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Hairdressers –
hand eczema, hair dyes
and hand protection

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To Peter, Anna and Johan

ABSTRACT

Hand eczema is a well-known problem in occupations that involve largely manual work in combination with long periods of wet exposure and skin contact with chemicals. Hairdressing involves dermal exposure to a number of skin-damaging substances. Hair cosmetic products such as hair dyes, permanent wave solutions and bleaches can cause contact allergy and extensive wet work can cause irritant contact dermatitis (ICD).

In this thesis the occurrence of hand eczema was studied in a nationwide retrospective longitudinal cohort study comprising 7,203 female hairdressers attending the vocational hairdressing programme during a period of 25 years. A total of 7,355 women from the general population constituted the control group. A hand rinse method for assessment of dermal exposure to permanent hair dyes on hairdressers' hands was developed and validated. A high-performance liquid chromatography (HPLC) method was used for analysis of the hair dye compounds. The validated hand rinse method was used during hair dyeing in hairdressing salons for assessment of the occupational dermal exposure to *p*-phenylenediamine (PPD), toluene-2,5-diaminesulfate (TDS), *m*-aminophenol (MAP), resorcinol (RES) and 2-methylresorcinol (MRE). Hand rinse samples were taken before the start of hair dyeing, after application of hair dyes to the hair and after cutting newly dyed hair. An HPLC analysis of hair dye compounds in extracts of newly dyed hair was also carried out. In another study we investigated the permeation of PPD, TDS and RES through protective gloves frequently used in hairdressing. The gloves were made of natural rubber latex (NRL), polyvinyl chloride (PVC), nitrile rubber (NR) and polyethene (PE).

The incidence of hand eczema was 23.8 cases/1,000 person-years for the hairdressers and 9.6 cases/person-years for the controls, incidence rate ratio (IRR) 2.5 (95% confidence interval, CI, 2.2–2.8), with an IRR of 3.1 (95% CI 2.6–3.5) for younger hairdressers (<25 years). Change of job due to hand eczema was reported by 5.5% of the hairdressers and 2.0% of the controls ($p < 0.001$). The attributable fraction (AF) of hand eczema cases from skin atopy was 9.6% in the hairdressers. A synergistic effect on the development of hand eczema was found between skin atopy and hairdressing. A high frequency of hair treatments involving risk of exposure to skin-damaging substances was reported by the hairdressers. The assessment of dermal exposure to permanent hair dyes in the salons showed that after application of hair dye, positive hand rinse samples were found in 26 out of 33 hairdressers. No statistically significant difference in the amount of hair dye compounds found on the hairdressers' hands was observed between users and non-users of protective gloves. Hair dye compounds were found in samples from 23 out of 29 hairdressers after cutting newly dyed hair. Eleven out of twelve extracts of newly dyed hair contained hair dye compounds. The exposure loadings of hair dye compounds found in the hand rinse samples are at a level at which there is a risk of sensitization. None of the tested protective gloves was permeated by the hair dye compounds before 30 minutes. The NRL glove gave protection for at least 4 hours. Permeation of TDS could not be detected for any glove.

In conclusion, the incidence of hand eczema among the hairdressers was remarkably high. Hand eczema starts early in life for many individuals. About 10% of the hand eczema cases would be prevented if no skin atopics entered the trade. Hairdressers are exposed to hair dye compounds during application of hair dyes and after cutting newly dyed hair. The exposure levels found on hairdressers' hands are at a level at which there is a risk of sensitization. All the tested protective gloves gave good protection against the hair dye compounds.

Key words: hand eczema, incidence, hairdresser, atopy, attributable fraction, skin exposure, permanent hair dye, aromatic amines, hand rinse sampling, sampling efficiency, skin, occupational dermal exposure, protective glove, permeability, hair dye compound

LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

- I. Lind M-L, Albin A, Brisman J, Kronholm Diab K, Lillienberg L, Mikoczy Z, Nielsen J, Rylander L, Thorén K, Meding B. Incidence of hand eczema in female Swedish hairdressers. Submitted.
- II. Lind M-L, Boman A, Surakka J, Sollenberg J, Meding B. A method for assessing occupational dermal exposure to permanent hair dyes. *Ann Occup Hyg* 2004; 48:533–9.
- III. Lind M-L, Boman A, Sollenberg J, Johnsson S, Hagelthorn G, Meding B. Occupational dermal exposure to permanent hair dyes among hairdressers. *Ann Occup Hyg* 2005; 49:473–80.
- IV. Lind M-L, Johnsson S, Meding B, Boman A. Permeability of hair dye compounds *p*-phenylenediamine, toluene-2,5-diaminesulfate and resorcinol through protective gloves in hairdressing. Manuscript.

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LIST OF ABBREVIATIONS

ACD	allergic contact dermatitis
AE	atopic eczema
AF	attributable fraction
ASTM	American Society for Testing and Materials
CI	confidence interval
DREAM	dermal exposure assessment model
EASE	estimation and assessment of substance exposure
EPA	Environmental Protection Agency
HRIPT	human repeat insult patch test
HSE	Health and Safety Executive
ICD	irritant contact dermatitis
i.d.	internal diameter
IgE	immunoglobulin E
INCI	International Nomenclature of Cosmetic Ingredients *
IR	incidence rate
IRR	incidence rate ratio
IVDK	Information Network of Departments of Dermatology
Lag-BT	time-lag breakthrough
LMW	low-molecular-weight
LOEL	lowest observed effect level
MAP	<i>m</i> -aminophenol [CAS 591-27-5]
MPA	Medical Products Agency
MRE	2-methylresorcinol [CAS 608-25-3]
NR	nitrile rubber
NRL	natural rubber latex
OCD	occupational contact dermatitis
P _s	permeation rate at steady state
PE	polyethene
PPD	<i>p</i> -phenylenediamine [CAS 106-50-3]
PVC	polyvinyl chloride
QDI	quinonedimine
RERI	relative excess risk due to interaction
RES	resorcinol [CAS 108-46-3]
SCCP	Scientific Committee on Consumer Products
SD	standard deviation
TDA	toluene-2,5-diamine [CAS 95-70-5]
TDS	toluene-2,5-diaminesulfate [CAS 615-50-9]
VITAE	Video Imaging Technique for Assessing Exposure

*The names of the hair dye compounds are given as INCI names.

CONCEPTS AND DEFINITIONS USED

Attributable fraction (AF): measure of the proportion of the disease cases among the exposed population that is related to the exposure

Conceptual model for dermal exposure: model for assessment of dermal exposure. It is a multi-compartment model comprising six different compartments, viz. source, air, surface contaminant layer, outer and inner clothing contaminant layer and the skin contaminant layer, which describes the mass transport processes between these compartments

Incidence rate (IR): measure of the frequency of disease occurrence in a population. The IR is calculated as the number of new cases per person-year of observation

Incidence rate ratio (IRR): relative measure of the risk, calculated as the ratio of the incidence in an exposed to the incidence in an unexposed group

Permeation: usually defined as the process by which a chemical migrates through the protective clothing material at a molecular level. The permeation process involves three stages, (a) sorption of the chemical into the outside surface of the material; (b) diffusion of the sorbed molecules through the material; and (c) desorption of the molecules from the inside surface of the material into the collecting medium

Permeation rate (PR): rate at which the test chemical permeates the material per unit area, in $\mu\text{g}/\text{min}/\text{cm}^2$ or $\text{nmol}/\text{min}/\text{cm}^2$

Penetration: usually defined as the flow of a chemical through closures, porous material, seams, and pinholes or other imperfections in a protective clothing material at a molecular level

Relative excess risk due to interaction (RERI): measure of the biological interaction (synergism) between two different causes of disease

Residence time: time elapsed between contamination of the skin and the start of sampling

Sampling efficiency: sampling performance characteristics of a sampling method

Skin loading: mass of contaminant present on the skin (can be given as mass or mass/skin surface area)

Time-lag breakthrough (Lag-BT): also called the “cumulative breakthrough”, the extrapolation of the steady-state permeation portion of the cumulative permeation curve to the time axis, in minutes

1 INTRODUCTION

Occupational contact dermatitis (OCD), which usually involves the hands, is among the most prevalent occupational diseases (Diepgen and Coenraads, 1999; Dickel *et al.*, 2001; Diepgen, 2003). Despite its common occurrence, population-based epidemiological studies on the disease are scarce. Data on incidence and prevalence of OCD are most often derived from occupational disease registers or from clinical studies of patients attending dermatological clinics. The cost of OCD in terms of medical costs, sick leave, social disability and other impairment of quality of life may be considerable. Hairdressing is an occupation with one of the highest incidences of OCD in several European countries. In a review by Diepgen the conclusion is that exposure without doubt is the most important determinant of risk but that exposure quantification techniques in occupational dermatology are underdeveloped (Diepgen, 2003).

In this thesis skin disease and dermal exposure in hairdressers were studied. The occurrence of hand eczema in hairdressers was estimated using epidemiological methods. A cohort was studied consisting of all female hairdressers attending hairdressing courses in Swedish vocational schools during a 25-year period. A hand rinse method to assess dermal exposure to hair dye compounds in permanent hair dyes was developed and validated and used to determine the actual dermal exposure on hairdressers' hands during hair dyeing. Finally, we tested the permeation of hair dye compounds through protective gloves commonly used by hairdressers in Sweden.

This work will hopefully contribute to the understanding of dermal exposure pathways in hairdressing. The results will be useful in preventing skin-damaging exposure and reducing OCD in hairdressers.

2 BACKGROUND

2.1 HAIRDRESSERS

Hairdressing is an occupation with a long history (Lindsköld, 1987). There are records of hairdressers among the Egyptians that date back as far as 5,000 years B.C. Hair colouring is known to have been common among the ancient Persians, Hebrews, Greeks and Romans as well as the Chinese and Hindus. The use of henna dates back to the 3rd dynasty of Egypt, some 4,000 years ago, while the Romans used lead combs that had been dipped in sour wine (vinegar) to hide grey hair. The professional hairdressers among the Egyptians were free men, but skilful slaves, men or women, could also practise the profession. They braided and curled hair and beards and they also performed other cosmetics arts such as doing make up and dyeing hair as well as constructing wigs. Around 1,500 B.C. the hairdressers even started to perform some surgery among the Babylonians, Greeks and Romans, as there was no medical profession. In Europe in the 5th century it was by tradition the hairdressers who practised surgery.

