestimating the true effects of machining work, as the office control group would be ‘enriched’ with allergic individuals.

Exposure assessment was conducted by three methods (current work tasks and reported exposures, aerosol measurements, and duration of metalworking) and all of these consistently showed significant adverse respiratory effects, which gives assurance concerning the observed effects. First, study subjects were categorized based on current occupation and questionnaire-answers on exposures. Both machining workers and office workers answered the computer-assisted interview in a similar way. Then, assessment of current exposure levels was based on measurements of aerosol concentrations by an aerosol photometer that has been widely used for exposure measurements in machine shops (15, 25-26). It has the advantage of measuring not just MWF concentration, but giving a measure of the actual exposure to an aerosol mix of different workplace exposures. DataRAM has been reported to overestimate exposure as compared to the gravimetric methods (15, 26), suggesting
that the exposure levels measured in our study would actually be even lower if measured by a gravimetric method. Measurements carried out in the breathing zone of the machining workers obviously give a better assessment of an individual’s exposure than the measurements in the general air of the workshops, but interestingly both assessment methods gave very similar results with respect to health effects. It is obvious that the short-term DataRam measurements are rough estimates of the long-term exposure, but it was not possible to conduct longer measurements for reasons of feasibility. In workplaces with poor ventilation oil mist could accumulate during the working day, but such accumulation was not observed in the short-term measurements or visually during worksite visits. Some misclassification of exposures is inevitable in this type of large epidemiological study, at least with respect to the dose, but as the exposure assessment components of the study were carried out without knowing the symptom/disease status of the individuals, any misclassification is likely to be random, thus leading potentially to some underestimation of the true risks.

One drawback in the exposure assessment was that only part of the interviewees could be combined reliably with the workplace aerosol measurements. The reasons for this were: 1) the aerosol measurements were conducted in only 57 machine shops, 2) not all machines were actively operated during the worksite visits and in those situations aerosols could not be measured, and 3) the ethics committee required us to delete the names of the interviewees from the data, so we had to use machine code and department codes for combining the questionnaire data to the measurements.

Synthesis with previous knowledge

O’Brien et al. (26) measured exposure to MWF in 23 small machining shops in USA using a real-time aerosol photometer (DataRAM). Time-weighted average for 8-hr exposure ranged from 0.04 to 1.82 mg/m³. Sprince et al. (15) also measured aerosol
concentrations using a same type of method in an automobile transmission plant and found the geometric mean of total aerosol to be 0.33 mg/m$^3$ (range 0.04-1.44). The mean total aerosol mass quantified with gravimetric analysis has generally been below 0.5 mg/m$^3$ in the North American studies (17, 31, 32). This comparison with recent literature on exposures suggests that occupational exposures in the Finnish machine shops are compatible with or lower than those in North America. The effect of the MWF type has been evaluated in some studies, but the results have been inconsistent (14, 15, 17, 26).

Some previous studies in automobile industries have investigated respiratory effects in relation to the aerosols. The study by Kennedy et al. (12) included 89 machine operators and 42 assembly workers and found that exposure to MWF was significantly related to $\geq$5% post-shift decrement in FEV$_1$. Such FEV$_1$ response is a predictor of occupational asthma, so these results could be compatible with ours on current asthma. The same group also found increased risk of cough, phlegm and wheeze in relation to current exposure to any MWF among 1042 machinists and 769 assembly workers from three automobile facilities in USA (14). Two other cross-sectional studies from USA (15, 17) found increased risks of respiratory symptoms, including throat irritation, cough, phlegm, and chest tightness among machinists. Thus, their results are compatible with those of our study.

**Conclusions**

This large study representing metal workshops in Southern Finland showed that despite rather high hygienic standards in the companies, machining workers had increased risk of upper respiratory symptoms, cough, breathlessness and current asthma compared to office workers. The aerosol concentrations in these workplaces
were in general low, but an internal comparison of the machining workers suggested that exposure to aerosol concentrations above the median, especially in the general workshop air (0.17 mg/m³) was related to both upper and lower respiratory symptoms and asthma. Our results indicate that improving the work environment of machining workers, for example by fitting machines with enclosures, installing local exhausts, and re-designing processes, could benefit the health of this workforce. Clinicians should be aware of the links of respiratory symptoms and asthma to machining work. This study also suggests that it is time to consider reducing the Finnish OEL value for oil mist and to use total aerosols or other more health-relevant indicators of exposure in machining environments.
ACKNOWLEDGMENTS

The authors would like to thank Marja Viluksela for conducting the CATI-interviews.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHORS’ CONTRIBUTIONS:

Maritta S. Jaakkola planned the respiratory part of the study, including the questionnaire, she planned the data analysis and has main responsibility for interpretation of the results, and she had major contribution to writing the article.

Katri Suuronen contributed to the study design and questionnaire design. She contributed to planning and performing exposure assessment. She participated in interpretation of the results and writing the article.

Ritva Luukkonen contributed to planning of the study, she conducted the statistical analyses and participated in writing the article.

Merja Hautamäki contributed to data collection, exposure data analysis and writing the article.

Timo Tuomi contributed to the study design, he contributed to designing the industrial hygiene measurements, their data analysis and interpretation of exposure data, and he participated in writing the article.

Kristiina Alanko contributed to designing the questionnaire, interpretation of results and writing the article.
Erja A Mäkelä contributed to the planning of the study, especially worksite visits and combining the air measurements to health data. She contributed to data collection (worksite visits) and participated in writing the article.

Riitta Jolanki was the PI of the large project on machining workers, she contributed to study design and questionnaire design. She contributed to exposure analysis, interpretation of results and writing the article.
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Table 1. Characteristics of machining and office workers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Machining</th>
<th>Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 726</td>
<td>N= 84</td>
<td></td>
</tr>
<tr>
<td>Smoking1 (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>283 (39 %)</td>
<td>21 (25 %)</td>
</tr>
<tr>
<td>ex</td>
<td>169 (23 %)</td>
<td>11 (13 %)</td>
</tr>
<tr>
<td>never</td>
<td>273 (38 %)</td>
<td>51 (62 %)</td>
</tr>
<tr>
<td>Childhood/ school age atopy (%)</td>
<td>107 (15 %)</td>
<td>17 (20 %)</td>
</tr>
<tr>
<td>Age (mean (SD) in yrs)</td>
<td>40.1 (10.9)</td>
<td>41.6 (9.6)</td>
</tr>
<tr>
<td>Duration of employment2</td>
<td>15.3 (10.7)</td>
<td>10.1 (9.6)</td>
</tr>
<tr>
<td>in metal industry for metal workers, office work for controls</td>
<td>(mean (SD) in years)</td>
<td></td>
</tr>
</tbody>
</table>

1 Smoking was missing for 1 metal and 1 office worker

2 Duration was missing for 2 machining workers
Table 2. Occurrence of upper and lower respiratory symptoms and respiratory conditions in machining and office workers, and crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI) in relation to machining work compared to office work (=reference category with OR 1).

<table>
<thead>
<tr>
<th>Symptom/disease</th>
<th>Machining workers N= 726</th>
<th>Office workers N= 84</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>Adj. OR(^1)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal symptoms</td>
<td>137 (18.9 %)</td>
<td>3 (3.6 %)</td>
<td>6.3</td>
<td>2.0- 20.3</td>
<td>6.2</td>
<td>1.9- 20.0</td>
</tr>
<tr>
<td>Throat symptoms</td>
<td>26 (3.6 %)</td>
<td>1 (1.2 %)</td>
<td>3.1</td>
<td>0.4- 23.0</td>
<td>3.6</td>
<td>0.5- 27.3</td>
</tr>
<tr>
<td>Eye symptoms</td>
<td>47 (6.5 %)</td>
<td>2 (2.4 %)</td>
<td>2.8</td>
<td>0.7- 11.9</td>
<td>2.8</td>
<td>0.7- 11.9</td>
</tr>
<tr>
<td>Cough</td>
<td>66 (9.1 %)</td>
<td>3 (3.6 %)</td>
<td>2.7</td>
<td>0.8- 8.8</td>
<td>2.5</td>
<td>0.8- 8.1</td>
</tr>
<tr>
<td>Phlegm production</td>
<td>90 (12.4 %)</td>
<td>7 (8.3 %)</td>
<td>1.6</td>
<td>0.7- 3.5</td>
<td>1.4</td>
<td>0.6- 3.3</td>
</tr>
<tr>
<td>Wheezing</td>
<td>39 (5.4 %)</td>
<td>5 (6.0 %)</td>
<td>0.9</td>
<td>0.3- 2.4</td>
<td>0.9</td>
<td>0.3- 2.3</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>29 (4.0 %)</td>
<td>2 (2.4 %)</td>
<td>1.7</td>
<td>0.4- 7.3</td>
<td>2.0</td>
<td>0.5- 8.8</td>
</tr>
<tr>
<td>Any symptom(^2)</td>
<td>223 (31.3 %)</td>
<td>13 (15.5 %)</td>
<td>2.5</td>
<td>1.4- 4.6</td>
<td>2.5</td>
<td>1.3- 4.6</td>
</tr>
<tr>
<td>Fever</td>
<td>15 (2.1 %)</td>
<td>1 (1.2 %)</td>
<td>1.8</td>
<td>0.3- 13.4</td>
<td>1.9</td>
<td>0.2- 14.7</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>31 (4.3 %)</td>
<td>3 (3.6 %)</td>
<td>1.2</td>
<td>0.4- 4.1</td>
<td>1.0</td>
<td>0.3- 3.5</td>
</tr>
<tr>
<td>Asthma current</td>
<td>12 (1.7 %)</td>
<td>1 (1.2 %)</td>
<td>1.4</td>
<td>0.2- 10.8</td>
<td>2.2</td>
<td>0.3- 17.7</td>
</tr>
<tr>
<td>Asthma ever</td>
<td>36 (5.0 %)</td>
<td>4 (4.8 %)</td>
<td>1.0</td>
<td>0.4- 3.0</td>
<td>1.3</td>
<td>0.4- 4.0</td>
</tr>
<tr>
<td>Upper respiratory symptom index (scale 0-3)</td>
<td>4.2(^3)</td>
<td>1.8- 9.9</td>
<td>4.2(^3)</td>
<td>1.8- 9.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower respiratory symptom index (scale 0-4)</td>
<td>1.7(^3)</td>
<td>0.9- 3.4</td>
<td>1.6(^3)</td>
<td>0.8- 3.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\)Adjusted for age, smoking habits, and atopic disorders during childhood and/or school age

\(^2\) Occurrence of any upper (nasal, throat or eye symptoms) or lower (cough, phlegm, wheezing or breathlessness) respiratory symptom

\(^3\) Calculated by ordinal regression, see Methods section
<table>
<thead>
<tr>
<th>Symptom/ disease</th>
<th>High exposure Breathing zone</th>
<th>High exposure Average in workshop</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 0.12 mg/m³</td>
<td>N=152</td>
</tr>
<tr>
<td>Nasal symptoms</td>
<td>1.8</td>
<td>1.0- 3.3</td>
</tr>
<tr>
<td>Throat symptoms</td>
<td>1.7</td>
<td>0.6- 5.0</td>
</tr>
<tr>
<td>Eye symptoms</td>
<td>1.1</td>
<td>0.5- 2.5</td>
</tr>
<tr>
<td>Cough</td>
<td>2.2</td>
<td>1.0- 4.8</td>
</tr>
<tr>
<td>Phlegm production</td>
<td>1.6</td>
<td>0.8- 3.1</td>
</tr>
<tr>
<td>Wheezing</td>
<td>4.8</td>
<td>1.6- 14.8</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>7.0</td>
<td>1.6- 31.9</td>
</tr>
<tr>
<td>Any symptom²</td>
<td>2.0</td>
<td>1.2- 3.2</td>
</tr>
<tr>
<td>Fever</td>
<td>1.3</td>
<td>0.2- 8.4</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>1.6</td>
<td>0.5- 4.5</td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>4.1</td>
<td>0.8- 20.5</td>
</tr>
<tr>
<td>ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory symptom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>index (0-3)</td>
<td>2.2</td>
<td>1.3- 4.0</td>
</tr>
</tbody>
</table>

Footnote for Table 3.