The late 19th century and the early 20th century heralded the era of new discoveries in the field of organic chemistry, which also affected hairdressing. The first synthetic dye, mauvine, was discovered in 1856 and permanent hair colourants have been in commercial use for more than 100 years (Corbett, 1991). Phenylenediamine was the first of the amino dyes to be used on human hair; the first compound of the kind was discovered in 1854 by A.W. Hofman. The possibilities of *p*-Phenylenediamine (PPD) as a dye for hair, fur and feathers were first made known in 1883 (Wall, 1957). Shortly after their introduction and for many years thereafter, the permanent hair colourants developed a reputation for producing allergic reactions. Other advances in hair cosmetic chemistry led to the discovery in 1906 of methods to make permanent waves in the hair by Charles Nestlé.

Today in Sweden there are about 20,000 active hairdressers. Hairdressing is well known as a high-risk occupation for occupational injuries. Occupational contact dermatitis is the most common, but airway diseases and musculo-skeletal disorders are also frequent. The majority are self-employed women working in smaller salons. The situation where self-employed hairdressers rent a chair (working place) from the owner of a larger salon has become increasingly common. This fact makes hairdressers a group that is hard to reach with conventional welfare work, making preventive work difficult.

Hairdressers are exposed to numerous different skin-damaging factors, such as wet work, skin irritants, friction and thermal changes. Many hair cosmetic products, such as hair dyes and permanent wave solutions, contain very potent contact allergens. Hairdressers also are exposed to other sensitizers such as fragrances, nickel and preservatives.

2.2 HAND ECZEMA

The skin is one of the larger organs in the body, which protects us from physical trauma, heat, cold, light, chemicals, micro-organisms and dehydration. It consists of three layers, the epidermis (0.05 mm thick), dermis (1–10 mm) and subcutis. The epidermis can be divided into different layers, with the stratum corneum outermost. The epidermis contains keratinocytes and the Langerhans cells that are of importance for the immune response.

Eczema is a generic name for many inflammatory conditions in the epidermis. The term “dermatitis” is often used as a synonym for “eczema”. Hand eczema is a common skin disease affecting about 10% of the general population of working age in Sweden. Hand eczema can be divided into different diagnostic subcategories, viz. allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), atopic hand eczema, nummular eczema on the hands, hyperkeratotic dermatitis of the palms, and pompholyx. Contact dermatitis caused by exogenous factors is the only type of eczema with a known aetiology.

It is known that persons with a history of atopy have an increased risk of developing ICD on the hands (Rystedt, 1985; Meding and Swanbeck, 1990; Coenraads and Diepgen, 1998; Bryld *et al.*, 2003; Dickel *et al.*, 2003; Meding and Järholm, 2004; Nyrén *et al.*, 2005). Today other constitutional risk groups for hand eczema besides skin atopics are discussed. (Bryld *et al.*, 2003) propose the hypothesis that a hitherto undescribed genetic factor, which is independent of atopic dermatitis and contact allergy, is likely to be of major importance for the development of ICD.

2.2.1 Allergic contact dermatitis

Contact allergy

Contact allergy is also referred to as “delayed contact hypersensitivity”, or “type IV allergy”. It develops after skin contact with sensitizing substances. Sensitizing substances are low-molecular-weight (LMW) molecules, usually of a molecular weight below 700, called “haptens”. They can penetrate the skin barrier and bind to soluble or cell-bound proteins forming an antigen complex, and thereby elicit an immune reaction. More than 3,500 chemical substances are known to cause contact allergy. Once an individual has become sensitized, very small amounts of the contact allergen are required to elicit the allergic reaction.

Sensitizing phase

The sensitizing phase starts with skin contact with the hapten and is completed when the person is sensitized, i.e. has an immunological memory of the hapten. The overall process can take 3 days to several weeks. When the hapten has penetrated into the epidermis and formed a hapten-protein antigen it is taken up by the antigen-presenting Langerhans cells. The Langerhans cells then migrate out of the epidermis and carry the hapten to regional lymph nodes and there present the hapten to initiate primary immune responses in T-cells. The T-cells become activated and release cytokines that lead to proliferation and differentiation of T-cells into specific memory cells.

Eliciting phase

A previously sensitized individual has specific inflammatory memory T-cells circulating in the body. During renewed contact with the hapten these cells will proliferate and induce a cascade of inflammatory events in the exposed skin area. An eczematous reaction usually develops 18–48 hours after contact with the hapten.

2.2.2 Irritant contact dermatitis

“Irritant contact dermatitis” may be defined as a non-immunological inflammatory reaction of the skin to an external agent. Irritant contact dermatitis may be acute or chronic. Irritants are the major cause, but mechanical, thermal and climatic effects can contribute to the disease. Irritant contact dermatitis can be caused by exposure to water/wet work, degreasing agents, detergents, solvents, metal working fluids, dust/friction and low humidity (English, 2004). The inflammatory events seen in the skin during ICD are the same as during ACD but the reaction is not immunologically triggered.

2.2.3 Hairdressers’ occupational contact dermatitis

It has been reported that 70–80% of all cases of OCD are cases of ICD and 20–25% are due to ACD (Nixon *et al.*, 2005). Hairdressers run a high risk of developing OCD due to exposure to skin irritants and sensitizers (van der Walle, 2000; Uter *et al.*, 2003). In the hairdressing profession ICD is most frequently seen in apprentices while ACD often occurs after some years in the occupation. A combination of ICD and ACD, as well as an association with atopy, is of course possible. Major irritants in hairdressing are water and shampoos, as well as permanent waving solutions and bleaches. Several clinical studies show that hairdressers run a high risk of developing occupational ACD. Thioglycolates in permanent wave solutions, persulphates in bleaches, and PPD, toluene-2,5-diamine (TDA) or its sulfate toluene-2,5-diaminesulfate (TDS), and resorcinol (RES) in permanent hair dyes can cause sensitization. *p*-Phenylenediamine and TDA/TDS are often the most common agents responsible for allergic reactions, between 17% and 58% of patch-tested hairdressers showing positive reactions to PPD in different studies and 14–25% to TDA or TDS (Armstrong *et al.*, 1999; Iorizzo *et al.*, 2002; Nettis *et al.*, 2003; Uter *et al.*, 2003).

In a German study among 856 hairdressers and barbers who were patch-tested for dermatitis, 88% had positive reactions and 72% were found to have an occupationally caused allergy (Dickel *et al.*, 2001). Another German study conducted by the Information Network of Departments of Dermatology (IVDK), in which patch test results were collected during 1995–2002, the most frequent sensitizers found among hairdressers in 2001–2002 were ammonium persulphate (27.6%), TDA (24.8%) and PPD (17.2%) (Uter *et al.*, 2003).

2.3 HAIR DYES

Modern hair dyes can be divided into five categories, each with a specific composition and action mechanism: gradual hair colouring (using metallic dyes such as salts of lead, bismuth or silver), vegetable hair dyes (such as henna), temporary dyes (water-soluble dyes that withstand only one shampooing), semi-permanent or direct dyes (which will withstand four to five shampooings) and permanent or oxidation hair colours, the most important category (Nater *et al.*, 1983). Permanent hair colourants currently represent the largest proportion of the world hair dye market (Corbett, 1991). The hair dye market in the European Union (EU) in 2004 was worth €2.6 billion. In Europe permanent hair dyes account for 70–80% of the colouring product market. More than 60% of women, and 5–10% of men, colour their hair, with the average frequency of use being six to eight times per year cited from Euromonitor (<http://www.euromonitor.se>). The annual consumption of hair dyes in Europe of PPD, TDA and RES amounted to 270 metric tons during 2002, according to the European Cosmetic Toiletry and Perfumery Association (Søsted *et al.*, 2004). A questionnaire investigation carried out by the Medical Product Agency in Sweden among 30 registered suppliers of hair dyes showed that of 73 products on the Swedish market in 1999, 30% contained PPD and 74% TDA (Wahlberg *et al.*, 2002). The EU's Scientific Committee on Consumer Products (SCCP) in 2001 concluded that the potential risk of using certain permanent hair dyes is of concern. In 2002 the SCCP stated that there is epidemiological evidence to indicate that regular and long-term use of hair dyes by women may be associated with development of bladder cancer (European Commission, 2006).

In this thesis dermal exposure to five hair dye compounds was studied: the aromatic amines PPD and TDS, and RES, 2-methylresorcinol (MRE) and *m*-aminophenol (MAP) (Figure 1). The compounds were selected after a survey of the current literature followed by an inventory of compounds in common commercial hair dye products in Sweden. *p*-Phenylenediamine, MAP, TDS and RES are known contact allergens and are included in hairdressing patch test series (van der Walle, 2000).

The colouring process is complex. The hair shaft consists of three layers, the cuticle (the outer layer), the cortex (the middle layer) and the medulla (the inner layer). It is the melanin in the cortex that gives hair its natural colour. The cortex cells contain amorphous sulphur protein matrix and keratin filaments. The cuticle is composed of keratin and consists of overlapping layers of scales, like tiles on a roof (Boldoc and Shapiro, 2001). The cuticle protects the underlying cortex and acts as a barrier. Permanent hair dye formulations contain colourless precursors called “intermediates” and “couplers”. During permanent hair colouring the LMW primary intermediates, like PPD and TDS, and couplers, like MAP, RES and MRE, are readily taken up by the hair cuticle and undergo oxidation, forming larger molecules that become entrapped in the hair shaft, making the colouring permanent (Figure 2). Under usual application techniques, direct hair colours penetrate only the outer cortex while oxidative colours penetrate more deeply into the medulla, facilitated by high-pH hair dye bases (Dressler, 1998). In the hair dyeing process the colour precursor is mixed with hydrogen peroxide prior to application to the hair. This triggers oxidation and also removes the natural (or previous synthetic) colour of the hair and enhances the penetration of the hair dye

compounds into the hair fibre. Different concentrations (6–12%) of hydrogen peroxide are used (Brown and Pohl, 1996).