1 Adjusted for age, smoking habits, and atopic disorders during childhood and/or school age
2 Occurrence of any upper (nasal, throat or eye symptoms) or lower (cough, phlegm, wheezing or breathlessness) respiratory symptom
3 There were too few observations to calculate OR
4 Calculated by ordinal regression, see Methods section
Table 4. Adjusted odds ratio (OR) with 95% confidence interval (CI) of upper and lower respiratory symptoms and respiratory conditions in relation to increasing aerosol exposure in the general workshop air. The reference category (with OR 1) was the lowest quartile of exposure.

<table>
<thead>
<tr>
<th>Exposure Level</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nasal symptoms</td>
<td></td>
<td>throat symptoms</td>
<td></td>
<td>eyes symptoms</td>
<td></td>
<td>cough</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.2 - 2.5</td>
<td>2.3</td>
<td>1.1 - 4.8</td>
<td>2.5</td>
<td>1.2 - 5.0</td>
<td>1</td>
<td>12.8 - 101.6</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.6 - 3.6</td>
<td>2.1</td>
<td>0.5 - 9.0</td>
<td>3.2</td>
<td>0.8 - 12.4</td>
<td>1</td>
<td>0.5 - 1.6</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.5 - 1.6</td>
<td>1.1</td>
<td>0.4 - 2.9</td>
<td>1.2</td>
<td>0.5 - 3.0</td>
<td>1</td>
<td>0.4 - 1.6</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.1 - 2.1</td>
<td>2.6</td>
<td>1.4 - 4.8</td>
<td>2.4</td>
<td>1.3 - 4.4</td>
<td>1</td>
<td>0.7 - 2.1</td>
</tr>
<tr>
<td>Condition</td>
<td>Value</td>
<td>Lower 95% CI</td>
<td>Upper 95% CI</td>
<td>Lower 90% CI</td>
<td>Upper 90% CI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>1</td>
<td>5.1</td>
<td>0.6 - 45.1</td>
<td>7.9</td>
<td>0.9 - 67.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma ever</td>
<td>1</td>
<td>2.1</td>
<td>0.4 - 12.5</td>
<td>3.2</td>
<td>0.6 - 17.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper resp. symptoms index (0-3)</td>
<td>1</td>
<td>0.9</td>
<td>0.4 - 1.7</td>
<td>1.9</td>
<td>1.0 - 3.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower resp. symptoms index (0-4)</td>
<td>1</td>
<td>1.9</td>
<td>0.8 - 4.4</td>
<td>3.3</td>
<td>1.5 - 7.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Adjusted for age, smoking habits, and atopic disorders during childhood and/or school age
2 Occurrence of any upper (nasal, throat or eye symptoms) or lower (cough, phlegm, wheezing or breathlessness) respiratory symptom
3 Calculated by ordinal regression, see Methods section
Table 5. Crude and adjusted odds ratio (OR) with 95% confidence interval (CI) of upper and lower respiratory symptoms and respiratory conditions in relation to ≥ 15 years of machining work compared to < 15 years work (= reference category with OR 1)

<table>
<thead>
<tr>
<th>Symptom/ disease</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>Adj. OR(^1)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal symptoms</td>
<td>1.1</td>
<td>0.7-1.5</td>
<td>1.3</td>
<td>0.8-2.0</td>
</tr>
<tr>
<td>Throat symptoms</td>
<td>3.0</td>
<td>1.2-7.3</td>
<td>3.3</td>
<td>1.1-9.9</td>
</tr>
<tr>
<td>Eye symptoms</td>
<td>1.4</td>
<td>0.8-2.6</td>
<td>1.0</td>
<td>0.5-2.2</td>
</tr>
<tr>
<td>Cough</td>
<td>1.5</td>
<td>0.9-2.4</td>
<td>2.1</td>
<td>1.1-4.2</td>
</tr>
<tr>
<td>Phlegm production</td>
<td>1.9</td>
<td>1.2-3.0</td>
<td>1.5</td>
<td>0.8-2.7</td>
</tr>
<tr>
<td>Wheezing</td>
<td>1.2</td>
<td>0.6-2.3</td>
<td>1.0</td>
<td>0.4-2.4</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>1.1</td>
<td>0.5-2.2</td>
<td>0.9</td>
<td>0.3-2.3</td>
</tr>
<tr>
<td>Any symptom(^2)</td>
<td>1.2</td>
<td>0.9-1.7</td>
<td>1.2</td>
<td>0.8-1.9</td>
</tr>
<tr>
<td>Fever</td>
<td>0.8</td>
<td>0.3-2.1</td>
<td>0.8</td>
<td>0.2-2.9</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>2.1</td>
<td>1.0-4.5</td>
<td>2.7</td>
<td>1.0-7.3</td>
</tr>
<tr>
<td>Asthma current</td>
<td>1.6</td>
<td>0.5-5.1</td>
<td>3.5</td>
<td>0.7-18.0</td>
</tr>
<tr>
<td>Asthma ever</td>
<td>1.0</td>
<td>0.5-2.0</td>
<td>1.9</td>
<td>0.7-4.9</td>
</tr>
<tr>
<td>Upper respiratory symptom index (0-3)</td>
<td>1.2(^3)</td>
<td>0.8-1.6?</td>
<td>1.2(^3)</td>
<td>0.7-1.8</td>
</tr>
<tr>
<td>Lower respiratory symptom index (0-4)</td>
<td>1.5(^3)</td>
<td>1.0-2.2</td>
<td>1.5(^3)</td>
<td>0.9-2.4</td>
</tr>
</tbody>
</table>

Footnote for Table 5.
1 Adjusted for age, smoking habits, and atopic disorders during childhood and/or school age
2 Occurrence of any upper (nasal, throat or eye symptoms) or lower (cough, phlegm, wheezing or breathlessness) respiratory symptom
3 Calculated by ordinal regression, see Methods section
IV

Respiratory exposure to components of water-miscible metalworking fluids

by

Suuronen K, Henriks-Eckerman ML, Tuomi T


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Respiratory Exposure to Components of Water-Miscible Metalworking Fluids

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Water-miscible metalworking fluids (MWFs) are capable of causing respiratory symptoms and diseases. Recently, much emphasis has been put on developing new methods for assessing respiratory exposure to MWF emulsions. The air concentrations of ingredients and contaminants of MWF and inhalable dust were measured in 10 metal workshops in southern Finland. Oil mist was determined by infra red spectroscopy analysis after tetrachloroethylene extraction from the filter. Aldehydes were collected on Sep-Pak chemosorbents and analysed by liquid chromatography. Volatile organic compounds (VOCs) were collected on Tenax adsorbents and analysed by gas chromatography with mass spectrometric detection after thermal desorption. Endotoxins were collected on glass fibre filter and analysed by enzyme-based spectrophotometry, and viable microbes were collected on polycarbonate filter and cultured. Inhalable dust was collected on cellulose acetate filter and quantified gravimetrically. Associations between the different exposures were calculated with Spearman’s correlations. The mean concentration of oil mist was 0.14 (range 0.010–0.60) mg m⁻³. The mean total concentration of aldehydes was 0.095 (0.026–0.38) mg m⁻³, with formaldehyde as the main aldehyde. The average total concentration of VOC was 1.9 (0.34–4.5) mg m⁻³ consisting mainly of high-boiling aliphatic hydrocarbons. Several potential sensitizing chemicals such as terpenes were found in small quantities. The concentration of microbial contaminants was low. All the measured air concentrations were below the Finnish occupational exposure limits. The exposure in machine shops was quantitatively dominated by volatile compounds. Additional measurements of MWF components such as aldehydes, alkanolamines and VOCs are needed to get more information on the chemical composition of workshops’ air. New air cleaning methods should be introduced, as oil mist separators are insufficient to clean the air of small molecular impurities.

Keywords: asthma; exposure; formaldehyde; metalworking fluid; volatile organic compounds

INTRODUCTION

Water-miscible metalworking fluids (MWFs) are complex chemical mixtures consisting of petroleum oil, vegetable oil or a synthetic lubricating component and various auxiliary substances such as emulsifiers, corrosion inhibitors, extreme pressure agents, antioxidants and preservatives (NIOSH, 1998). Fluids are mixed with water to form 2–10% emulsions, which are used for cooling and lubricating the metalworking process as well as for removing metal chippings formed in machining. The chemical and physical nature of the MWF emulsions as well as their environmental contaminants, such as leaking machine oils and bacteria, make the chemistry of the fluids even more complex, as these factors enable the fluid composition to change over time.

Ingredients of MWF are well-known causes of dermatitis in machinists (Geier et al., 2004; Suuronen et al., 2007a). Epidemiological and clinical studies suggest that both chemical ingredients and microbiological contaminants in MWF may also cause various respiratory symptoms and diseases (Gordon, 2004). The reported respiratory health effects have been e.g. irritation of upper respiratory tract and eyes (Rosenman

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et al., 1997), allergic alveolitis (Gupta and Rosenman, 2006), chronic bronchitis, changes in pulmonary function and asthma (Greaves et al., 1997; Rosenman et al., 1997; Zacharisen et al., 1998) and the symptoms have been abundant even in an environment rated as fairly clean according to occupational exposure limits (OELs) (Robertson et al., 2007). In a recent Finnish study, various upper and lower respiratory symptoms were very frequent (M. Jaakkola, K. Suuronen et al., submitted for publication), although according to the Finnish Register of Occupational Diseases, incidence of occupational asthma (OA) in machinists has been about the same as in total working population (Suuronen et al., 2007a). The specific causing factor of OA has been identified in only a few cases, the reported causatives including pine oil odorant and colophony (Hendy et al., 1985) and alkanolamines (Savonius et al., 1994; Piipari et al., 1998).

Respiratory exposure to both MWF emulsions and straight oils has been assessed with a variety of methods, a common one being mineral oil mist collection on a filter followed by solvent extraction and infra red spectroscopy (IR) analysis (NIOSH, 1996). It has been discussed widely that the traditional methods for oil mist collection are not sufficient when assessing exposure to water-miscible MWF. In the US, thoracic particulate, quantified with a gravimetric analysis, has been recommended as the measure of MWF exposure (NIOSH, 1998; Ross et al., 2004). However, gravimetric analysis alone is not able to differentiate soluble MWF from solid particulate originating in other sources than MWF, and thus new methods for determining all classes of MWF have emerged. The American Society for Testing and Materials (ASTM) method P-42-97 includes collection of air samples on polytetrafluoroethylene filter followed by gravimetric analysis and extraction with a ternary solvent blend (Glaser et al., 2003). In National Institute for Occupational Safety and Health (NIOSH) method 5524, an additional binary blend of methanol and water is used to enhance the removal of water-soluble components (NIOSH, 2003). Other methods include, e.g. measurement of boron or potassium (HSE, 2003) as markers of MWF. We have recently also shown that exposure to MWFs can be assessed by measuring alkanolamines (Henriks-Eckerman et al., 2007). Collecting the volatile component of the oil mist with, e.g., sorbent traps subsequent to filters has been reported in the laboratory (Simpson, 2003), but field investigations remain scarce (Woskie et al., 2003).

Most of the current methods used to assess exposure to MWF measure either the total oil component of MWF or the total MWF aerosol. Recently, we have also investigated respiratory symptoms in relation to total aerosols in metal workshops using a real-time aerosol photometer (M. Jaakkola, K. Suuronen et al., submitted for publication). Little is known about respiratory exposure for instance to the volatile constituents of MWF, and the need for new methods and strategies for assessing exposure to the airborne components of water-miscible MWF is evident. The purpose of this study was to measure small molecular weight ingredients as well as microbial impurities of MWFs capable of causing skin and respiratory sensitization and irritation. The section of this study presenting respiratory and skin exposure assessment to alkanolamines has recently been reported in detail elsewhere (Henriks-Eckerman et al., 2007).

MATERIALS AND METHODS

Workplaces

Exposure measurements were carried out in 10 metal workshops in southern Finland during the year 2004. The companies were selected from a pool of 60 metal workshops where machining was one of the main activities. In all 60 companies, an assessment of total aerosol exposure and a questionnaire concerning respiratory and skin symptoms was carried out (Suuronen et al., 2007b; M. Jaakkola, K. Suuronen et al., submitted for publication). Subsequently, the 10 workshops included in this analysis were chosen to represent different types of companies based on the MWFs, products and raw materials as well as the number of machinists in the workshop.

The 10 companies chosen for the present study were involved in different kinds of machining including the manufacturing of tools and bodies and parts for machines and vehicles. The most common processes were turning, grinding and milling. Both manual and computer numerical control machines were used, and in one machine shop, a fully automated machining centre was also used. The number of machinists in the workshops varied from 10 to 100, whereas the number of the machines ranged from 5 to 70. All the 17 MWFs observed were water miscible. Safety data sheets (SDSs) were available for 16 MWFs, and according to them, 10 (59%) were mineral oil-based soluble oils or semi-synthetic MWFs; 2 (12%) were vegetable oil-based semi-synthetic and 4 (24%) were synthetic MWFs. In seven of the 10 workshops, more than one MWF was used; the number of MWFs per workshop was one to three. One of the semi-synthetic MWFs was designed to be used without any preservatives, and another one did not contain any alkanolamines. Typically, MWFs were changed every 6–12 months, but the observed fluids’ age still varied from 1 week to almost 3 years. Ventilation measures and use of enclosures varied in the workshops, and some of the local exhaust equipment were found ineffective. Overall standard of exposure control was nevertheless found to be reasonably good throughout the companies.

Sampling strategy

Airborne exposure to the components of MWF was determined by personal sampling in the
breathing zone of the machinists and with stationary sampling. The workers were chosen so that different parts and processes in the workshops were evenly represented. Also, the machines producing the highest concentration of total aerosol, as measured with a real-time aerosol photometer (Data-Ram, MIE Inc., Bedford, MA, USA), were included. The number of workers with personal air sampling at each workshop was three to six, depending on the total number of machinists and machines. A maximum of three samplers were attached to the workers simultaneously. Personal air samples of volatile organic compounds (VOCs), aldehydes, endotoxins, alkanolamines (Henriks-Eckerman et al., 2007) and inhalable dust were collected from the breathing zone of the workers. A total of 42 breathing zone samples were taken for each substance. The VOCs were collected on Tenax adsorbents. Thermal desorption was used to increase the sensitivity of the analytical method compared to conventional methods with liquid desorption. Oil mist and microbes were measured from the breathing zone of the workers in the first three workshops and in the remaining seven workshops from one stationary site. The total number of samples was 21 for oil mist and 21 for microbes.

Sampling and analytical methods

The methods for air sampling and analysis (SFS, 1976; Palmgren et al., 1986; NIOSH, 1996; US Environmental Protection Agency, 1999; CEN, 2002; ISO, 2004) are presented in Table 1. The sampling pumps were calibrated with the relevant samplers for accurate flow rates prior to the measurements. The flow rates were checked for accuracy after sampling back in the laboratory.

Statistical analysis

Spearman’s correlations were used when studying associations between the exposure variables, namely oil mist, dust, endotoxins, total aldehydes, formaldehyde, total VOCs and alkanolamines (Henriks-Eckerman et al., 2007). A P-value of <0.05 was considered to indicate statistical significance.

RESULTS

The mean concentration of mineral oil mist in 10 metal workshops was 0.14 (range <0.010–0.60) mg m\(^{-3}\). All the oil mist concentrations were well below the Finnish OEL (5.0 mg m\(^{-3}\)), and in all machine shops except for one, the oil mist concentrations were <0.2 mg m\(^{-3}\), as recommended by the American Conference of Governmental Industrial Hygienists (ACGIH, 2005). The average concentration of inhalable dust was 0.78 (<0.14–2.0) mg m\(^{-3}\), which is small as compared to the Finnish OELs for both inorganic and organic dust (10 and 5.0 mg m\(^{-3}\), respectively). In two of the 10 workshops, inhalable dust was the main impurity. The average air concentrations of the measured impurities in each workshop are presented in Fig. 1. The air concentrations of alkanolamines reported earlier

<table>
<thead>
<tr>
<th>The measured substance</th>
<th>Number of samples</th>
<th>Sampling time</th>
<th>Approximate duration of sampling (h)</th>
<th>Approximate air flow (l min(^{-1}))</th>
<th>Sampling method/collection medium</th>
<th>Analysis method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing zone samples</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VOCs</td>
<td>42</td>
<td>A</td>
<td>1</td>
<td>0.1</td>
<td>Tenax sorbent tube</td>
<td>Thermodesorption, gas chromatography–mass spectrometry (ISO, 2004)</td>
</tr>
<tr>
<td>Aldehydes</td>
<td>42</td>
<td>M</td>
<td>2</td>
<td>1</td>
<td>Sep-Pak collector</td>
<td>Liquid chromatography–mass spectrometry (US Environmental Protection Agency, 1999)</td>
</tr>
<tr>
<td>Endotoxins</td>
<td>42</td>
<td>A</td>
<td>2</td>
<td>2</td>
<td>IOM cartridge/glass fibre filter</td>
<td>Enzyme-based spectrophotometry, BIOWhittager-QCL (CEN, 2002)</td>
</tr>
<tr>
<td>Stationary samples(^{a})</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oil mist</td>
<td>21</td>
<td>A</td>
<td>4–6</td>
<td>2</td>
<td>IOM cartridge/teflon or glass fibre filter</td>
<td>Extraction to tetrachloromethane, IR (NIOSH, 1996)</td>
</tr>
<tr>
<td>Microbes</td>
<td>21</td>
<td>A</td>
<td>2</td>
<td>2</td>
<td>Camnea cartridge/polycarbonate filter</td>
<td>Cell culture, microscopy (Palmgren et al., 1986)</td>
</tr>
</tbody>
</table>

M = morning; A = afternoon.

\(^{a}\)Personal breathing zone samples from three workplaces and stationary samples from seven workplaces.
(Henriks-Eckerman *et al.*, 2007) are also included in Fig. 1 for comparison.

The mean concentrations of viable bacteria and endotoxins were 120 (50–220) colony forming unit (CFU) m\(^{-3}\) and 18 (<1.3–290) endotoxin unit (EU) m\(^{-3}\), respectively. Fungi were found in all workshops in small amounts [average concentration 550 (<100–1600) CFU m\(^{-3}\)], and in four samples, the Finnish reference value for homes and offices of 500 CFU m\(^{-3}\) was exceeded (Reponen *et al.*, 1992). Endotoxin concentrations were generally below the Dutch health-based exposure limit of 50 EU m\(^{-3}\), but in one endotoxin sample, the concentration was clearly higher, exceeding the Dutch legal limit of 200 EU m\(^{-3}\) (Douwes *et al.*, 2003).

The air concentrations of aldehydes (42 samples) other than those in the VOCs are presented in Table 2. The mean concentration of total aldehydes was 0.095 (0.026–0.38) mg m\(^{-3}\). The main aldehyde, formaldehyde, constituted about half of the total aldehyde concentration, and its mean concentration was ~11% of the Finnish OEL of 0.370 mg m\(^{-3}\).

The concentrations of VOCs (42 samples) are presented in Table 3. Total VOCs formed the main fraction of all airborne impurities in eight of the 10 metal workshops (Fig. 1). The mean concentration of total VOCs was 1.9 (0.34–4.5) mg m\(^{-3}\). The main components were different high-boiling (150–330°C) hydrocarbons. Aromatic hydrocarbons consisted of, e.g., xylene and toluene. In organic nitrogen compounds, 5-methyl-oxazolidine, 3-methyl-oxazolidine, morpholine and morpholineborane were identified. Although the collection and analysis method used in the present study is not designed for collecting...
aliphatic and acyclic hydrocarbons (alkanes, alkenes, and cycloalkanes), nitrogen compounds, terpenes, alcohols (mono-, di-, and polyhydric), ketones, aromatic hydrocarbons (benzene, toluene, and xylene), phenolic compounds, other (phenolic ethers, aldehydes, esters, and lactones), and hydrocarbon mixtures (boiling point 150–250°C). The highest concentration of any VOC was 2.6 mg m⁻³ for di-tert-butylphenol and 2,6-di-tert-butyl-4-methylphenol. The average total concentration of terpenes was 0.016 mg m⁻³, with the highest concentration of limonene being 0.070 mg m⁻³. Among terpenes, limonene, 3-carene, α-pinene, and β-pinene were identified as the most common, and among phenolic compounds, di-tert-butylacetate and 2,6-di-tert-butyl-4-methylphenol were identified.

In Spearman’s correlation test, statistically significant associations were found between (i) oil mist and alkanolamines, (ii) formaldehyde and alkanolamines, (iii) total aldehydes and alkanolamines, and (iv) total aldehydes and the VOCs. The correlation coefficients (r) were 0.463 (P-value 0.002), 0.776 (<0.001), 0.432 (0.005) and 0.365 (0.017), respectively.

**DISCUSSION**

In the present study, several small molecular weight chemicals were measured in the air of 10 metal workshops. The companies were of different sizes, and various machining techniques and MWFs were used. The overall standard of exposure varied in the companies as there were different degrees of local ventilation and MWF maintenance. However, in most of the workshops adequate care was taken to control exposure, and serious defaults were not observed. The concentrations of dusts, oil mist and bacteria were generally small when compared to the present Finnish OELs.

Mineral oil mist has traditionally been measured in machine shops in Finland. In the present study, the concentration of extractable oil mist was well below the Finnish OELs in all the samples. The highest concentration, 0.60 mg m⁻³, was measured from a process with several open-face grinders connected to a central MWF system without local ventilation. In most of the samples, the concentration was also below the recommendation of the ACGIH (2005). A guidance value for mineral oil mist of 3 mg m⁻³ has been used in the UK as a target value for good industrial practice. The guidance value for water-miscible MWF has been 1 mg m⁻³, but it was recently withdrawn due to a multitude of asthma and allergic alveolitis cases observed in concentrations below it and considered to be caused by microbial impurities (Robertson et al., 2007). The average concentration of inhalable dust exceeded the NIOSH recommended exposure limit for total particulate mass (0.50 mg m⁻³). The value is compatible with recently reported concentrations in machining industries in North America (Abrams et al., 2000; Piacitelli et al., 2001). Inhalable dust measurement is likely to represent total inhalable aerosol (oil mist and dust) rather than just dust, as also oil droplets may retain on the filter.

In our study, the levels of viable bacteria and endotoxins were generally lower than in some North American studies, where viable bacteria were reported in concentrations up to 8300 CFU m⁻³ (Virji et al., 2000) and 148 500 CFU m⁻³ (Sprince et al., 1997) and total bacteria up to 2.66 × 10⁹ cells m⁻³ (Abrams et al., 2000); the average concentrations of endotoxin in the studies ranged from 0.27 to 98.4 ng m⁻³ (~2.7 to 980 EU m⁻³). There are no OELs for bacteria and fungi in Finland. Concentrations above the

<table>
<thead>
<tr>
<th>VOC component</th>
<th>Median concentration², mg m⁻³</th>
<th>Mean concentration (range)³, mg m⁻³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocarbon mixtures (boiling point 250–330°C)</td>
<td>0.39</td>
<td>0.70 (0.15–2.6)</td>
</tr>
<tr>
<td>Hydrocarbon mixtures (boiling point 150–250°C)</td>
<td>0.46</td>
<td>0.59 (0.035–2.4)</td>
</tr>
<tr>
<td>Aromatic hydrocarbons (n = 42)</td>
<td>0.054</td>
<td>0.32 (0.0060–2.5)</td>
</tr>
<tr>
<td>Alcohols (mono-, di-) (n = 42)</td>
<td>0.11</td>
<td>0.14 (0.025–0.60)</td>
</tr>
<tr>
<td>Alcohol and phenolic ethers (n = 40)</td>
<td>0.062</td>
<td>0.13 (0.0020–0.55)</td>
</tr>
<tr>
<td>Ketones (n = 42)</td>
<td>0.015</td>
<td>0.13 (0.0020–1.3)</td>
</tr>
<tr>
<td>Aliphatic and acyclic hydrocarbons (n = 18)</td>
<td>0.0</td>
<td>0.039 (0.0010–0.35)</td>
</tr>
<tr>
<td>Terpenes (n = 39)</td>
<td>0.0085</td>
<td>0.017 (0.0035–0.092)</td>
</tr>
<tr>
<td>Nitrogen compounds (n = 31)²</td>
<td>0.0095</td>
<td>0.058 (0.018–0.27)</td>
</tr>
<tr>
<td>Esters + lactones (n = 29)</td>
<td>0.0070</td>
<td>0.029 (0.020–0.052)</td>
</tr>
<tr>
<td>Phenolic compounds, other (n = 20)</td>
<td>0.0</td>
<td>0.011 (0.0055–0.043)</td>
</tr>
<tr>
<td>Aldehydes (n = 35)</td>
<td>0.012</td>
<td>0.020 (0.0065–0.061)</td>
</tr>
<tr>
<td>Total VOCs</td>
<td>1.8</td>
<td>1.9 (0.34–4.5)</td>
</tr>
</tbody>
</table>

n = number of positive samples.
²If a compound is not found in the analysis, its concentration is marked as zero.
³If a compound is not found in the analysis, its concentration is marked as 50% of the detection limit.
⁴The components of cigarette smoke are excluded.