In the absence of couplers the primary intermediate still undergoes colour-forming oxidation. The primary intermediates are ortho- or para-diamino-, or aminohydroxybenzenes that develop colour on oxidation. They usually oxidize very readily. Typical couplers are phenols, meta-disubstituted phenylenediamines and aminophenols and various RES derivatives.

Oxidative reactions that occur in the presence of hair are known to be more complex than those occurring in simple aqueous solutions (Brown and Pohl, 1996; Dressler, 1998). The presence of hair protein, melanin, free metal ions or metal ions bound to protein is likely to modify the reactive chemistry and may alter the hair dye compounds formed. Metabolism in the skin, including reductive processes and N-acetyltransferase, can potentially alter the rate and adsorption of hair dyes but data on the subject are scarce.

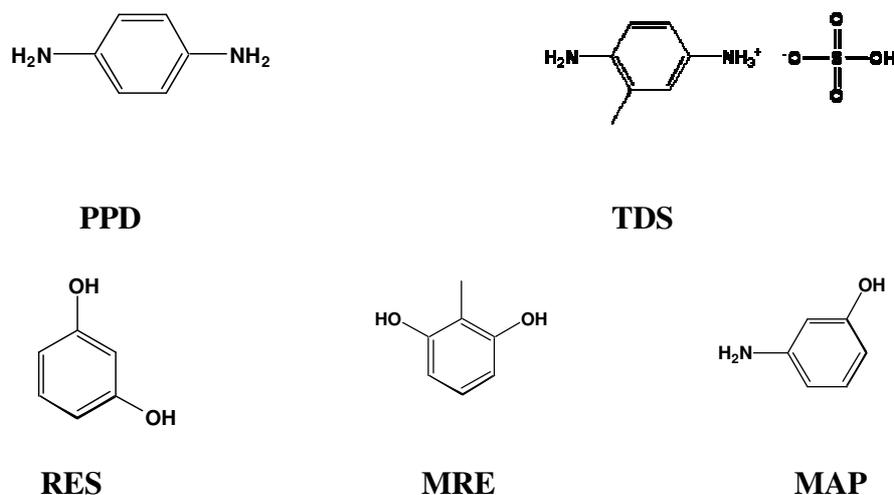


Figure 1. Molecular structure of *p*-phenylenediamine (PPD), toluene-2,5- diaminesulfate (TDS), resorcinol (RES), 2-methylresorcinol (MRE) and *m*-aminophenol (MAP).

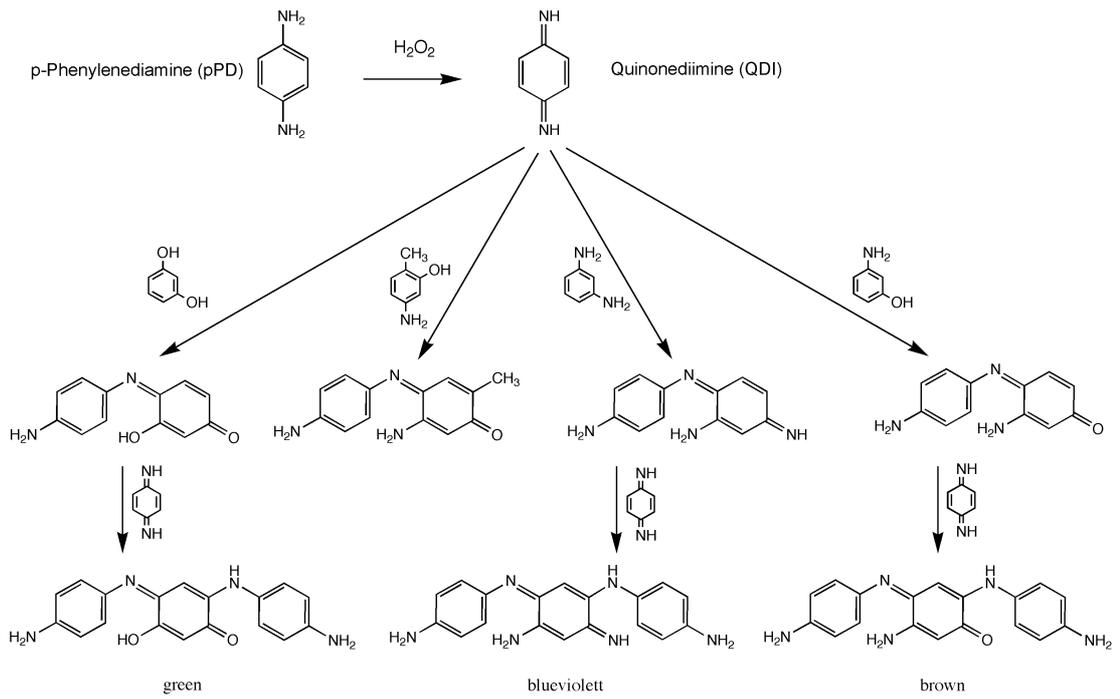


Figure 2. Schematic representation of reaction pathways of *p*-phenylenediamine (PPD) with different couplers (Spengler and Bracher, 1990).

2.4 DERMAL EXPOSURE

Dermal exposure occurs in many occupations. While the methods of assessing airborne exposure are well developed there are few validated methods for measuring dermal exposure. The existing methods usually measure the mass of the material deposited on the skin, while many with expertise in the field argue that it is the concentration of the substance that drives the diffusive process and should consequently be of greater interest for assessment of dermal uptake. However, no accepted sampling methods exist for measuring concentration and instead, the mass per unit area is often used as a surrogate (Semple and Cherrie, 2003). Dermal exposure measurements are complicated by interactions between the substances under study and the skin. Factors such as evaporation from the skin and dermal uptake through the skin make quantitative assessment difficult. The complexity of assessment of dermal exposure is demonstrated by the conceptual model developed by Schneider *et al.* (1999; 2000). For assessment of dermal exposure in ICD and ACD, the amount of chemical per surface area is of interest since this is the measure used when ranking the sensitizing potential of a substance.

The techniques for assessing dermal exposure can be divided into the following categories:

2.4.1 Removal techniques

Removal techniques have a widespread use and have the advantage of low capital costs and ease of application. The techniques remove chemicals deposited on the skin followed by chemical analysis of these compounds. Chemicals can be removed by washing, wiping with a piece of fabric or a cotton swab, brushing, skin stripping using adhesive tape, or suction. Hand wash sampling will be discussed in detail later. Tape stripping removes the outer layer of the stratum corneum of the skin and quantifies the compounds present in the skin. Stripping gives an indication of the amount of a substance that has already been absorbed into the skin, but no standardized method exists to quantify the amount of chemical measured to the number of stratum corneum cells removed (Cherrie *et al.*, 2005). Tape stripping has been used for assessment of dermal exposure to acrylates (Surakka *et al.*, 1999; Nylander-French, 2000; Surakka *et al.*, 2000) and jet fuel (Chao *et al.*, 2006) etc. Suction methods have in the past been mainly used for assessment of contamination on surfaces but a vacuuming technique for dermal exposure to particles has recently been constructed and evaluated (Lundgren *et al.*, 2006).

Hand wash sampling

Hand wash sampling has been reviewed by (Brouwer *et al.*, 2000). Hand wash sampling can be divided into hand washing and hand rinsing. During hand washing the contaminant is removed from the skin in a routine washing fashion by rubbing the hands against each other. The contaminant is detached from the skin by a combination of mechanical forces and wet chemical action (dissolution). In hand rinsing the contaminant is removed by a combination of hydrodynamic drag, and wet chemical action (dissolution) during liquid-skin contact. During hand rinsing one hand is

immersed in a solvent in a bag that is sealed tightly just above the wrist by a technician or by a rubber band to prevent leakage. The person cups the hand slightly and holds the fingers a short distance apart. The hand is shaken vigorously, either by the person or by the technician, for a fixed time (Fenske and Lu, 1994; Fenske *et al.*, 1998), a fixed number of shakes, e.g. 50 times (US EPA, 1996), or a fixed number of shakes in a fixed time (Fenske *et al.*, 1999).

Hand wash sampling for a variety of pesticides has been employed internationally in field studies and remains a standard procedure for assessing occupational exposure to pesticides in the USA (US EPA, 1986). When developing a method using hand wash sampling it is essential to study sampling performance characteristics. Sampling efficiency can be affected by sample load, i.e. the amount of contaminant on the surface contaminant layer, and residence time, i.e. the time elapsed between contamination and the start of wash sampling. The removal efficiency has been defined by Fenske and Lu (1994) as the percentage of chemical removed from the skin by the skin sampling procedure. Sampling efficiency is used by Brouwer *et al.* (2000) and includes parameters that are determined by the sampling strategy. The sampling efficiency must be determined for each chemical substance of interest since factors such as residence time and sample load may influence these parameters differently for each substance. The matrix in which the substance is present is also important since compounds in the matrix may influence the solubility of the compounds in the sampling medium, and may also influence the dermal uptake of the compounds.

2.4.2 Surrogate skin techniques

Patches, gloves or whole body overalls are used and the contaminant in the collected patches is measured with the aim of sampling the total amount of the substance that would be deposited on the skin or clothing. The primary weakness of patch sampling is the potential to introduce large errors when the exposure is non-uniform. Surrogate skin methods are likely to overestimate the amount of a chemical on the skin because the materials used for body suits and patches often absorb the fluids more readily than the skin does and the fluids are therefore less likely to evaporate. In Sweden patches have been used for assessment of dermal exposure to styrene and terpenic resin acids (Eriksson and Wiklund, 2004; Eriksson *et al.*, 2004) A review of patches and whole body sampling has been done by (Soutar *et al.*, 2000).

2.4.3 Visualization techniques

Fluorescent tracers can be used in both qualitative and quantitative methods (Cherrie *et al.*, 2000). A suitable tracer agent is added to the source of exposure. Long-wave ultraviolet light is normally used to identify and characterize the extent of contamination on surfaces, workers' clothing and skin. Fluorescent tracer in combination with image processing (using the Video Imaging Technique for Assessing Exposure, VITAE) is a quantitative method which translates the intensity of the fluorescence to the amount of contaminant on the skin using a computer program, and can also be used to measure the exposed area. Semi-quantitative methods using a visual score system are also available. These techniques have recently been used for measuring dermal exposure to pesticides in Nicaragua (Aragon *et al.*, 2006).