In the present Finnish OELs.

The components include 0.50 mg m⁻³. The value is compatible with recently reported concentrations in machining industries in North America (Abrams et al., 2000; Piacitelli et al., 2001). Inhalable dust measurement is likely to represent total inhalable aerosol (oil mist and dust) rather than just dust, as also oil droplets may retain on the filter.

In our study, the levels of viable bacteria and endotoxins were generally lower than in some North American studies, where viable bacteria were reported in concentrations up to 8300 CFU m⁻³ (Virji et al., 2000) and 148 500 CFU m⁻³ (Sprince et al., 1997) and total bacteria up to 2.66 × 10⁹ cells m⁻³ (Abrams et al., 2000); the average concentrations of endotoxin in the studies ranged from 0.27 to 98.4 ng m⁻³ (~2.7 to 980 EU m⁻³). There are no OELs for bacteria and fungi in Finland. Concentrations above the
reference values for homes and offices are often considered normal in industrial workplaces, while atypical species may be suggestive of a harmful microbial source (Reponen et al., 1992). In the present study, the only machine shop where the Dutch legal endotoxin level was exceeded was the one using MWF designed to be used without preservatives. Due to the resulting massive growth of gram-negative bacteria and because of multiple reports of endotoxin-induced respiratory symptoms (Douwes and Heederik, 1997), use of such MWFs does not seem advisable. Overall, careful maintenance of the fluid to maintain its microbiological quality as well as control measures to avoid exposure to aerosols are essential when controlling health risks due to MWF (Stear, 2005).

Finland has established OELs only for individual aldehydes, such as formaldehyde and acetaldehyde. Formaldehyde was found in all workshops. The mean concentration, 0.04 mg m\(^{-3}\), was well below the Finnish 8-h OEL and in line with another study from machine shops in Finland (Linnainmaa et al., 2003). Only few other studies of aldehydes in machine shops could be identified (Cohen, 1996; Thorne and DeKoster, 1996; Godderis et al., 2007). In a recent study from Belgium (Godderis et al., 2007), formaldehyde was found in a concentration of 0.03 mg m\(^{-3}\), whereas in another study from the US (Thorne and DeKoster, 1996), the average concentration of formaldehyde was higher, 0.22 mg m\(^{-3}\).

Aldehydes in general may originate from the oil component and fatty acid derivatives in MWF as a result of oxidative decomposition. However, the formaldehyde-releasing biocides in MWF are the most important source of formaldehyde; this was also supported by the strong correlation between formaldehyde and alkanolamines, as many of the common biocides in MWFs are composed of formaldehyde and alkanolamine derivatives. Even though individual aldehydes were found only in small quantities, the total average concentration of aldehydes may be enough to cause respiratory irritation. Formaldehyde is a skin sensitizer (Herbert and Rietschel, 2004), and it is also known to cause OA (Piipari and Keskinen, 2005). In indoor air studies, association between asthma or other respiratory symptoms and formaldehyde in concentrations clearly below the Finnish OEL has been found (Norback et al., 1995; Delfino, 2002).

Aldehydes probably pass through oil mist sampling filter, meaning that they are not discovered in the analysis of oil mist. The present Sep-Pak method is likely to be specific for aldehydes as it is based on an ‘in situ’ reaction of aldehydes with 2,4-dinitrophenylhydrazine in the acidified Sep-Pak cartridge, followed by analysis of the resulting hydrazone derivatives.

The most pronounced class of impurities was the VOCs (Fig 1, Table 3). The mean concentration of total VOCs was ~20-fold as compared to aldehydes, >10-fold as compared to oil mist and more than double the concentration of inhalable dust. In Finland, there is no OEL for total VOCs, but the recommended limit for good air quality in industrial workplaces is 5 mg m\(^{-3}\) and in houses and offices 0.6 mg m\(^{-3}\).

The main components in the VOCs were high-boiling hydrocarbons. High-boiling hydrocarbons with a boiling point >250\(^\circ\)C are expected to appear mainly as mist in the air. However, the measured oil mist concentrations were well <10% of the total VOCs, indicating that airborne hydrocarbons from water-miscible MWFs were not well retained by the filter during oil mist sampling. This conclusion could be verified by using an appropriate adsorbent as backup during oil mist sampling. In such cases, both filter and adsorbent should be analysed separately by gas chromatography. It is also possible that high-boiling hydrocarbons collected by the Tenax adsorbent without pre-filter represent a part of the oil mist despite the low sampling rate (0.1 l min\(^{-1}\)) that is not optimal for aerosols.

The aromatic hydrocarbons and butylacetate possibly originate from solvent mixtures used in, e.g., cleaning, mounting and painting in the surroundings. The terpenes probably originate from odorants in MWFs. Terpenes such as limonene and \(\alpha\)-pinene are known to sensitize the skin (Matura et al., 2005), and they have also been connected with bronchial hyperresponsiveness (Norback et al., 1995) and OA (Hendy et al., 1985). Morpholine and oxazolidine compounds are quite common formaldehyde-releasing preservatives in MWF, and the formaldehyde released from them is known to cause skin sensitization (Herbert and Rietschel, 2004), respiratory symptoms (Norback et al., 1995) and asthma (Piipari and Keskinen, 2005). The phenolic antioxidant 2,6-di-tert-butyl-4-methylphenol may cause allergic contact dermatitis (Flyvholm and Menne, 1990). The only ethanolamine found in the VOC analysis was triethanolamine borate, which, like other ethanolamines, is a well-known skin sensitizer (Geier et al., 2004) and may also cause asthma (Savonius et al., 1994).

In nine of the 10 metal workshops studied, the alkanolamines were also measured separately with a new filter sampling method with liquid chromatography–mass spectrometry analysis, the median concentrations for mono-, di- and triethanolamine being 0.057 (range 0.004–0.345), 0.064 (<0.004–0.180) and 0.006 (0.001–0.166) mg m\(^{-3}\), respectively. The study has been reported in detail elsewhere (Henriks-Eckerman et al., 2007). A statistically significant association was found between oil mist and alkanolamines. Alkanolamines are common in modern MWFs, their collection is easy with the newly developed method and their detection limit is low, ~0.001 mg m\(^{-3}\) for 2-h sampling. Thus, it seems that alkanolamines could be useful indicators of exposure to all classes of water-miscible MWFs.
There are some investigations of the vapour losses from aerosol samplers (Simpson, 2003; Woskie et al., 2003), but we were able to identify only one report of active sampling of VOCs in machining facilities; it had only a few samples and an apparently less sensitive method (Godders et al., 2007). The need for evaluating the extent and composition of the volatile compounds in machine shops has been emphasized (Woskie et al., 2003), and indeed, based on the present results, VOCs provide plenty of information not only on the total volatile hydrocarbons but also on the reactive and possibly sensitizing small molecular weight compounds in MWF. In addition, the VOC method used in the present study is well established and gives reliable results with a mean analytical precision of 20% for individual volatiles at a 95% confidence level. Although the amount of VOCs was below the recommended industrial level, the total airborne impurities were dominated by volatile compounds. VOCs and small molecules in general may also increase their concentration in workplace air because they are not well retained by oil mist separators. According to a recent review of indoor investigations, the low level of total VOCs cannot be regarded as a potent reason for asthmatic symptoms (Nielsen et al., 2007). However, MWF-originated VOCs may play a role in a machining environment.

CONCLUSIONS

On the whole, there is great need for assessing and regulating exposures to water-miscible MWFs. Specific ingredients are not merely markers of total MWF exposure but important in themselves as some of them may cause respiratory sensitization or irritation even in small concentrations. We have shown that the total exposure in machine shops was quantitatively dominated by volatile compounds. In order to get more information on the chemical composition of the air in machine shops, additional measurements of VOCs, aldehydes and alkanolamines are needed. Present Finnish OELs for alkanolamines should be revised to account for multiple exposures, and the OEL for oil mist should be adjusted based on the recent development in workplaces towards a concentration clearly <5 mg m\(^{-3}\). Overall, careful maintenance of the fluid to maintain its microbiological quality is essential when controlling health hazards due to MWF. Another important step in occupational hygiene would be to develop new air cleaning methods, as oil mist separators are insufficient for cleaning the air of small molecules.

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Determination of occupational exposure to alkanolamines in metal-working fluids

by

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Determination of Occupational Exposure to Alkanolamines in Metal-Working Fluids

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Overall exposure to alkanolamines in metal-working fluids (MWFs) in machine shops was studied by determining alkanolamines in air samples and in rinse-off samples from the hands of machinists. Methods for collecting airborne alkanolamines and alkanolamines absorbed to the skin of the hands were developed and tested. The exposure measurements were carried out in nine machine shops. After a 2 h working period the dominant hand of 37 machinists was rinsed with 200 ml of 20% isopropanol for 1 min in a plastic bag. Personal air samples were also collected during the 2 h working period onto acid-treated glass fibre filters. The filter samples were desorbed with methanol and analysed by liquid chromatography with mass spectrometric detection (LC-MS). The rinse-off samples were also analysed for alkanolamines by LC-MS.

The median air concentration of monoethanolamine (EA) was 57 µg m⁻³, diethanolamine (DEA) 64 µg m⁻³ and triethanolamine (TEA) 6 µg m⁻³. The workers’ overall exposure to alkanolamines was estimated by calculating the amount in inhaled air and the amount on the skin. The median amount of EA on the skin of the dominant hand was 9-43 times the median amount in inhaled air during 2 h exposure. The corresponding ratio for DEA was 100 and for TEA 170. According to this study the exposure to alkanolamines occurs mainly through the skin. EA was the only alkanolamine with a noticeable inhalation uptake compared to the skin uptake. Total exposure to MWFs may be reduced by reducing skin exposure. The hand rinsing method can be used to assess the efficiency of protective gloves.

Keywords: alkanolamines; dermal exposure; filter sampling; hand rinsing; inhalation; liquid chromatography; mass spectrometry

INTRODUCTION

Skin and respiratory symptoms are very common among machinists using water-miscible metal working fluids (MWFs) (Suuronen et al., 2004). MWFs are used e.g. to cool the work piece, and to protect the work piece from corrosion and to wash away the removed metal swarf. Airborne exposure to MWFs is usually assessed by measuring oil mist concentrations, though nowadays the concentrations are usually well below the occupational exposure limit (OEL) due to changes in the compositions of the fluids (NIOSH, 1998; Simpson et al., 2000). Alkanolamines, such as monoethanolamine (EA), diethanolamine (DEA), triethanolamine (TEA), methyldiethanolamine (MDEA), act as corrosion inhibitors and pH adjusters and they are often added as borates to the MWF. They may induce asthma even at air concentrations below OELs (Savonius et al., 1994; Piipari et al., 1998). EA, DEA and TEA can cause irritant contact dermatitis due to their alkalinity. They have also been frequently reported to cause allergic contact dermatitis. (Bruze et al., 1995; Geier et al., 2004). However, none of them has so far been classified in the EU as a substance which can cause sensitization by skin contact. Carcinogenic nitrosamines can be formed from DEA and other secondary alkanolamines. (NIOSH, 1998).

Airborne alkanolamines have been collected in impingers with acidified water (NIOSH, 1994; Serbin and Birkholz, 1995), on silica gel adsorbents (Serbin and Birkholz, 1995; Giachetti, 1998) and on coated XAD-2 chemosorbents (OSHA, 1987, 1988). EA and DEA have been analysed by liquid chromatography (LC) with fluorescence detection
after derivatization with fluorenyl methyl chlorofor- 
mate (Serbin and Birkholz, 1995) or with UV-detect-
tion after *in situ* derivatization with naphthyl 
isothiocyanate on XAD-2 adsorbents (OSHA, 1987,
1988). In Finland, primary and secondary 
alkanolamines have been analysed as dansyl chloride 
derivatives after collection of air samples in diluted 
sulphuric acid (Henriks-Eckerman and Laijoki,
1985). However, tertiary alkanolamines cannot be 
derivatized using those derivatization reagents. 
TEA has been determined by gas chromatography-
mass spectrometry (GC-MS) after silylation of the 
hydroxyl groups (Giachetti, 1998). Before silylation 
the extracted samples should be evaporated to dryness 
(Giachetti, 1998). All types of alkanolamines can be 
determined without derivatization using ion exchange 
liquid chromatography (IC) by measuring the con-
ductivity of the eluent (NIOSH, 1994). MS detection 
in combination with IC separation is nowadays used 
to determine alkanolamines in environmental sam-
ple extracts (Headley *et al*., 1999; Peru *et al*.,
2004).

Alkanolamines can appear simultaneously both as 
aerosol and as vapour in the workplace air, and there-
fore the sampling device should be able to collect 
both phases efficiently including both free and 
bound alkanolamines. Acid-treated glass fibre filters 
are used to collect air samples of semivolatile 
aromatic diamines by transforming them to the 
corresponding sulphate salts on the filter (OSHA,
1989a, 1989b). Filters are user friendly collection 
devices making personal sampling easy, and as 
sulphate salts of volatile alkanolamines are non-vol-
atile, acid-treated filters should be expected to be an 
efficient collection device for alkanolamines.

In order to evaluate the overall exposure of machin-
ists to alkanolamines or MWFs, reliable information 
about quantitative skin exposure data are also needed. 
As far as we know, there are no biomonitoring 
methods reported for alkanolamines. A biomonitor-
ing method for *N*-nitrosodietanolamine, which 
can be formed from DEA, has been published 
(Spiegelhalder *et al*., 1984). Dermal exposure to 
MWFs in the UK was assessed by measuring 
boron adsorbed to oversuits and to white cotton 
gloves worn underneath the protective gloves by the 
machinists (Roff *et al*., 2004). According to that study 
the main dermal exposure was found to occur through 
the skin of the hands, but the surrogate skin sampling 
media were not generally accepted by the workers.
It is also possible that the surrogate skin method over-
estimates the dermal exposure. (van Wendel de Joode 
*et al*., 2005). Other quantitative methods for measur-
ing dermal exposure to, for example, MWF have been 
the fluorescent tracer method and the video-recording 
method. However, both of these methods are expen-
sive and difficult to apply. (Wassenius *et al*.,
1998; van Wendel de Joode *et al*., 2005). The aim of this study was to measure overall 
exposure, both dermal and airborne, to alkanolamines 
contained in MWFs. A sampling method was de-
veloped utilizing acid-treated glass fibre filters, with 
which both vapours and aerosols could be collected 
simultaneously. Work place air concentrations were 
determined by LC-MS after a slight modification of 
the method for alkanolamines in water extracts. The 
same analytical method was used to analyse simulta-
neously collected rinse-off samples from the dominant 
hands of the machinists. Assessment of exposure to 
MWFs by using alkanolamines as markers is discussed.

**MATERIALS AND METHODS**

**Chemicals**

The solvents used in the experiment were methanol 
(HPLC gradient grade, J.T. Baker), isopropanol 
(Merck, purity 99%) and acetonitrile (HPLC grade 
S, Rathburn). The acids used were formic acid (purity 
98%, J.T. Baker) and sulphuric acid (purity 95–97%,
Merck). EA, DEA, TEA and *N,N*-diisopropyl 
aminoethanol (DIPAE) with the purity of all 
>99% were purchased from Fluka, and MDEA (purity 
99%) from Aldrich. Water was purified by a 
Milli-Q-academic plus Elix S water purification 
system to 18.2 MΩ cm. Whatman GF/B glass fibre 
filters (25 mm I.D.) free from organic binders were 
used to prepare the sampling devices, which were 
kept in Svinnex® filter holders from Millipore during 
sampling. A Millex HV type filter (PVDF Durapore,
13 mm I.D., 0.45 µm, Millipore) was used to clean 
up the filter sample desorption solution before 
injection.

**Instrumental**

A single quadrupole mass spectrometer (Waters 
Platform LCZ MS Detector) was used in the electros-
pray mode monitoring positive ions (ESI+). The 
cone voltage was 23 V, and the temperature of the 
ion source was 100°C. The mass spectrometer 
was connected to a Waters Alliance 2690XE separa-
tion module consisting of a quaternary solvent 
delivery system, a refrigerated, integrated autosam-
pler, a column heater and a variable volume injection 
system.

The alkanolamines were analysed using a mobile 
phase of methanol–water (1 + 1) containing 1% 
formic acid. The flow rate was 0.2 ml min⁻¹. The 
LC column was a cation exchange column IonPac 
CS14 (250 × 2.1 mm I.D., Dionex Corp.). The column 
temperature was held at 30°C and the autosampler 
temperature was 10°C. The retention times varied 
between 5 and 8 min depending on the alkanolamine 
and on the condition of the column.
Laboratory testing of the desorption and retention efficiency of the acid-treated filters

The testing was performed in a chamber with constant temperature (23°C ± 1°C) and relative humidity (RH, 50% ± 3%). Air was pumped through the filter with a Gilian 3500 air sampling pump at an airflow rate of about 2 l min⁻¹ for 2 h. Air sampling was simulated at two different concentration levels with six replicates of each level. With the airflow on, 10 µl of acetonitrile containing a mixture of alkanolamines (5 µg of each) or 50 µl of acetonitrile containing the same alkanolamine mixture (25 µg of each) were injected onto the filter. The following alkanolamines were tested: EA, DEA, TEA and MDEA. A back-up sampler with an acid-treated filter was coupled to each collection device. Retention and desorption efficiency (DE) was calculated as the mean value of 5 or 6 parallel, successfully performed spiking collections. Freshly prepared standards in methanol containing acid-treated filters were used for the calculations. A seventh collection performed with only acetonitrile was used as a blank. The total air volume was about 240 l.

Laboratory testing of the recovery efficiency of the hand rinsing method

Diluted MWF (1.0 and 3.0 ml) (a mineral oil-based semisynthetic MWF-emulsion, 5% in water) was added to each hand of the test subjects (three people) in portions of 0.5 ml during 30 min with six replicates of each dose. Some sample loss occurred throughout the 3 ml dose experiment, and the remaining dose was estimated to be a total of 2.5 ml per hand. The test subjects held their palms upwards for another 30 min after the last addition. The right hand was not in contact with the left hand. After that (a total of 60 min from the beginning of the experiment) the hand was rinsed for 1 min using 200 ml of 20% isopropanol in a plastic bag. The rinsing was repeated with 100 ml to determine the recovery efficiency. Portions of 0.5 ml were also added to test tubes in order to determine the alkanolamine content of the added dose and the precision of the addition. According to our analysis results, the MWF concentrate contained 5.9% of EA and 5.4% of TEA. The pH of the diluted MWF was 9.3, as stated in the material safety data sheet. The storage stability of the rinse-off samples at +4°C was determined by analysing the samples 7 days and 4 weeks after sampling. The risk of adverse skin effects in the subjects was discussed with an experienced toxicologist. The risk was assessed as minor, as the exposure was very small compared to a normal MWF exposure of machinists.

Work-up procedure and quantification

The filter samples were desorbed with methanol (5 ml). The hand rinse-off samples were analysed as such or after dilution. The samples of the MWF were analysed after dilution with methanol. After sampling, a known amount (10 µg) of internal standard (DIPAE) in acetonitrile was added to the sample solutions (5 ml of each) and to the standard solutions. Standards containing acid-treated filters were prepared by adding 5–50 µl of a 0.5 mg ml⁻¹ standard solution to the liquid phase. Standards and samples in pure methanol or in 20% isopropanol were acidified with formic acid (50 µl). The sample and standard vials were placed in an ultrasonic bath for 10 min. The solutions from the filter samples were passed through a Millex filter into an autosampler vial. Four different concentrations, 2.5–25 µg per sample, were used for the calibration curve. The injection volume was 5 µl. The 25 µg sample and the corresponding standards were analysed after dilution, as the detector response was linear only up to about 15 µg per sample (3 µg ml⁻¹). The analyte was quantified using the internal standard method by monitoring protonated molecular ions in the single ion monitoring mode. The protonated ions to be used were determined separately for each alkanolamine by scanning mass spectra from m/z 50–300. The limit of detection (LOD) was 0.01 µg ml⁻¹ for EA and MDEA, 0.02 µg ml⁻¹ for TEA and 0.15 µg ml⁻¹ for DEA. These LODs correspond to air concentrations of 0.002–0.03 mg m⁻³ for 15 min sampling or rinse-off amounts of 4–20 µg per hand for undiluted samples. The chromatographic performance of the analytical method has been thoroughly studied by Headley et al. (1999).

Stability of air samples and sample solutions

Spiked filters from the retention efficiency testing were stored at +4°C for 1 day, 4 days and for 4 weeks before desorption. After desorption the sample solutions were analysed within 1–2 days. One sample set was desorbed after 4 days storage of the filters at +4°C and these sample solutions were further stored at +4°C for 4 weeks before analysis. Freshly prepared standards in methanol containing acid-treated filters were used for the calculations.

Field sampling in machine workshops

Exposure measurements were carried out in nine machine work shops during the year 2004. The companies did different types of machining, including making tools, manufacturing of bodies and parts of machines and vehicles. All of the MWFs observed in the companies were water-miscible. About 70% of the MWFs were mineral oil-based, and about 20% were synthetic MWFs. There was one vegetable oil-based MWF, and a MWF of a new type that did not contain alkanolamines at all. Samples of diluted MWFs in use were collected in plastic bottles to be analysed for their alkanolamine content. After 2 h
working period the dominant hand of 37 machinists was rinsed for 1 min using 200 ml of 20% isopropanol in a plastic bag. After that, the machinists washed their hands with soap and warm water, and then samples were collected by using the same rinse-off method. Personal air samples were also collected during the two working hours onto acid-treated glass fibre filters. The measurements took place in the morning between coffee break and lunch. The workers were not informed that their hands were to be washed after about 2 h work in order to avoid influence on their working habits.

The filters for air sampling were prepared by soaking each filter with 0.5 ml of 0.26 N sulphuric acid (OSHA, 1989a, 1989b). The filters were then dried in an oven (100°C, 1 h). One filter per filter holder was used. Air was pumped through the filter with personal sampling pumps calibrated to give an accurate airflow of 1.5–2 l min⁻¹.

RESULTS

Retention efficiency and breakthrough of acid-treated filters

The retention efficiency of the acid-treated filters was calculated by comparing the amount found on the first filter to the total amount of both filters in series in the laboratory testing. As no alkanolamines were detected in the back-up filters, the LODs were used to calculate the retention efficiency, which then was found to be >85% for DEA and >97% for EA, TEA and MDEA. The tested total amount of 20 g (4.5 g) per filter corresponded to a total alkanolamine concentration of 0.7 mg m⁻³ (15 min sampling) or 0.08 mg m⁻³ (2 h sampling) in air. The higher amount 100 µg (4 x 25 µg) corresponded to a total alkanolamine concentration of 3.3 mg m⁻³ (15 min sampling) or 0.4 mg m⁻³ (2 h sampling) in air. The breakthrough was also tested in two work places, where the air concentrations of alkanolamines were 0.04–0.12 mg m⁻³ (EA, n = 6) and 0.05–0.12 (DEA, n = 3). No detectable amounts were found in the back-up filters after 2 h sampling.

Recovery efficiency of the hand rinsing method

The recovery efficiency was about 55% for EA and about 67% for TEA. The detailed results of the recovery experiment are presented in Table 1. The second rinsing increased the recovery efficiency by <10% to about 60% for EA and about 71% for TEA.

Stability of air samples, sample solutions and rinse-off samples

Storage of alkanolamines spiked onto acid-treated filter and storage of the filter samples in methanol after desorption was performed to test the stability of alkanolamines after air sampling. The stability was calculated as DE by using freshly prepared standards containing acid-treated filters (Table 2). As can be seen from column B in Table 2, a DE of in general 85% or more is achieved, if the filter samples are desorbed within 4 days after sampling and standards solutions prepared simultaneously. Therefore, field desorption is not needed.