2.4.4 Modelling

Modelling of dermal exposure has received much attention over the past decade. The estimation and assessment of substance exposure (EASE) system that has been developed by the UK Health and Safety Executive (HSE) and a similar technique developed by the US Environmental Protection Agency (EPA) (Mulhausen and Damiano, 1998) are generic models primarily used for risk assessment. Another generic model is the DREAM method (Van-Wendel-de-Joode *et al.*, 2003) for occupational exposure. Deterministic modelling of dermal exposure during spray painting has also been developed (Brouwer *et al.*, 2001).

2.5 HAND PROTECTION

Gloves can be made of rubber or plastic materials, leather and textile and combinations of these materials (Mellström *et al.*, 2005). The protective effect of a glove does not only depend on the material formulation but also on the manufacturing process, material combinations and material thickness. Standardized tests exist to evaluate penetration (leakage) and permeation (resistance) of protective gloves. A standardized test cannot represent all conditions likely to be found in working situations but the test data should be restricted to comparison of the glove materials on a relative basis. For examining the ability of the material to resist degradation against chemicals, no standardized test so far exists. The protective glove materials commonly used in hairdressing are natural rubber latex (NRL), nitrile rubber (NR), polyethene (PE) and polyvinyl chloride (PVC).

Natural rubber latex

Natural rubber latex comes from the rubber tree *Hevea brasiliensis* and contains about 36% rubber (cis-isoprene), 60% water, 1.7% resin and 2% proteins, as well as ash and sugars. In the manufacturing process several additives are added to the latex dispersion. Gloves made of NRL have a superior elasticity compared with other gloves and are relatively inexpensive, which probably explains their widespread use. However, NRL gloves can cause immunoglobulin E (IgE)-mediated allergic reactions against latex proteins or contact allergy to additives and are often not recommended as first choice today. Natural rubber latex is still one of the most common glove materials used by hairdressers in Sweden, usually in gloves with a thickness of about 0.20 mm.

Nitrile rubber

Nitrile rubber is a synthetic rubber made of nitrile butadiene rubber, a co-polymer of acrylonitrile and butadiene. They have good resistance to oils, fuels and certain solvents and very good tensile strength.

Polyethene

Polyethene gloves are available as thin disposable gloves. In contrast to NRL, NR and PVC gloves, which are manufactured by a dipping procedure, PE gloves are manufactured by punching or welding thin sheets of PE. They are often used in non-sterile hospital work, food handling, etc. Their protective effect is more dependent on

the strength of the welded seams than on the chemical resistance of the material itself. Polyethene has a very low elasticity.

Polyvinyl chloride

These gloves are made of a polymer of vinyl chloride. All types of glove are available. They give good protection against water and most aqueous solutions, detergents, diluted bases and acids. The resistance to permeation of organic solvents is, however, restricted.

3 AIMS OF THE THESIS

The primary aim of this thesis was to study the occurrence of hand eczema in hairdressers and to study risk factors, such as skin atopy and dermal exposure to skin-damaging substances, particularly to permanent hair dyes. The ultimate goal was to provide knowledge to be used as a basis for prevention in order to reduce occupational hand eczema in hairdressers.

Specific aims were to –

estimate the incidence of hand eczema and occupational skin exposure in female Swedish hairdressers using a self-administered questionnaire (Paper I);

develop and validate a method of assessing actual occupational skin exposure to permanent hair dyes on hairdressers' hands (Paper II);

apply the previously validated method for assessment of hairdressers' occupational dermal exposure to permanent hair dyes on hairdressers' hands, in relation to given work tasks (Paper III); and

determine the resistance of protective gloves used in hairdressing to permeation by PPD, TDS and RES (Paper IV).

4 MATERIALS AND METHODS

4.1 OCCURRENCE OF HAND ECZEMA (PAPER I)

4.1.1 Study population

The design was a retrospective longitudinal cohort study with a self-administered postal questionnaire. The study population consisted of women born after 1945 who had graduated from hairdressing classes in Swedish vocational schools during the years 1970–1995. Altogether 7,203 trained hairdressers were sent a questionnaire. A total of 7,355 women, stratified for age and randomly selected from the Swedish population register, were selected as the population-based control group.

4.1.2 Questionnaire

Hairdressers and controls were sent a questionnaire containing questions about hand eczema and history of childhood eczema. The hairdressers were asked about their working periods and about the number of hair treatments they gave per week. After two reminders answers were obtained from 4,061 (56%) hairdressers and 5,034 (68%) controls. An analysis of non-responders was made: 584 of the hairdressers and 217 of the population controls (about one-fifth and one-tenth, respectively) who had not returned the questionnaire were randomly selected for a telephone interview by a nurse. Interviews were performed with altogether 392 of the hairdressers (67%) and 134 of the population controls (62%).

4.1.3 Statistics

For statistical analysis, SAS Software, release 8.2, was used (SAS Institute Inc., Cary, NC, USA). Age was stratified into the categories <25, 25–34 and >34 years. For the hairdressers, only times of active hairdressing were included in the calculations. The incidence rates (IRs) were calculated as the number of new cases of hand eczema per person-year of observation. Hairdressers without previous hand eczema were followed from the year of certification, usually the age of 18, and during years as active hairdressers. The referents were followed from 18 years of age. Onset of hand eczema or 1996 (end of the study) were regarded as individual endpoints. Incidence rate ratios (IRRs) of hand eczema, with 95% confidence intervals (95% CIs) were estimated by a Poisson regression using EGRET software (Statistics and Epidemiology Research Corporation, Seattle, WA, USA). For comparison of proportions, χ^2 -test was used, while for comparison of means, we used Student's *t*-test.

The relative excess risk due to interaction (RERI) was calculated to conclude whether there exists a biological interaction (synergism) between childhood eczema and hairdressing (Rothman, 1986; Andersson *et al.*, 2005). The attributable fraction (AF), i.e. the proportion of hand eczema cases that is attributable to childhood eczema, was calculated (Rothman and Greenland, 1998). Confidence intervals were established for both RERI and the AF. For details of the calculations, see Paper I.

4.2 DERMAL EXPOSURE TO PERMANENT HAIR DYES (PAPERS II AND III)

Paper II is an experimental study in which a hand rinse method for assessment of dermal exposure to compounds in permanent hair dyes was developed and validated. In the subsequent field study (Paper III) the method was used to assess the actual dermal exposure during hair dyeing in nine hairdressing salons in Stockholm.



Application of hair dye product.



Hand rinse sampling.

4.2.1 Test procedure (Paper II)

The hand rinse method was validated by studying the sampling efficiency for five different hair dye compounds at three different residence times and sample loads. “Residence time” is defined as the time the compound is in contact with the skin. The hands of 30 healthy volunteers were exposed to two hair dye products and a mixture of five reference compounds. The hair dye compounds used as reference were PPD, TDS, MAP, RES and MRE. Reference solutions with 20 mM and 40 mM of the reference compounds were made in borate buffer, with ascorbic acid added as antioxidant. Hair dye product A contained TDS, RES and MRE while product B contained PPD, MAP, RES and MRE. One hair dye product at a time was applied to one hand and the reference solution to the other hand. After different residence times the hair dye compounds were sampled. The hands of the test subjects were immersed in 50 ml of rinse liquid, 0.2 M ascorbic acid in a borate buffer with 10% ethanol, inside a PE bag sealed tightly above the wrist with a rubber band. The test subjects shook their hands vigorously for 2 minutes and then the rinse liquid was collected in 100 ml glass bottles. Two hand rinses were performed in succession. The hand rinse liquids were stored in a refrigerator until high-performance liquid chromatography (HPLC) analysis within 24 hours. The HPLC method used was a modification of the method developed by Vincent *et al.* (1999).

4.2.2 Dermal exposure assessment (Paper III)

The third study was a field study in which the dermal exposure to permanent hair dyes was assessed using the method described in Paper II. The study population was 33 hairdressers working in nine hairdressing salons in Stockholm.

Hand rinse samples were taken in the hairdressing salons during normal working hours. Hand rinsing was performed on three occasions during the hair dyeing process. The first sample was taken before mixing the hair dye cream with hydrogen peroxide, the second after application of the hair dye to the hair and the third after cutting the newly dyed hair. Samples were taken from both hands simultaneously. The samples were immediately transferred to 20 ml glass vials and stored in a cold box during transport to the laboratory freezer (-18°C). Samples of the hair dye mixtures were also collected, and dissolved in rinsing solution with a magnetic stirrer. All samples were analysed within 14 days. Twelve samples of newly dyed hair cuttings were extracted in rinse solution and their content of hair dye compounds compared with that found in the hair dye mixtures and on the hairdressers' hands.

4.3 PERMEATION TESTING OF PROTECTIVE GLOVES (PAPER IV)

4.3.1 Gloves

Four different gloves commonly used by hairdressers in Sweden and provided by the Swedish hairdressers' trade association (Frisörföretagarna) were selected for the permeation testing. The glove materials tested were PVC, NR, NRL and PE. All gloves were disposable and non-powdered, with thicknesses of 0.02 mm to 0.20 mm (see Table 1).

Table 1. Description of the tested protective gloves.

Glove	Material	Thickness, mm
A	Polyvinyl chloride, PVC	0.12 ± 0.008
B	Nitrile rubber, NR	0.11 ± 0.005
C	Natural rubber latex, NRL	0.20 ± 0.008
D	Polyethene, PE/copolymer	0.02 ± 0.01

4.3.2 Permeation test procedure

Samples were cut from the palm and back of unused gloves and mounted inside the test cell. The permeation was tested according to the European standard EN 374-3: 2003. A standard American Society for Testing and Materials (ASTM) test cell was used, a

glass (internal diameter, i.d., 1 inch (2.54 cm)), two-compartment chemical permeation cell. The exposure compartment contained the exposure solution, and the collecting compartment contained borate buffer with 0.2 M ascorbic acid as the collecting medium. The collecting medium was circulated in a closed-loop system with a flow rate of 5 ml/min, and mixed with a magnetic stirring bar. The material to be tested was placed vertically without tension as a barrier between the two compartments, the glove's normal outside surface facing the exposure compartment. The exposure solutions were 10% RES (w/v), 5% PPD and 0.75% TDS in borate buffer with 0.2 M ascorbic acid. Each glove was tested five times for PPD and RES and three times for TDS.

The permeation through the glove material was followed by taking 200 μ l samples from the collecting medium at 15 minute intervals. The samples were analysed with HPLC. The volume of the collecting medium was kept constant by adding 200 μ l of borate buffer with 0.2 M ascorbic acid directly after each sample was taken.

The permeation rate at steady state (P_s) and the cumulative breakthrough, the so-called "time-lag breakthrough (Lag-BT)", were calculated for each glove-substance combination, as was the estimated amount permeated after 2 and 4 hours.

5 RESULTS

5.1 OCCURRENCE OF HAND ECZEMA (PAPER I)

5.1.1 Hand eczema

The IR of self-reported hand eczema was 23.8 cases/1,000 person-years in hairdressers compared with 9.6 for the controls. For hairdressers who were younger than 25 years, the IR was even higher, 37.1 cases/person-years, v. 12.2 for the controls. A comparison between hairdressers and population controls gives an incidence rate ratio (IRR) of 2.5 (95% CI 2.2–2.8), and of 3.1 (95% CI 2.6–3.5) for the younger hairdressers.

The mean age at onset of hand eczema was 21.6 years for hairdressers and 21.2 years for the population controls. Forty per cent of the hairdressers reported that their hand eczema had started during time for vocational school.

The 1-year prevalence of self-reported hand eczema was 18.0% for the hairdressers compared with 12.1% for the controls ($p < 0.001$) and the cumulative lifetime prevalence was 29.1% for the hairdressers and 19.2% for the controls ($p < 0.001$).

Change of job due to hand eczema was reported by 5.5% of the hairdressers and 2.0% of the controls ($p < 0.001$). Twenty per cent of the hairdressers who reported ever having had hand eczema stated that they had changed jobs due to the disease.

5.1.2 History of atopy

A significantly lower proportion of the hairdressers (15.9%) compared with controls (21.1%) reported a history of childhood eczema ($p < 0.001$). The IR of hand eczema was higher among individuals who had had childhood eczema, both in hairdressers and in controls, giving an (age-adjusted) IRR of 1.9 and 2.2, respectively, compared with individuals without a history of childhood eczema.

The RERI was calculated to be 1.21 (95% CI 0.21–2.21; $p = 0.01$). The AF due to skin atopy was 9.6% (95% CI 5.7–12.4%).

For hairdressers reporting childhood eczema, the mean age at onset of hand eczema was 18.8 years, while it was 15.8 years for controls who had had eczema during childhood ($p < 0.001$). For 66% of the hairdressers reporting childhood eczema, the hand eczema had started before 21 years of age, compared with 34% among those without childhood eczema ($p < 0.001$). For the controls, the corresponding figures were 67% v. 33% ($p < 0.001$). Among those with onset of hand eczema during time for vocational school 28% reported childhood eczema.

5.1.3 Exposure and skin protection

The hairdressers reported a large number of potentially skin-damaging treatments per week. For alkaline permanent waving, hair colouring and bleaching, between two and

seven treatments per week was most common. A total of 58% of hairdressers stated that they performed shampooing more than 30 times a week. Glove use was most frequent during colouring and bleaching, but during permanent waving and shampooing there was less use of gloves. Of the glove users 64% reported using vinyl (i.e. PVC) gloves, while 50% used NRL gloves and 4% did not know the glove material (more than one answer was possible). Sixty-five per cent reported discolouration of the hands as the reason for using gloves, while 72% gave prevention and 19% gave alleviation of skin problems as the reason (more than one answer possible). Whereas 64% reported use of hand cream one to three times a day, 18% used cream more than four times a day and 18% never used hand cream. As many as 73% stated that they used rings or bracelets while working.

5.1.4 Non-responders

The dropout analysis showed no statistically significant difference between responders and non-responders regarding occurrence of hand eczema, childhood eczema and change of job. Lack of time was the most common reason for not returning the questionnaire.

5.2 DERMAL EXPOSURE TO PERMANENT HAIR DYES (PAPERS II AND III)

5.2.1 Sampling efficiency of the hand rinse method (Paper II)

The sampling efficiency varied for different hair dye compounds and residence times. Sampling efficiency after 5 minutes was between 67% and 90% for the different compounds in the different hair dye products (see Figure 3).

Sampling efficiency decreased with increasing residence time for the compounds in the different hair dye products; however, residence time did not have the same effect on the compounds in the reference solution. The sampling efficiency in the hair dye product was reduced by 40% for PPD and by about 30% for TDS after 30 minutes compared with 5 minutes' residence time. Different sample loads had little or no effect on the sampling efficiency. The amount of hair dye compounds found in the second hand rinse was between 0% and 10% of that in the first (not shown in the Figure).

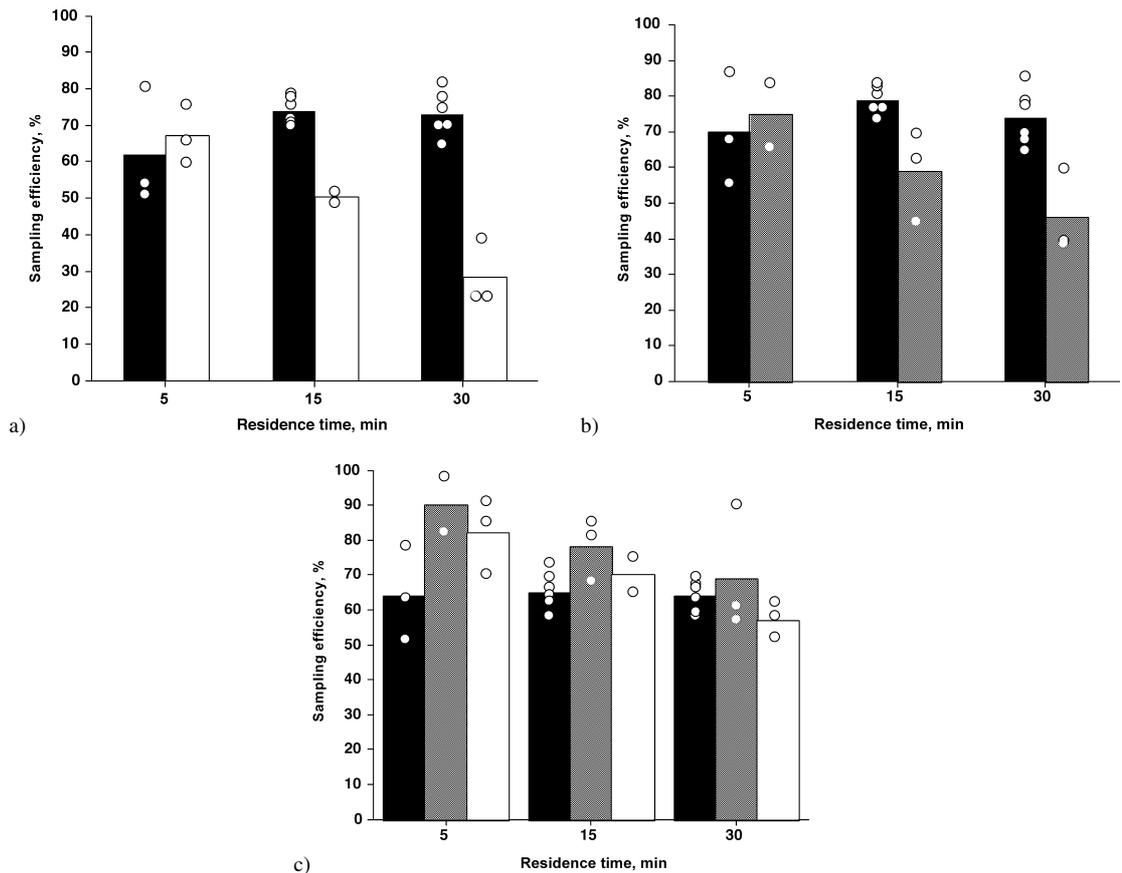


Figure 3 (a–c). Effect of residence time on sampling efficiency for (a) *p*-phenylenediamine (PPD); (b) toluene-2,5-diaminesulfate (TDS); and (c) resorcinol (RES) in the reference solution and hair dye products A and B (see Section 4.2.1). The sample load was 400 nmol for the reference substance, 20 mg for product A and 50 mg for product B. Black = reference substance; grey = product A; white = product B.

5.2.2 Dermal exposure assessment (Paper III)

Hair dye mixtures

The contents of the hair dye mixtures used by the hairdressers are shown in Table 2. Note that the mixtures could contain other hair dye compounds besides the five compounds analysed; however, they are not accounted for.

Table 2. Amount of *p*-phenylenediamine (PPD), *m*-aminophenol (MAP), toluene-2,5-diaminesulfate (TDS), resorcinol (RES) and 2-methylresorcinol (MRE) in the hair dye mixtures used, according to high-performance liquid chromatography (HPLC) analysis and the declaration of ingredients.

Compound	Amount found in hair dye mixtures, analysed using HPLC, % w/w (n=22)*	Number of hair dye mixtures that contained the compound, according to HPLC analysis (n=54)	Number of hair dye mixtures that contained the compound, according to the declaration of ingredients** (n=54)
PPD	0.004–0.250	10	5
MAP	0.001–0.051	33	33
TDS	0.019–0.447	40	40
RES	0.001–0.271	44	44
MRE	0.007–0.147	18	18

*Quantitative analysis of hair dye compounds was performed in 22 of the 54 hair dye mixtures.