Rinse-off samples in 20% isopropanol were analysed for their EA and TEA concentrations after 7 days and after 4 weeks in the refrigerator after the rinse-off experiment. The decline was 3% (TEA) and 8% (EA), when the concentration was about 8 µg ml⁻¹. The decline was 1% for both alkanolamines when the concentration was about 20 µg ml⁻¹. The declines were within the relative standard deviations of the determinations, meaning that no deterioration took place.

Work place measurements

Diluted MWFs in use during the work place measurements were analysed for their main alkanolamine contents (Table 3). In one machine a MWF containing MDEA as alkanolamine additive was used. The concentration was 0.51%. Two

<table>
<thead>
<tr>
<th>Alkanolamine</th>
<th>n⁶</th>
<th>Applied dose (mg hand⁻¹)</th>
<th>RSDb (%)</th>
<th>Recovery efficiency and standard deviationc (%)</th>
<th>First rinse-off</th>
<th>Second rinse-offd</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA (0.5 ml dose)</td>
<td>4</td>
<td>2.8</td>
<td>6.4</td>
<td>59.1 ± 4.5</td>
<td>5.5 ± 0.90</td>
<td></td>
</tr>
<tr>
<td>EA (3 ml dose)</td>
<td>5</td>
<td>7.5</td>
<td>7.4</td>
<td>51.3 ± 7.8</td>
<td>4.6 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>TEA (0.5 ml dose)</td>
<td>4</td>
<td>2.6</td>
<td>4.9</td>
<td>64.8 ± 11</td>
<td>4.2 ± 0.95</td>
<td></td>
</tr>
<tr>
<td>TEA (3 ml dose)</td>
<td>5</td>
<td>6.8</td>
<td>3.4</td>
<td>69.2 ± 15</td>
<td>4.1 ± 1.3</td>
<td></td>
</tr>
</tbody>
</table>

EA, monoethanolamine; TEA, triethanolamine.

n⁶ is the number of samples analysed to determine the alkanolamine content in the applied dose and the precision of addition. 1–2 samples per dose have been discarded due to wrong handling.

bPrecision of the applied dose expressed as relative standard deviation (RSD).

cn = 6.

d100 ml was used.
machinists used a MWF with no alkanolamine additives. The main results of the work place measurements are presented in Tables 4 and 5. The following alkanolamines were also identified and quantified in some of the air samples: N,N-dimethylethanolamine (4–8 \( \mu \)g m\(^{-3} \), \( n = 4 \)), amino-2-propanol (27–47 \( \mu \)g m\(^{-3} \), \( n = 6 \)) and aminoethylpropanediol (3 \( \mu \)g m\(^{-3} \)). Morpholine was afterwards identified in most samples taken, when bismorpholine containing MWFs were in use. It could not be quantified as a pure standard was not in use and the protonated molecular ion was not monitored during analysis. The amounts of alkanolamines in the rinse-off samples from the dominant hand corresponded to a retainment of 1–2 ml of diluted MWF during 2 h work. After collection of the rinse-off samples...
the machinists washed their hands with soap and warm water, and then samples were collected by using the same rinse-off method. These samples contained alkanolamine residues well below 1 mg hand⁻¹. Two exceptions were noticed: a TEA residue of 1.3 mg hand⁻¹ (2% of the content in the ordinary rinse-off sample) and a DEA residue of 1.4 mg hand⁻¹ (4% of the content in the ordinary rinse-off sample).

Estimation of overall exposure to alkanolamines

The workers’ overall exposure to alkanolamines was estimated by using the measurement results of alkanolamines to calculate the amount in inhaled air and the amount on the skin (Table 6). According to this estimation, exposure to EA took place both through the airways as well as through the skin, when the machinists were exposed to both EA and TEA containing MWF at the same time. The exposure to TEA was mainly dermal, as the ratio of median amount on the skin compared to the median amount in inhaled air was 170. When the machinists used only EA or only DEA containing MWFs, the median amount on the skin of the dominant hand was 43 times (EA) or 100 times (DEA) the median amount in inhaled air during 2 h of exposure.

DISCUSSION AND CONCLUSIONS

Impinger methods are usually used when collection of all types of alkanolamines (primary, secondary and tertiary) is needed (NIOSH, 1994). However, an impinger is not a user-friendly collection device. Therefore, we tested if acid-treated glass fibre filters could be used instead. According to our test results the alkanolamines were efficiently captured by the sulphuric acid on the first filter in series at a sampling rate suitable for aerosols (2 l min⁻¹), as no evaporation from the sampling filter to the backup filter took place, neither with pure reference substances nor in the field sampling. The retention efficiency was tested at an RH of 50% with pure reference substances. Testing at other RHs was not considered necessary, as water-based MWFs are used as 2–10% solutions in water and therefore the aerosols and vapours during machining are expected to give enough moisture to the filter during sampling, thereby promoting efficient collection at any RH. However, if the filters are to be used in extreme conditions during field sampling, further laboratory testing and also method comparisons should be done to check for breakthrough of especially alkanolamine vapours. Method comparisons should also be done before this convenient method can be accepted as a standard method, for example, the influence of different types of MWFs should be checked.

Some of the tested alkanolamines (DEA and TEA) showed a little instability at the low test concentration (5 μg per filter) during prolonged sample storage (Table 2, columns C and D), resulting in a DE below 85%. Therefore we recommend desorbing the samples within 4 days after sampling and to prepare standard solutions containing acid-treated filters at the same time.

Hand rinsing with a liquid containing 20% of isopropanol in water was used to determine dermal exposure. A recovery efficiency of 55% in general was achieved with 200 ml of this liquid. According to results from preliminary experiments a higher isopropanol per cent did not improve the sampling efficiency, but was more irritating to the skin. A second rinse-off improved the sampling efficiency with only about 10% (Table 1) and was therefore not considered necessary in field sampling. Acid washing may have improved the recovery efficiency of alkanolamines from the hands, but it was not considered due to the risk of increased skin irritation. A pure water-acid washing liquid may also negatively influence the storage stability of the samples. After our field measurements were finished, a draft of a CEN (2005) standard for measurement of dermal exposure has been published (prCEN/TS 15279). In this draft 250 ml of rinsing solvent and a rinsing time of 30 s are recommended. The differences in volume and rinsing time between our procedure and the standard draft are small and are not expected to have a great

### Table 6. Estimation of the workers’ exposure to alkanolamines in machine work shops during 2 h work with MWFs

<table>
<thead>
<tr>
<th>Identified alkanolamine in the MWFs</th>
<th>nᵃ</th>
<th>Amountᵇ of alkanolamine in inhaled air (mg)</th>
<th>Amountᶜ of alkanolamine retained on the skin (mg/dominant hand)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>Monoethanolamine</td>
<td>10</td>
<td>0.23</td>
<td>0.03–0.65</td>
</tr>
<tr>
<td>Diethanolamine</td>
<td>5</td>
<td>0.19</td>
<td>&lt;0.02–0.44</td>
</tr>
<tr>
<td>Monoethanolamine and Triethanolamine</td>
<td>19</td>
<td>0.21</td>
<td>0.03–1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.02</td>
<td>0.003–0.60</td>
</tr>
</tbody>
</table>

ᵃNumber of personal measurements.
ᵇAn inhalation rate of 30 l min⁻¹ was assumed.
ᶜThe amount in rinse-off samples were corrected for the recovery efficiency of the method (59% for EA and 65% TEA) and for sampling time. The recovery efficiency for TEA was also used for DEA.
influence on the sampling efficiency in this case. Despite some application difficulties during the validation, the repeatability of the rinse-off method was good with standard deviations of 15% or lower for TEA and of 8% or lower for EA (Table 1).

The Finnish 8 h OEL is 2.5 mg m\(^{-3}\) for EA and 2 mg m\(^{-3}\) for DEA. For TEA the Swedish OEL, 5 mg m\(^{-3}\), can be applied. Assuming that the machinists were exposed to the measured alkanolamine concentrations during the whole working day, the OELs were in none of the cases exceeded. The measured maximum air concentration for EA, 345 μg m\(^{-3}\), was 14% of the OEL. Generally, airborne exposure to MWF is assessed by measuring oil mist. Nowadays the measured oil mist concentrations are usually very low, below 0.5 mg m\(^{-3}\) (NIOSH, 1998; Simpson et al., 2000). During oil mist sampling volatile compounds like EA are missed as they break through the filter during sampling (Volkens et al., 1999). By using alkanolamines as markers it is possible to get much more reliable information about airborne exposure to MWF than by measuring only the oil mist. For example, commonly used biocides are built up of formaldehyde and of alkanolamines or amines. According to our measurement results these biocides can be analysed as their corresponding alkanolamines. Also morpholine, the ingredient of the biocide bismorpholine, was afterwards identified in most of the air samples. Whether the biocides are collected on the filters as such or as their corresponding alkanolamines or amines, we do not know yet.

As alkanolamines can cause both irritant and allergic contact dermatoses as well as asthma, the exposure should be kept as low as reasonably achievable. Other exposure routes than inhalation should also be considered. In machine shops, skin exposure was considered important. The main skin exposure was expected to occur through the hands and consequently the dominant hand was chosen as the target of skin exposure measurements. About the same time as our measurements were performed Roff et al. showed by measuring boron in surrogate skins that the main skin exposure route is by the hands, as the deposition rates of the hands were about 20 times that of the body. In order to compare inhalation and skin exposure the measurement results were recalculated as follows: the air concentrations were expressed as amount of inhaled alkanolamine and the amount of alkanolamines in the rinse-off samples were expressed as amount retained on the skin of one hand during 2 h exposure. The amount per cm\(^2\) of skin provides information about skin exposure and the risk to develop allergic or irritant contact dermatitis. The bigger amount is retained on the skin the higher is the risk. According to our comparison (Table 6) the exposure to alkanolamines was mainly dermal. The only alkanolamine with a noticeable inhalation uptake compared to skin exposure was EA. Dermal exposure was quite high probably due to the fact that most machinists did not use proper chemical protective gloves. Permeable leather and textile gloves were commonly used. Many machinists did not use gloves at all or used them only occasionally.

According to results from the testing of the hand rinsing method (Table 1) about 60% of EA and about 70% of TEA could be recovered, if a two step rinsing was applied. This means that theoretically 30% of TEA could have penetrated the stratum corneum. For EA the systematic uptake is probably much smaller than the theoretical 40%, as EA is a fairly volatile compound compared to TEA. However, in order to evaluate more thoroughly the role of systemic uptake during skin exposure, further studies, such as biomonitoring, are needed.

New information about overall exposure to MWFs was obtained by developing simple methods for measuring alkanolamines in air as well as in rinse-off samples from the hands of machinists. These collection methods are easy to perform and well accepted by the machinists. The efficiency of protective gloves may also be assessed by this hand rinsing method. The conclusions of this study were that in machine shops skin exposure to alkanolamines is considerable compared to inhalation exposure. Consequently, the overall exposure may be markedly reduced by reducing skin exposure with correct work habits and by use of nitrile rubber protective gloves or protective gloves coated partly with nitrile rubber as they are impermeable to metalworking fluids and their ingredients.

Acknowledgements—We thank the Finnish Work Environment Fund for financial support.

REFERENCES


OSHA (1989a) 4,4'-Methylenedianiline. Method No 57.
OSHA (1989b) Benzidine, 3,3'-dichlorobenzidine, 2,4-toluenediamine, 2,6-toluenediamine. Method No 65.


VI

Analysis of allergens in metalworking fluids

by

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Analysis of allergens in metalworking fluids

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Background: Metalworking fluids (MWFs) are well-known causes of occupational contact dermatitis in machinists.

Objective: To gain information about skin sensitizers in MWFs and to compare it with the information in safety data sheets (SDSs).

Methods: A total of 17 samples of MWF concentrates were analysed for skin sensitizers known or suspected to be used in MWF. Alkanolamines, formaldehyde, isothiazolinones, methylidibromo glutaronitrile (MDBGN), and iodopropynyl butylcarbamate (IPBC) were separated by liquid chromatography. Resin acids of colophonium (colophony) were separated by gas chromatography. The substances were identified with mass spectrometric detection and ultraviolet detection.