**Five of the hair dye creams had no declaration of ingredients. All five contained PPD.

Hand rinse samples

Analysis of the hand rinse samples showed that hairdressers are exposed to compounds in permanent hair dyes. In Tables 3-5 we give the amount of PPD, TDS and RES found in the hand rinse samples; for results regarding all five analysed compounds, see Paper III. Table 3 shows the amount of hair dye compound found on both the dominant and the serving hand before mixing the hair dye cream with oxidizing cream. The amount of PPD, TDS and RES found in the hand rinse samples taken after application of the hair dyes to the client's hair is shown in Table 4. *p*-Phenylenediamine was found in samples from four hairdressers, TDS in twelve (dominant hand) and RES in 21. Seventeen of the hairdressers used gloves during application of the dye but no statistically significant differences in the measured dermal exposure were found between glove users and non-glove users.

Table 3. Amounts of *p*-phenylenediamine (PPD), toluene-2,5-diaminesulfate (TDS) and resorcinol (RES) found in hand rinse samples taken before mixing hair dye cream with hydrogen peroxide.

Compound	Dominant hand (n=33)		Serving hand (n=33)	
	Positive samples, n	Mean amount, nmol/hand (range)	Positive samples, n	Mean amount, nmol/hand (range)
PPD	3	294 (197–406)	3	263 (201–311)
TDS	7	149 (26–386)	6	192 (55–323)
RES	6	138 (24–433)	5	133 (24–397)

Table 4. Amount of *p*-phenylenediamine (PPD), toluene-2,5-diaminesulfate (TDS) and resorcinol (RES) found in hand rinse samples taken after application of hair dye.

Compound	Dominant hand		Serving hand	
	Positive samples, n	Mean amount, nmol/hand (range)	Positive samples, n	Mean amount, nmol/hand (range)
Total hairdressers (n=33)				
PPD	4	454 (22–939)	4	426 (36–839)
TDS	12	118 (19–379)	11	142 (13–741)
RES	21	185 (30–513)	21	136 (24–773)
Hairdressers using gloves (n=17)				
PPD	3	598 (209–939)	3	556 (173–839)
TDS	5	65 (19–197)	4	50 (13–149)
RES	11	183 (30–443)	10	98 (24–176)
Hairdressers not using gloves (n=16)				
PPD	1	22	1	36
TDS	7	156 (36–379)	7	194 (15–741)
RES	10	187 (42–513)	11	170 (31–773)

In hand rinse samples from 23/29 hairdressers measurable amounts of hair dye were found after cutting newly dyed hair. There was a tendency for the serving hand, the hand holding the hair, to be more exposed (Table 5). This difference in exposure loading between the dominant and the serving hand was statistically significant for RES ($p < 0.05$) and for TDS $p = 0.06$.

Table 5. Amount of *p*-phenylenediamine (PPD), toluene-2,5-diaminesulfate (TDS) and resorcinol (RES) found in hand rinse samples taken after cutting newly dyed hair.

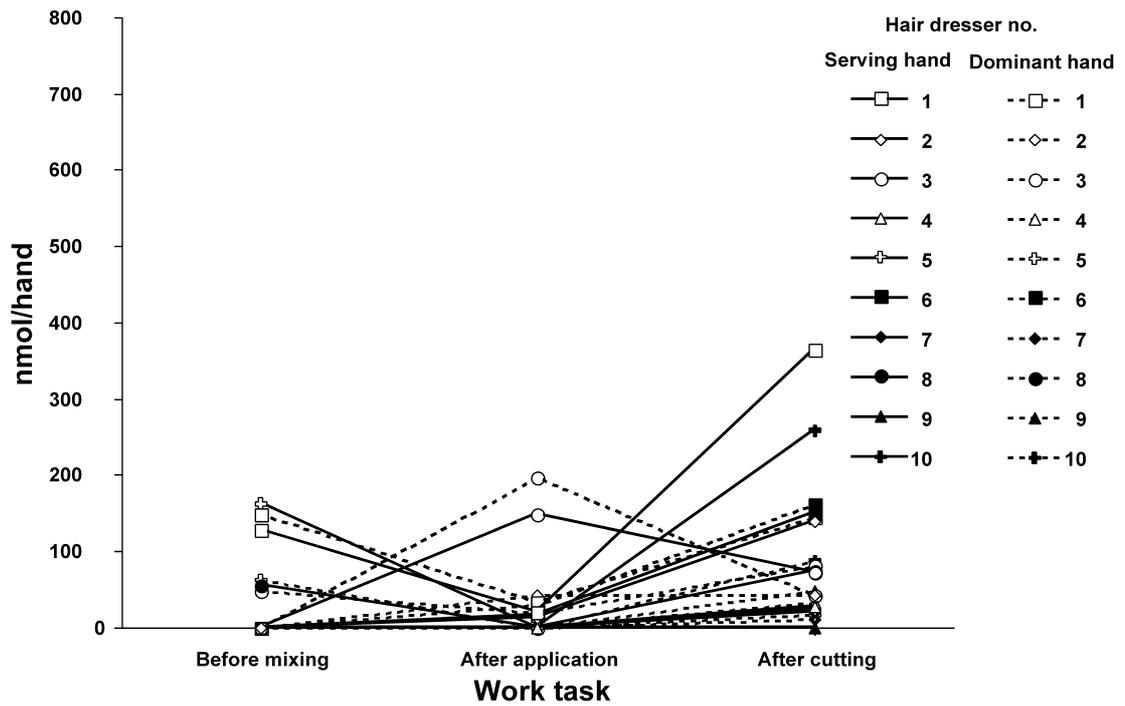
Compound	Dominant hand (n=29)		Serving hand (n=29)	
	Positive samples, n	Mean amount, nmol/hand (range)	Positive samples, n	Mean amount, nmol/hand (range)
PPD	5	178 (33–360)	5	153 (36–324)
TDS	14	71 (11–162)	13	120 (19–365)
RES	20	99 (19–364)	20	158 (22–736)

Measurable amounts of hair dye compounds were found in eleven out of twelve extracts from newly dyed hair cuttings. The same hair dye compounds as found in the extracts were also found in hand rinse samples after cutting newly dyed hair and in the hair dye mixtures used by the hairdressers. This indicates that the compounds found in the hand rinse samples originate from the newly dyed hair and that the hairdressers are exposed during cutting.

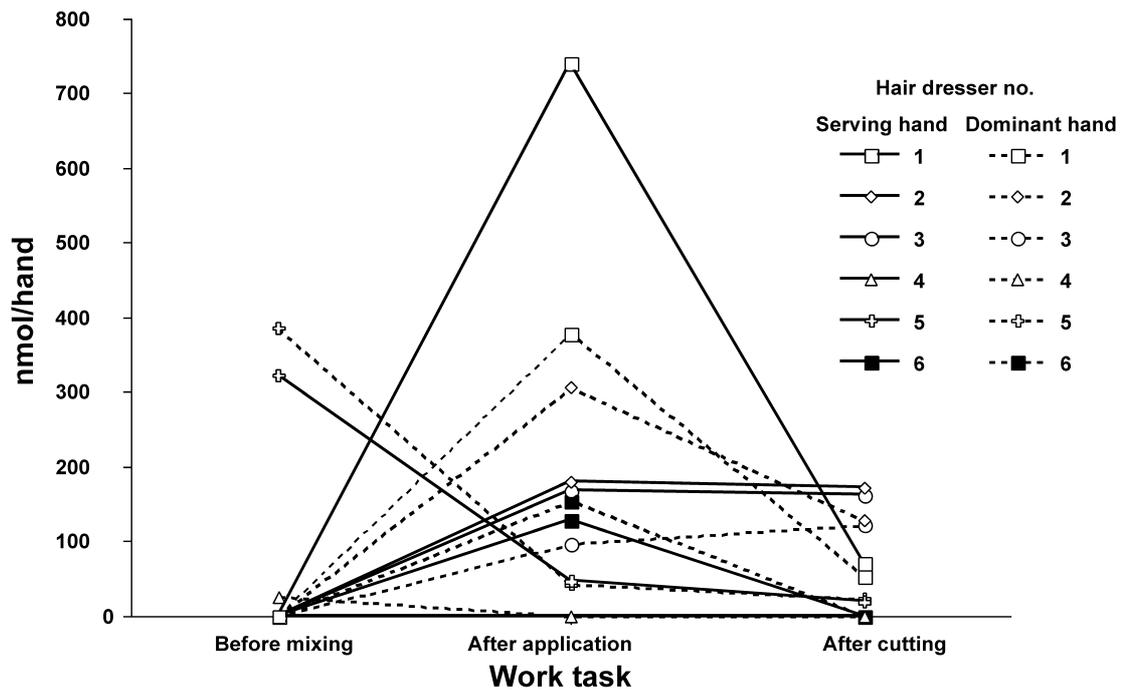
Figure 4 illustrates the contribution of TDS exposure from different work tasks and the dermal exposure level on each occasion for the individual hairdresser.

5.3 PERMEATION TESTING OF PROTECTIVE GLOVES (PAPER IV)

The Lag-BT and P_s of RES and PPD are summarized in Table 6. Two typical permeation curves are shown in Figure 5. All gloves gave good protection against the tested compounds. None of the gloves was permeated before 30 minutes and most of the gloves resisted permeation for more than 1 hour. None of the tested substances permeated glove C in 4 hours. Glove B was the second best glove, with only RES being able to permeate it, in a Lag-BT of more than 3 hours. Glove A gave the lowest protection against PPD and RES. Glove D, the thinnest glove, had the shortest Lag-BT but the permeation rate through the glove was very low. The estimated amount of PPD and RES permeated after 4 hours is presented in Table 7. The estimated amount permeated after 4 hours was highest for glove A, for both RES and PPD. Toluene-2,5-diaminesulfate did not permeate any of the tested gloves.



a)



b)

Figure 4. Amounts of toluene-2,5-diaminesulfate (TDS) found in hand rinse samples from hairdressers (a) using; and (b) not using gloves during application of hair dyes. The samples were taken before the start of the dyeing procedure, after application of hair dyes to the hair, and after cutting newly dyed hair. Hairdressers who had TDS-negative hand rinse samples on all occasions and hairdressers who did not cut the newly dyed hair are not included in the Figure.

Table 6. Arithmetic means and standard deviation (SD) for time-lag breakthrough (Lag-BT) (min) and permeation rates at steady state (P_s) ($\text{nmol cm}^{-2} \text{min}^{-1}$) for resorcinol (RES) and *p*-phenylenediamine (PPD).

Glove	RES		PPD	
	Lag-BT, min	P_s , $\text{nmol cm}^{-2} \text{min}^{-1}$	Lag-BT, min	P_s , $\text{nmol cm}^{-2} \text{min}^{-1}$
A	90±3.9 n=5	3.6±0.7 n=5	86±4.6 n=5	0.88±0.1 n=5
B	183±2.1 n=5	3.9±0.6 n=5	>240 n=5	n.b.
C	>240 n=5	n.b.	>240 n=5	n.b.
D	119±6.8* n=5	0.0079±0.0006* n=5	32±23 n=4	0.031±0.0031 n=4

For a description of the tested protective gloves, see Table 1.

n.b. = no breakthrough detected.

*permeates in small quantities (near the detection limit); very low permeation rate.

Table 7. Estimated amount of resorcinol (RES) and *p*-phenylenediamine (PPD) permeated after 240 minutes (nmol cm^{-2}).

Glove	RES	PPD
	Estimated amount permeated, nmol cm^{-2}	Estimated amount permeated, nmol cm^{-2}
A	543	135
B	223	n.b.
C	n.b.	n.b.
D	1.0	6.4

For a description of the tested protective gloves, see Table 1.

n.b. = no breakthrough detected.

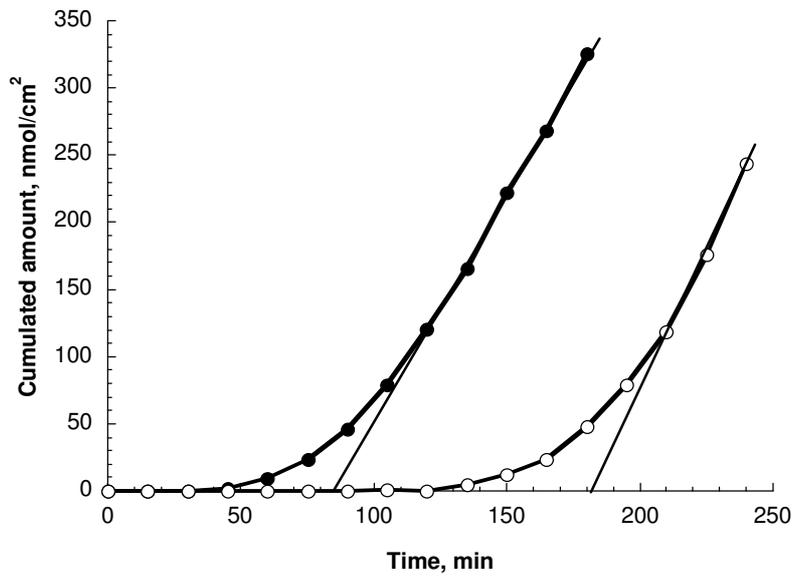


Figure 5. Permeation curves for resorcinol (RES), with glove A (polyvinyl chloride, PVC) to the left and glove B (nitrile rubber, NR) to the right. The time-lag breakthrough (Lag-BT) is achieved as the intercept with the x-axis.

6 DISCUSSION

6.1 HAND ECZEMA

The first study (Paper I) included in this thesis work was a nationwide retrospective longitudinal cohort study. The main result was that the occurrence of hand eczema is high among hairdressers and that hairdressing is a high-risk occupation for hand eczema, with extensive exposure to skin-damaging substances. Remarkably high IRs and IRRs of hand eczema among hairdressers were found. Previous studies on the occurrence of hand eczema in hairdressers give a cumulative prevalence of 17–42% (Holm and Veierod, 1994; Leino *et al.*, 1998). A high prevalence (24–70%) and IR (152–328 cases per 1,000 person-years) of hand eczema among apprentice hairdressers have been reported (Budde and Schwanitz, 1991; Smit *et al.*, 1994; Uter *et al.*, 1998). The only studies presenting IRs of hand eczema in active hairdressers are based on registers of industrial injuries, which report incidences of 5.6–9.7/1,000 person-years (Dickel *et al.*, 2001; Skoet *et al.*, 2004). Registers of occupational skin diseases probably underestimate the actual occurrence of disease owing to underreporting (Diepgen and Coenraads, 1999). In Sweden only 5–10% of the hand eczema cases in hairdressers are reported. The incidence of hand eczema reported to industrial registers in Germany and Denmark is considerably lower than that found in this study, which seems to suggest that there must be some underreporting (Dickel *et al.*, 2001; Skoet *et al.*, 2004).

In our study we found that hand eczema occurs early in life for many individuals. For about half of the hairdressers, the onset of hand eczema occurred before the age of 20, which also was true for the controls. For 40%, the hand eczema started during time for their vocational training. An early age of onset has also been reported by other authors (Budde and Schwanitz, 1991; Smit *et al.*, 1994; Uter *et al.*, 1998; Uter *et al.*, 1999a; 1999b).

In the present study “hand eczema” is defined as “self-reported hand eczema”. The questions used concerning self-reported 1-year prevalence of hand eczema and childhood eczema have been previously validated (Meding and Barregård, 2001; Stenberg *et al.*, 2006). The question, “Have you had childhood eczema?”, overestimates the prevalence of childhood atopic eczema (AE). Persons reporting ever having had hand eczema tend to report more false-positive cases of childhood AE than do people without hand eczema. The authors conclude that the question may overestimate AE as a risk factor for hand eczema in adult population surveys by a factor of 1.6. The question regarding 1-year prevalence of hand eczema was shown to lead to some underestimation; however, using IRs gives a better understanding of the risk of developing hand eczema considering the long duration of the disease. The “true” relative risk would have been higher considering that the prevalence of skin atopics was lower among the hairdressers than among the controls. Comparison with a low-risk group instead of the general population would also have resulted in a higher IRR.

In the present study population the self-reported number of skin-damaging treatments was high, with most of them being performed several times a week. Hair dyeing, permanent waving, and bleaching were performed between two and seven times a week. Shampooing was performed more than 30 times a week by more than half of the hairdressers. Glove use was most frequently reported during hair dyeing and bleaching, but during permanent waving and shampooing, gloves were used less frequently, which is consistent with findings by other authors (Nixon *et al.*, 2006). Use of PVC gloves was reported by the largest group of hairdressers, followed by NRL gloves.

The reported number of treatments and amount of glove use reflect the exposure at the time of answering the questionnaire. An investigation of possible associations between incidence of hand eczema and specific hairdressing activities was not performed owing to the retrospective design of the study. To study this association would have been desirable but the information about exposure, e.g. frequency of hair washes or colouring, many years back in time may have been biased (recall bias). To make such associations it would be better to perform a prospective study.

Even though individuals with a history of childhood eczema have an increased risk of developing hand eczema as an adult, as confirmed by our and other studies (Rystedt, 1985; Meding and Swanbeck, 1990; Coenraads and Diepgen, 1998; Bryld *et al.*, 2003; Dickel *et al.*, 2003; Meding and Järholm, 2004), occupational exposure in hairdressing is a factor that contributes strongly to the development of hand eczema. A synergistic effect was seen between hairdressing and childhood eczema, showing that work as a hairdresser highly contributes to the outcome of the disease. In a German study 19% of occupational skin diseases among hairdressers could be ascribed to atopy (Dickel *et al.*, 2003). In our study the AF of hand eczema in hairdressers from skin atopy was 9.6%, indicating that only one out of ten hand eczema cases could be ascribed to atopy. The prevalence of childhood eczema in the hairdressers was lower than in the general population, which implies a selection away from hairdressing for skin atopics. Another German study found lower prevalence of childhood eczema among hairdressers compared with office workers (Uter *et al.*, 1999a). The low AF from skin atopy in hairdressers leads to the conclusion that the exposure in hairdressing is a strong risk factor for hand eczema regardless of atopic disposition.

The hairdressers in this study reported change of job almost three times more often than did the controls. A high frequency of hairdressers having to leave their job because of contact dermatitis has also been reported by other authors (Budde and Schwanitz, 1991; Leino *et al.*, 1999). In our study one out of five hairdressers who had ever had hand eczema had left the profession because of eczema. This implies that the burden to society and to the individual is of considerable proportions.

6.2 HAIR DYES: DERMAL EXPOSURE AND HAND PROTECTION

A removal technique, hand rinse sampling, was chosen for validation of sampling performance characteristics. The sampling efficiency for the substances contained in permanent hair dyes was high. Pilot studies performing sampling with tape stripping

were initially carried out. Advantages of the hand rinse method were that the sampling efficiency was higher than with tape stripping; also, hand rinsing makes it possible to assess the exposure of the whole hand. Our intention was to assess the contribution of different work tasks to dermal exposure. For this, the hand rinse method is a good choice. The approach enabled us to make a direct comparison between different work tasks, which provides useful knowledge for preventive measures. In the present study we assumed that dermal exposure of other parts of the body is negligible. Removal techniques such as hand rinse sampling measure the amount of substance on the surface of the skin, in the so-called “skin contaminant layer”. They do not measure the exposed area. This is a disadvantage since the local dose cannot be measured, nor can the dose per area be calculated, which factor is important for sensitization. To assess the exposed area a visualization technique needs to be used. In hairdressing the exposure locations may vary depending on the work task and consequently it is desirable to choose a method that measures the exposure of the whole hand. However, the dermal exposure is not evenly distributed across the hand and to use the total area of the hand for calculation of dose per area would not be a correct approximation. For assessment of dermal uptake, sampling methods that measure the concentration of the substance in the skin contaminant layer should be chosen according to the conceptual model of Schneider (Semple and Cherrie, 2003), but no such methods are available today. Study II showed that the sampling efficiency decreases with residence time, which probably is an effect both of oxidation of the hair dye compounds and of percutaneous penetration. These results are consistent with results of Fenske and Lu (1994), who found that for pesticides, the removal efficiency of hand washing decreased with increasing residence time. During hair dyeing in the hairdressing salons the hair dye products are mixed with an oxidation cream containing hydrogen peroxide to trigger oxidation. The amounts of aromatic amines such as PPD and TDS decrease rapidly, which makes quantification of the exact exposure load over time difficult. The measured value is the amount of hair dye compounds on the hand(s) at the precise moment of the hand rinse. To avoid effects of decreasing sampling efficiency due to oxidation and percutaneous penetration the sampling should be performed directly after the work task to be assessed.