Results: Of the MWFs, 15 contained 6–39% of alkanolamines, mostly monoethanolamine and triethanolamine. Formaldehyde was detected in all MWFs; the concentrations of total formaldehyde ranged between 0.002% and 1.3%. Benzisothiazolinone and octylisothiazolinone were detected in one fluid each. IPBC was detected in nine MWFs, and the highest concentration was 0.09%. Methylisothiazolinone and MDBGN were not detected in any of the fluids. Resin acids of colophonium were detected in seven MWFs in concentrations ranging from 0.41% to 3.8%. On the whole, the allergens analysed were poorly declared in the SDSs.

Conclusions: The content of total formaldehyde was not declared in any SDS. IPBC, a relatively new allergen, seems to be common in MWFs. Isothiazolinones may be relevant allergens of machinists, and they should be analysed in MWFs in case other sources are not identified. The occupational relevance of positive patch test results to MWF ingredients in machinists is difficult to determine if information in the SDSs is relied upon.

Key words: alkanolamines; analysis; antimicrobial agents; biocides; colophonium; contact allergens; formaldehyde; iodopropynyl butylcarbamate; isothiazolinones; metalworking fluids; resin acids; safety data sheet. © Blackwell Munksgaard, 2008.

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Water-miscible metalworking fluids (MWFs) are complex mixtures consisting of a lubricating component (mineral or vegetable oil or synthetic lubricant) and various auxiliary substances such as emulsifiers, corrosion inhibitors, antioxidants, and antimicrobial agents. The MWF concentrates are mixed with water and used for cooling and lubricating as well as for removing metal chip-pings formed in the machining process.

MWFs are well-known causes of occupational contact dermatitis in machinists (1), and they have also been reported to cause asthma (1–3). The adverse health effects are partly due to the irritancy of the fluids, but several MWF ingredients are also known to be skin sensitizers. In recent studies, the most common causes of occupational allergic contact dermatitis (ACD) in machinists have been alkanolamines, formaldehyde, formaldehyde releasers, and colophonium (colophony) (1, 4), but other ingredients of MWF may also cause contact allergy (1, 4–9).

In the safety data sheets (SDSs), information on sensitizing substances has found to be deficient (10). The aim of this study was to obtain information about the occurrence of skin-sensitizing additives in MWFs by analysing commonly used MWF concentrates. The accordance of the analytical results with the information given in the SDSs is discussed.
Materials and Methods
A total of 17 samples of MWF concentrates were acquired from nine machine shops in Southern Finland. The samples were acquired in parallel with occupational hygiene measurements performed to assess airborne and skin exposure to the components of MWFs (11, 12). SDSs were provided for 16 of the studied concentrates. According to them, 10 were mineral oil based, 2 were vegetable oil based, and 4 were synthetic MWFs. The MWFs were analysed for the following substances: (i) alkanolamines, (ii) total formaldehyde (free and easily released), (iii) other antimicrobials, (iv) resin acids of colophonium, and (v) other skin-sensitizing additives identifiable by mass spectrometric (MS) analysis after gas chromatographic (GC) separation. In addition, the efficiency of the formaldehyde analysis after gas chromatographic (GC) separation was verified by analysing the total amount of released formaldehyde from four commercially available and undiluted formaldehyde releasing biocides: Acticide EF (N,N-methylenedibismorpholine, CAS 5625-90-1, Thor, Speyer, Germany), Bioban CS 1135 (a mixture of 3,4-dimethyloxazolidine and 3,4,4-trimethyloxazolidine, CAS 81099-36-7, Dow Chemical Company, Horgen, Switzerland), Biocide OX/Grotan OX [N,N′-methylenebis(5-methylloxazolidine), CAS 66204-44-2, Schülke & Mayr, Norderstedt, Germany], and Grotan BK [hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, CAS 4719-04-4, Schülke & Mayr]. The theoretical amount of released formaldehyde was calculated by dividing the sum of molar masses of released formaldehyde molecules with the molar mass of the biocide and multiplying with the reported percentage purity.

Chemicals
For quantification, the following chemicals with at least 98% purity were used: monoethanolamine (MEA, CAS 141-43-5, Fluka, Buchs, Switzerland), diethanolamine (DEA, CAS 111-42-2, Fluka), triethanolamine (TEA, CAS 102-71-6, Fluka), methyl-diethanolamine (MDEA, CAS 105-59-9, Aldrich, St Louis, MO, USA), morpholine (CAS 110-91-8, Alfa Aesar, Heysam, England), benzyl alcohol (CAS 100-51-6, Merck, Darmstadt, Germany), dodecane (CAS 112-40-3, Aldrich, Steinheim, Germany), and 2-(2-ethoxyethoxy)ethanol (CAS 111-90-0, Merck) and as internal standards: N,N-dimethylamine acetate (CAS 96-80-0, Fluka), heptadecanoic acid (CAS 506-12-7, Fluka), and heneicosanoic acid (CAS 2363-71-5, Fluka).

Chemicals with purity lower than 98% were amino-2-propanol (AP, CAS 78-96-6, purity 93%, Fluka), 2-amino-2-ethyl-1,3-propanediol (AEPD, CAS 115-70-8, purity 97%, Acros organics, Geel, Belgium), TEA borate (CAS 15277-97-1, purity 97%, Aldrich, Gillingham, England), formaldehyde (CAS 50-00-0, minimum 37% in water, Merck), MDBGN (1,2-dibromo-2,4-cyano- butane, MDBGN, CAS 35691-65-7, Schülke & Mayr), dehydroabiotic acid (CAS 1740-19-8, >95% purity, Promochem), isopimaric acid (CAS 5835-26-7, >95% purity, Promochem, Borås, Sweden), and 7-oxodehydroabiotic acid (CAS 18684-55-4) > 95% purity, Promochem).

The following antimicrobial agent standards were bought from Chemotechnique Diagnostics (Malmö, Sweden): Kathon CG (mixture of 2-methyl-4-isothiazolin-3-one (MI, CAS 2682-20-4) 0.375% and 5-chloro-2-methyl-4-isothiazolin-3-one (MCI, CAS 26172-55-4) 1.25%), 1,2-benzoisothiazolin-3-one (BIT, CAS 2634-33-5, purity 94%), 2-N-octyl-4-isothiazolin-3-one (OIT, CAS 26530-20-1, purity 45%), iodopropynyl butylcarbamate (IPBC, CAS 55406-53-6), Bioban P 1487 (a mixture of 4-(2-nitrobutyl)morpholine (70%), and 4,4-(2-ethyl-2-nitrotrimethyl)dimorpholine, CAS 37304-88-4), Grotan BK (CAS 4719-04-4, hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, purity 76%).

For derivatization, extraction, and chromatographic analysis, the following chemicals were used: methanol [high-performance liquid chromatography (HPLC) gradient grade; J.T. Baker, Deventer, Holland], acetonitrile (HPLC grade S; Rathburn, Walkerburn, Scotland), acetone (Lichrosolv; Merck, Darmstadt, Germany), formic acid (purity 98%, J.T. Baker), dinitrophenylhydrazine (DNPH, Merck, 97%), hydrochloric acid (tuning 37%, Merck), tert-butylmethylether (TBME; Uvasol, Merck), tetramethylammonium hydroxide (TMAH, 10% in methanol; Fluka), and phenolphthalein (1% in ethanol; J.T. Baker).

Instrumental
All liquid chromatographic (LC) analyses were performed with Waters Alliance 2690XE connected to Waters Platform LCZ MS detector and to Waters 2487 Dual Absorbance Detector. The GC analyses were performed with Agilent 6890N GC systems connected to an Agilent 5973N Mass Selective Detector (MSD). The compounds were separated on a Varian Factor Four capillary column VF-5ms (30 m × 0.25 mm inner diameter, df = 0.25) with the MSD in the electron ionization (EI) scan mode. The injection temperature was 250°C, which was high enough to completely methylate the acids but only partly methylate the hydroxy/keto groups in the oxidized resin acids.
LC analysis

Alkanolamines. The samples were desorbed in methanol, and the methanol extracts were analysed by LC with MS detection as described earlier (11).

Total formaldehyde. The specimens of the MWF concentrates were accurately weighed and emulsified in a known amount of water (50 mg/14 ml and 100 mg/10 ml, Millipore purified) to obtain concentrations of about 3 mg/ml and 10 mg/ml. After ultrasonic treatment for 15 min, 0.5 ml was removed to another test-tube containing 3 mg of recrystallized DNPH-hydrochloric acid and 90 μl of concentrated hydrochloric acid in 1.5 ml acetonitrile. The mixture was kept at 70°C for 1 h to completely release formaldehyde from the biocides and to achieve a complete formation of the corresponding hydrazone. The formaldehyde hydrazone was analysed with LC and ultraviolet (UV) detection at 372 nm on a Chromsep C18 column (200 mm, 3 mm ID) with 0.5 ml/min, a mixture of acetonitrile (55%) and water (45%). Ten microlitres was injected. For quantification, a solid hydrazone derivative of formaldehyde with DNPH was prepared in the laboratory. The LC purity was determined to be over 98%, as no other peaks appeared in the chromatogram during the analytical conditions of the analysis. The repeatability of the method was determined to be within 5%. The detection limit for formaldehyde was 15 ng/ml. This method was determined to be within 5%. The detection limit for formaldehyde was 15 ng/ml. This method was developed from a method used to determine free formaldehyde in foundry resins (13).

Other antimicrobial agents. MCI, MI, BIT, OIT, IPBC, Bioban P 1487, and MDBGN were determined in methanol–water (1 + 3, v + v) solutions of accurately weighed specimens (about 10 mg/ml) of the MWF concentrates. The biocides were separated by LC on a Symmetry shield C18 column (150 × 2 mm ID, 3.5 μm particles) with methanol–water containing 2 mM of ammonium acetate as eluent. A gradient elution was used starting with 34% methanol for 5 min. After that, the methanol content was increased to 95% in 6 min and then kept at 95% for 7 min. The column temperature was 30°C, and the autosampler temperature was 10°C. The injection volume was 5 μl, and the flow rate was 0.2 ml/min. The biocides were quantified using the external standard method by monitoring protonated molecular ions in the single ion monitoring mode (cone voltage 20 V) in MS and by UV detection at 230 nm and 270 nm, but MDBGN was monitored by the positive ions 282 and 284 as no protonated molecular ions were seen in the scan. Isothiazolinones were calculated using the UV detection signals and IPBC using the MS monitoring. Two standard concentrations of each biocide were used to calculate the quantitative results: 5 μg/ml and 10 μg/ml. Results from peaks with a signal to noise level of at least 10 were accepted. The extraction efficiency was determined by the standard addition method of six parallel samples at the 0.02% level and was found to be 89 ± 12% for IPBC. The corresponding extraction efficiency for BIT was 100 ± 25% and for OIT 95 ± 2%.

GC analysis

Resin acids. The specimens of the MWF concentrates were accurately weighed and dissolved with a mixture of TBME and methanol (90:10, v/v) to obtain concentrations of 5–10 mg/ml. The fatty acids, heptadecanoic acid and heneicosanoic acid, were added as internal standards (about 10 μg to 10 ml) before methylation. After addition of one to two drops of 1% phenolphthalein in ethanol as indicator, 0.1 m of the methylation reagent TMAH in methanol was added dropwise until a stable red–dish colour was formed. To allow complete methylation of the acid groups, the samples were stored for at least 1 day after the TMAH addition, and subsequently analysed with GC. The standards for quantification were treated in the same way. The resin acids were identified by comparing their MS to MS in the Wiley and NIST library. A probability of 85% or more was considered as a positive identification. Pimaric-type resin acids were quantified using the response of isopimaric acid, and abietic-type resin acids were quantified using the response of dehydroabietic acid. Heptadecanoic acid was used as internal standard in the calculations.

Other MS-identified allergens. The specimens of the MWF concentrates were accurately weighed and diluted in acetone to achieve a concentration of max 1 mg/ml. The following external standards in acetone were used: triethanolamine borate (for oxazolidinediones compounds), benzyl alcohol (for aromatics), dodecane (for aliphatics), and ethoxyethyloxethanol (for aliphatic alcohols). In order to test whether oxazolidines could be formed during the GC–MS analysis, a mixture of DEA and formaldehyde was injected into the GC–MS with injector temperature of 250°C. The compounds were identified by comparing their MS to MS in the Wiley and NIST library. A probability of 85% or more was considered as a positive identification.