In the present study the hand rinse method was successfully used to assess dermal exposure to permanent hair dyes in hairdressers during hair dyeing in salons. Hair dye compounds were found in samples taken after application of hair dyes and also, after cutting newly dyed hair. There was a tendency that the amount of hair dyes found in samples taken after cutting was higher from the serving hand than from the dominant hand, probably because the former holds the hair during cutting. An analysis of extracts of hair cuttings showed that hair dye compounds are in fact released from the hair. The same compounds were also found in the hair dye mixtures and on the hairdressers’ hands. In a study by Rastogi *et al.* the content of dye precursors in hair dye products was analysed 30–40 minutes after mixing with hydrogen peroxide (the time recommended for dyes to stay in the hair after application) and high amounts of aromatic amines remaining in the mixtures were found (Rastogi *et al.*, 2006). These findings support our results that there are indeed hair dye precursors left in the hair dye mixtures after the subscribed reaction time with hydrogen peroxide. The results from the hand rinse samples taken after cutting indicates that these compounds are not rinsed off but remain in the hair and that hairdressers are exposed while cutting the hair. The exposure loadings found on the hands of the hairdressers were at a level at which there

is a risk of sensitization and/or elicitation of contact allergy (e.g. for PPD, 22–939 nmol/hand). For PPD, the lowest observed effect level (LOEL, derived from the human repeat insult patch test, HRIPT) in humans has been found to be 93 nmol/cm² (Marzulli and Maibach, 1974), with an elicitation threshold in patch testing of 28 nmol/cm² (Mc Fadden *et al.*, 1998).

Hairdressers were exposed to permanent hair dyes irrespective of whether they used gloves or not. In Study IV we found that the permeation through the gloves most commonly used by hairdressers is low. Our field observations, however, made it clear that it is the way the gloves are used that is the major problem. The majority of the hairdressers used disposable gloves more than once, and the gloves were often turned inside-out after rinsing with water, and then reused. Natural rubber latex gloves were often used for 2–3 months or until they were discarded as damaged or torn. Under these conditions the gloves themselves may be a source of contamination.

In the present study positive samples were taken before mixing the hair dye cream with oxidizing cream (Table 3 and Figure 4). This exposure may have derived from previous hair dyeing on the same day or from so-called “background exposure” from contaminated surfaces such as workbenches, trolleys and telephones or equipment such as scissors, combs or hair dryers. Preliminary wipe samples taken from surfaces confirmed that many were contaminated with hair dye compounds (data not shown). Owing to their formulation hair dye creams easily stick to such surfaces. In future studies we recommend that surface sampling is included in the investigation. Figure 4 shows that some of the hairdressers in the present study were exposed to relatively high amounts of hair dyes before the start of hair colouring.

6.3 PREVENTION

Prevention of occupational dermatitis among hairdressers is a matter of great concern. Other authors have shown a considerable impact of hand eczema on both quality of life and economic circumstances for individuals and society (Skoet *et al.*, 2003; Colgan *et al.*, 2006).

There are several ways to achieve prevention, such as substitution of skin irritants and contact allergens by less harmful compounds, use of protective gloves, introduction of work routines that prevent skin contact with hair cosmetic products and water, and education about work-related hazards and preventive measures during vocational training. A recent published study confirms that information about preventive measures during the educational period is important (Wong *et al.*, 2005). It was found that knowledge about chemicals and preventive measures increases the intention to acquire information about chemical safety and to use personal protective equipment.

Substitution

The Swedish Work Environment Act states that personal protective equipment shall be used when adequate security from ill health or accidents cannot be achieved by other means (Anonymous). According to their stipulation, substitution of the most potent

allergens used in hairdressing would be desirable. The constituents in hair dyes most known to cause contact allergy are the aromatic amines PPD and TDA (or its sulfate TDS). In Sweden between 1943 and 1992 PPD was prohibited in cosmetics and hygiene products because of its sensitizing properties. Toluene-2,5-diamine was prohibited during the years 1943–1964. From 1964 to 1992 TDA instead of PPD was used in permanent hair dyes (Wahlberg *et al.*, 2002). When Sweden entered the EU in 1992 the national prohibition was lifted in line with the European Economic Community (EEC) Cosmetic Directive that allows PPD in hair dye products with a concentration limit of 6%, and TDA with a limit of 10%. In a report from the Medical Products Agency (MPA) in Sweden in 1993, figures after 1982, of incidence of positive PPD patch testing among hairdressers at dermatology clinics in countries without prohibition, were higher than in countries with a prohibition of PPD, including Sweden. The recommendation from the MPA was to continue the prohibition against PPD in Sweden. Attempts were made by the Swedish National Board of Occupational Safety and Health, now renamed the “Swedish Work Environment Authority”, to control the professional use of PPD by adding it to the list of chemicals to be handled only with permission. This prohibition did not have the desired effect, since no hairdressers applied for permission, despite the fact that PPD was used in hairdressing salons. One can only speculate on the reasons for this, one of which probably is lack of knowledge about the ingredients in the products hairdressers use. According to the EEC Cosmetic Directive, all cosmetic products handled in EU/EEC countries since January 1999 must bear a declaration of ingredients using the International Nomenclature of Cosmetic Ingredients (INCI) name of each ingredient. In spite of this we have seen in the course of our investigations that some products that are used in hairdressing salons still lack information on ingredients. In the present study five out of 54 hair dye products lacked a list of ingredients and these contained PPD. The hairdressers themselves had imported these products. This lack of knowledge of the content of hair dye products can be hazardous to the health of both hairdressers and their clients.

Of course removal of dangerous chemicals can only be made on condition that a substitute exists. A substitute for both PPD and TDA in permanent hair dyes does not exist today and a change in the nearby future is hard to foresee. According to the manufacturers there is little demand for an alternative to the oxidative hair dyes among hairdressers and hair dye users.

Protective glove use and educational training

The glove permeation tests showed that the protective gloves commonly used by hairdressers give good protection against the tested substances. Observations during our field study showed poor knowledge among the hairdressers about how protective gloves should be used. The gloves were put on too late; and they were reused for very long periods or until they showed tears. Some hairdressers even wore torn gloves. A simple way of reducing contact with skin-damaging substances would be to use disposable gloves, and change them often. Introducing proper work routines is also important, as is carefully avoiding contamination of surfaces and work tools. Hair should be cut before it is coloured. Information on proper glove use should be introduced at an early stage in hairdressing training in order to establish good routines and habits.

Vocational guidance

The result of the first study can be interpreted as indicating that the importance of an atopic disposition in development of hand eczema has been overestimated. From the individual point of view it is essential to have knowledge of the importance of skin atopy as a risk factor for hand eczema and to get vocational guidance. However, regardless of atopic disposition, hairdressing is a high-risk occupation for the development of hand eczema. The main focus in prevention should be on information and education on skin-damaging substances and how to avoid skin contact. The exposure in a high-risk occupation such as hairdressing is apparently of great importance for development of hand eczema.

Hair dye consumers

Prevention of OCD in hairdressers does not overcome the problems with these substances for the hair dye clients. In a Danish population-based interview study, 5.3% of the individuals who had ever used hair dyes reported adverse skin reactions to hair dyes and of these only 15% had been in contact with health care services after the hair dye reaction (Søsted *et al.*, 2005). In 2002 a clinical investigation in Sweden sought to examine whether the reintroduction of PPD in hair dyes had caused an increase in the number of cases of contact allergy among patients attending dermatological clinics (Wahlberg *et al.*, 2002). This study showed no increase or trend in line with figures from the 1980s. It is, however, hard to estimate the number of individuals in the general population who are exposed to PPD from hair dyes. There is reason to believe that at least some PPD-containing hair dye products were used during the prohibition, especially since no inventory or analysis of hair dye products was conducted during this period. To the best of my knowledge, no population-based survey of skin reactions to hair dyes has ever been performed in Sweden. Some systemic diseases, such as bladder cancer, are associated with the use of hair dyes, both in hairdressers and in hair dye consumers. A thorough risk analysis of the use of hair dyes is therefore justified.

7 CONCLUSION

Hairdressers are highly exposed to skin-damaging substances. The self-reported incidence of hand eczema in female hairdressers in the present study was substantially higher than previously found in register-based studies and also higher than in control persons from the general population. Onset of hand eczema often occurs early in life. The risk of hand eczema is increased in relation to a history of childhood eczema, but only 10% of the hand eczema cases would be prevented if no atopics entered the trade, according to the calculation of the AF.

Hand wash sampling with bag rinsing has proved to be a useful tool for studying occupational dermal exposure to permanent hair dyes in hairdressers. The sampling efficiency during hand rinsing was found to be adequate for measuring the amount of hair dye on the hands at the time of sampling.

Hairdressers are exposed to hair dye compounds during hair dyeing. Exposure occurs while applying hair dyes to the client's hair, during cutting of newly dyed hair and from background exposure, e.g. contact with contaminated work tools and surfaces. The exposure loadings in the present study were at levels that constitute a risk of sensitization and/or elicitation of contact allergy. Gloves were often used improperly, and glove use was insufficient to prevent exposure. The group of hairdressers who wore gloves were exposed to permanent hair dyes to the same extent as hairdressers who did not wear gloves. The gloves most commonly used in hairdressing all gave considerable protection against PPD, TDS and RES in the standardized permeation test, EN 374-3:2003. The glove materials were all seen to withstand permeation well, which confirms that it is the improper use of gloves, and not the gloves per se, that cause the problem.

Measures to prevent development of hand eczema in hairdressers should be given high priority. This can be achieved by reducing exposure to skin-damaging substances such as hair dye cosmetic products that are irritants or sensitizers, by reducing wet work and, if possible, through removal of the most potent allergens used in hairdressing. Finally, education about preventive measures, both at an early stage and later during training, can have a significant impact on glove use and, consequently, on prevention.

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