Results

The results of both GC and LC analysis and their accordance with the SDSs are presented in Table 1.
Two MWFs did not contain any detectable amounts of alkanolamines (DEA < 0.1% and the others < 0.02%). The rest of the products contained mostly MEA and TEA, and the total concentrations of alkanolamines were 6–39%.

Formaldehyde was detected in all products. Three concentrates contained 0.01% of total formaldehyde. The others contained 0.08–1.3% of total formaldehyde.

3-Oxazolidine-ethanol (CAS 20073-50-1) was detected by GC–MS in all DEA-containing MWFs (three products) in the concentration range 0.5–1.8%. Oxazolidine (CAS 504-76-7) was detected in most MWFs (seven products) that also contained formaldehyde and MEA at the same time. The concentration of oxazolidine was about the same as the total formaldehyde concentration (0.5–0.9%). 3-Oxazolidine-ethanol was also found to be formed from the standard mixture of DEA and formaldehyde in the GC–MS analysis.

The efficiency of the method for determination of total formaldehyde is reported in Table 2. In all the tested biocides, the total amount of formaldehyde released was between 85% and 114% of the theoretical maximum amount.

BIT or OIT were detected in two MWFs. MCI, MI, MDBGN, or Bioban P 1487 were not detected in any samples. The detection limit for MI/MCI was < 0.0005% and for MDBGN and Bioban P 1487 0.001%. IPBC was detected in nine products. The highest concentration was 0.09%.

Table 1. Concentrations of skin-sensitizing compounds in 17 metalworking fluid concentrates and the accordance of the results with the information given in material SDS

<table>
<thead>
<tr>
<th>Analysed compound</th>
<th>Concentrations (%, w/w)</th>
<th>Accordance with SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Median</td>
</tr>
</tbody>
</table>

- Alkanolamines and alkanolamine derivatives
  - Monoethanolamine: 1.4–11 | 7.2 | 4/12
  - Diethanolamine: 20–39 | 21 | 1/3
  - Triethanolamine: 5.9–26 | 11 | 1/7
  - Methyldiethanolamine: 10 | 1 | 1
  - Triethanolamineborate: 5.3–24 | 10 | 1/7
  - 2-Amino-2-ethyl-1,3-propanediol\(^a\): 0.06–0.39 | 0.09 | 0/3
  - Amino-2-propanol\(^b\): 0.09–2.3 | 1.4 | 0/5
  - Morpholine\(^c\): 1.7–4.6 | 3.6 | 3/4\(^d\)

- Formaldehyde
  - Total formaldehyde (free and easily released): 0.002–1.3 | 0.59 | 0/17

- Biocides other than formaldehyde releasers
  - Benzisothiazolinone\(^e\): 0.011 | 1/1
  - Octylisothiazolinone: 0.036 | 0/1
  - Iodopropynyl butylcarbamate: 0.0002–0.089 | 0.0021 | 1/9

- Colophonium\(^f\)
  - Resin acids: 0.41–3.8 | 1.7 | 0/7
  - Other mass spectrometric-identified allergens: 3 | 0/1

\(n\), number of concentrates containing the analysed compound; SDS, safety data sheets; \(x\), number of products, where the analysed additive was declared in the safety data sheet of the corresponding product.

\(^a\) Added as such or indicates addition of Bioban CS 1246 (7-ethylbicyclooxazolidine).

\(^b\) Added as such or indicates addition of 3,4-dimethyloxazolidine.

\(^c\) Indicates addition of N,N-methylenebismorpholine.

\(^d\) Declared as methylenebismorpholine.

\(^e\) Classified as skin sensitizer in the EU.

Table 2. Amounts of total formaldehyde (free and easily released) from four formaldehyde releasing biocides (\(n = 3\))

<table>
<thead>
<tr>
<th>Biocide</th>
<th>Released formaldehyde (%, w/w)</th>
<th>Total amount</th>
<th>Theoretical maximum amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acticide EF(^a) (N,N-methylenebismorpholine)</td>
<td>15.9</td>
<td>16.1</td>
<td></td>
</tr>
<tr>
<td>Bioban CS 1135 (contains 77% of the active components 3,4-dimethyloxazolidine and 3,4,4-trimethyloxazolidine)</td>
<td>26.0</td>
<td>22.8</td>
<td></td>
</tr>
<tr>
<td>Biocide OX/Grotan OX(^a) (methylenebis(5-methylloxazolidine))</td>
<td>41.3</td>
<td>16.0–48.4(^b)</td>
<td></td>
</tr>
<tr>
<td>Grotan BK (contains 76% of the active component hexahydro-1,3,5-tris(2-hydroxyethyl)triazine)</td>
<td>29.1</td>
<td>31.2</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Per cent of active components in the biocide not reported.

\(^b\) Depending on whether 1, 2, or 3 formaldehyde molecules are released from one.
Resin acids were detected in seven concentrates. The concentration ranged between 0.41% and 3.8%. No 7-oxodehydroabetic acid was detected (<0.005%).

Discussion

In the present study, ingredients of MWF capable of causing skin sensitization were analysed in 17 MWFs in the Finnish market, and a new method was developed for determining total formaldehyde content in MWFs. In addition, a method for determining preservatives other than formaldehyde releasers in a single analysis was also developed.

According to present EU legislation, sensitizers that appear in concentrations of at least 0.1% in chemical preparations need to be declared in the SDS with a danger phrase R43, ‘May cause sensitization by skin contact’ (14). Of the substances analysed in the present study, formaldehyde, BIT, MCI/CI, and colophonium are classified as skin sensitizers according to the Annex I of the European Commission Directive 67/548/EEC (European Community) (15). However, not all substances known to cause contact allergy are listed in the Annex I.

Contact sensitizers were found in all the MWFs, the most common ones being formaldehyde, MEA, and IPBC. MEA has been reported to be the most common contact allergen in machinists in Germany (4, 16). As a whole, alkanolamines seem to be poorly declared in the SDSs, although some of them are present in high concentrations. Additions of MEA, DEA, and TEA and their corresponding borates were listed in the SDSs as ‘boron amine esters’ or ‘alkanolamine borates’ in 11 of the SDSs without any specification of the alkanolamine. Thus, relevance of contact allergies of machinists to each alkanolamine may be difficult to show due to the defective information in SDS. Although not classified as sensitizers in the EU, MEA, MDEA, and DEA are classified as irritant or corrosive according to Annex I of the European Commission Directive 67/548/EEC (15), and they should thus be declared in the SDS if their concentration is ≥1%. TEA is not listed in the Annex, and therefore, it does not have to be declared.

The AP detected in five products in the LC analysis of alkanolamines indicates addition of a N,N-methylenebis(5-methylloxazolidine) containing biocide. In three of the four products’ SDSs, this biocide was declared in concentrations of up to 5%. It was recently reported that N,N'-methylenebismorpholine may be a potent contact allergen in machinists and that more research is needed to evaluate its clinical relevance (16). At Finnish Institute of Occupational Health, N,N-methylenebismorpholine has been routinely tested with machinists since 2005, and occasional positive patch test reactions in patients with formaldehyde allergy have occurred, suggesting that formaldehyde is the underlying cause of the reactions (17). Small amounts of AEPD were found in three products. AEPD may be used as such, e.g., emulsifier (16), or it could have been released from Bioban CS 1246 (7-ethylbicyclooxazolidine). Bioban CS 1246 was declared in none of the SDSs.

Two oxazolidine derivatives not used in common MWF antimicrobials were identified in the present GC–MS analysis: 3-oxazolidine-ethanol is theoretically formed from formaldehyde and DEA, and oxazolidine is theoretically formed from MEA and formaldehyde. We tested if oxazolidines could have been formed during analysis by injecting a mixture of DEA and formaldehyde into the GC–MS, and indeed, a peak identified as 3-oxazolidine-ethanol was detected. Whether oxazolidine compounds can be formed during machining processes and released into the air probably depends on the processing temperature.

Formaldehyde was found in all the MWFs, which emphasizes the importance of formaldehyde as an occupational allergen in machinists. In 14 products of 17, the total concentration of formaldehyde was more than 0.008% (80 p.p.m.), which is probably enough to cause dermatitis in some sensitized individuals (18). The measured total formaldehyde concentration gives information about the potential for sensitizing, as it is a sum of free formaldehyde in the fluid and formaldehyde that may be released from the anti-microbial agent. Free formaldehyde was not determined in this study because we were not able to analyse the fresh samples immediately after the work places visits.

Formaldehyde releasers in MWFs were not quantified in the present study as such because their analysis is demanding due to their instability when in contact with heat or neutral or acidic water. However, some oxazolidine and morpholine compounds can be identified by LC analysis as formaldehyde and alkanolamine derivatives specific for the respective antimicrobial. This was the case with AEPD, AP, and morpholine. In rare cases, when allergy to formaldehyde releasers without concomitant formaldehyde allergy
is found, it could be useful to analyse specific antimicrobials.

The total amounts of formaldehyde released from the studied commercial preservatives (Table 2) were close to the theoretical amounts, when the reported purity of the commercial biocide was taken into account (85–114%). Consequently, our method for determining total formaldehyde content has an efficiency of at least 85%, especially as the percentages of active components in the biocides Acticide EF and Biocide OX were not known and could be expected to be below 100%. The repeatability of the method was also excellent, within 5%.

In the present study, we found that antimicrobials other than those releasing formaldehyde are also noteworthy. IPBC was common in the MWFs analysed (Table 1); although so far, only a few cases of contact allergy to it have been reported in machinists (3, 8). The highest concentration, 0.09%, was found in the only product with a declaration of the IPBC content. Based on the present results, isothiazolinones may be relevant allergens of machinists, and they should be analysed in MWFs in case other sources are not identified. It is recommendable to analyse isothiazolinones from the used MWFs, as they may originate either from the concentrate or from the separate antimicrobials added to the fluids in use. The developed method for isothiazolinones with both UV and MS detection will provide more reliable qualitative results than UV detection only (19).

In the present study, the sum of resin acids was used to indicate colophonium in the products. Colophonium itself could not be quantified as the proportion of resin acids is not constant in it. However, colophonium, resin acids, or tall oil addition was mentioned in any of the SDSs. According to the GC analysis, all MWFs with resin acids also contained fatty acids, but not every product containing fatty acids contained detectable amounts of resin acids. Colophonium in MWFs originates mainly from distilled tall oil, which contains typically 10–30% colophonium. Colophonium is a frequent cause of ACD in machinists (20), and it is classified as a skin sensitizer in the EU (15). Thus, it should be declared in concentration at or above 0.1%, even if the amount of oxidized resin acids considered as the allergens in colophonium is low (21). The low level of oxidized resin acids in MWFs (20) is supported by our results, as we detected no 7-oxodehydroabietic acid, one of the main colophonium allergens, in any of the present products.

As a whole, not all MWF ingredients known to cause ACD are classified as skin sensitizers in the EU, and their declaration thus is not required. In addition, according to present EU legislation, only sensitizers that appear in concentrations of at least 0.1% need to be declared (14). Many of the alkanolamines, formaldehyde releasers, and other harmful ingredients may either have several chemical names or may be present in a very low concentration, thus making the interpretation of the chemical information in SDSs demanding. Other reasons for the shortcomings in SDSs might be lack of knowledge or carelessness of the producer or distributor regarding the ingredients of their preparations. To overcome some of the problems listed, market surveillance is needed.

Patch testing of a patient’s own MWFs at 10%, 3.2%, and 1% in petrolatum (22) detects contact allergy to the fluid ingredients fairly well. Exceptionally, patients may have a false negative test reaction to their own MWF due to the fact that the concentration of the ingredient in the MWF test preparation is too small. It is recommended to analyse the MWF, especially if the patient has an allergic reaction to a possible MWF ingredient. Specific information obtained from the manufacturer and that stated in SDS may be incomplete.

To summarize the results of this study, all MWFs contain some skin-sensitizing substances, but the specific substances and their concentrations vary. The relevance of positive patch test results in connection with MWF ingredients may be difficult to determine due to deficiencies in SDSs, especially if the patch test result to MWF itself is negative. The content of total formaldehyde was not declared in any of the SDSs. IPBC, a relatively new allergen, seems to be a common additive in present MWFs. Isothiazolinones may be relevant allergens for machinists, and they should be analysed in MWFs in case other sources are not identified.

References


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