Percutaneous absorption of aromatic amines in rubber industry workers: impact of impaired skin and skin barrier creams

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Background: Several aromatic amines (AA) could cause bladder cancer and are an occupational hygiene problem in the workplace. However, little is known about the percutaneous absorption of chemicals via impaired skin and about the efficacy of skin protection measures to reduce internal exposure.

Aims: To determine the impact of skin status and of skin protection measures on the internal exposure to AA in workers manufacturing rubber products.

Methods: 51 workers occupationally exposed to aniline and o-toluidine were examined. The workplace conditions, risk factors for skin and the use of personal protective equipment were assessed by means of a self-administered questionnaire. The skin of hands and forearms was clinically examined. Exposure to aniline and o-toluidine was assessed by ambient air and biological monitoring (analyses of urine samples and of haemoglobin adducts).

Results: Haemoglobin-AA-adduct levels in workers with erythema (73%) were significantly higher ($p < 0.04$) than in workers with healthy skin (mean values: aniline 1150.4 ng/l vs 951.7 ng/l, o-toluidine 417.9 ng/l vs 118.3 ng/l). The multiple linear regression analysis showed that wearing gloves significantly reduced the internal exposure. A frequent use of skin barrier creams leads to a higher internal exposure of AA ($p < 0.03$). However, the use of skincare creams at the workplace was associated with a reduced internal exposure ($p < 0.03$). From these findings we assume that internal exposure of the workers resulted primarily from the percutaneous uptake.

Conclusions: The study demonstrates a significantly higher internal exposure to AA in workers with impaired skin compared with workers with healthy skin. Daily wearing of gloves efficiently reduced internal exposure. However, an increased use of skin barrier creams enhances the percutaneous uptake of AA. Skincare creams seem to support skin regeneration and lead to reduced percutaneous uptake.

Occupational exposure to aromatic amines (AA) could be a significant cause of ill health. Several AA are well-known carcinogens to humans and/or animals, and exposure to them in the workplace should be well controlled.¹ Occupational exposure to AA could be the most common source of urinary bladder cancer in Germany, and the number of bladder cancers due to occupational exposure has been increasing in the past decade.^{2,3} Replacement of AA and the corresponding intermediates is not possible in some industries. In the rubber industry, AA aniline and o-toluidine are released from the accelerators di-ortho-tolylguanidine and diphenylguanidine, especially during the vulcanisation process of rubber products. In Germany, o-toluidine is considered to be carcinogenic to humans.¹ The International Agency for Research on Cancer classified o-toluidine as probably carcinogenic to humans, but could not find sufficient data to classify aniline as a human carcinogen.⁴

For some chemicals in the workplace—for example, glycol ethers, percutaneous absorption can be the main route of uptake.^{5,6} Several AA can also be absorbed percutaneously.^{1,7,8} Percutaneous absorption of AA can result from direct dermal contact, and also from airborne vapour, aerosols and particulates. Little is known about the absorption of workplace chemicals via impaired skin. We have recently demonstrated that over 70% of workers in the printing industry had hands with impaired skin.^{9,10} The breakthrough time of aniline through protective gloves is often only few minutes.¹¹ All these factors complicate the provision of effective safety measures to prevent systemic absorption in the workplace.

In this study, we determined the impact of skin status and of skin protection measures (among others, gloves, skin barrier and skincare creams) on the internal exposure of AA in workers manufacturing rubber products at a supplier for the automobile industry.

METHODS

Groups

A total of 51 workers (46 men, 5 women) at three plants of one supplier for the automobile industry were examined. In our study, all workers exposed to aniline and o-toluidine were considered. The workers were selected by occupational hygienists at the plants. According to the hygienists' information, the participation rate of the exposed workers was 98%. The workers were exposed to aniline and o-toluidine during the manufacturing of rubber products. The workers carried out mixing of raw materials, semi-finishing/assembly, curing (vulcanisation), deburring and final inspection of the products. In workers, we expected skin exposure from dermal contact with vapours and particles in the air during vulcanisation and from direct dermal contact when handling raw rubber materials and rubber products in all other jobs.

Ambient air and biological monitoring

The exposure of the workers was assessed by ambient air and biological monitoring. The analyses were performed with

Abbreviations: AA, aromatic amines; Hb, haemoglobin; RIE, relative internal exposure; TEWL, transepidermal water loss

validated analytical methods.^{12–14} The concentration of aniline and o-toluidine in the workplace air was measured by personal air monitoring (National Institute for Occupational Safety and Health method no 2017).¹² The current internal exposure in workers was determined by analysis of AA in post-shift urine samples and the cumulative internal exposure was determined by analysis of the corresponding haemoglobin (Hb) adducts using gas chromatography with mass-selective detection and negative chemical ionisation. The AA were determined in urine after hydrolysis to give the total amount of AA. The analytical procedures for the determination of AA in biological materials have been described previously.^{13, 14}

The assessment of the risk of percutaneous absorption to aniline and o-toluidine was calculated by the relative internal exposure (RIE) index¹⁵:

$$\text{RIE} = \frac{\text{Chemical concentration in urine } (\mu\text{g/l})}{\text{Chemical concentration in the air } (\mu\text{g/m}^3)}$$

This equation leads to an index that increases with an increase in percutaneous absorption, and allows a standardisation of the internal exposure that all workers would be exposed to from the same concentration in the air. RIE can compare the relationships between internal and external exposure for individuals and help to estimate the part of percutaneous absorption contributing to the total AA uptake.¹⁵ The influences of smoking habits of the workers on the internal exposure were assessed by the analysis of urinary excretion of cotinine. A cut-off of 100 µg cotinine per litre of urine was used to distinguish between smokers and non-smokers.¹⁶

Questionnaire investigation

The workers were asked to complete a self-administered questionnaire to report on the conditions at the workplace, and on occupational risk factors for skin complaints, lesions, history of skin diseases, hand washing frequency at the workplace and the use of occupational personal protective equipment (breathing masks, gloves, skin barrier and skincare creams¹). These factors are considered to be important as the cause of skin irritation and potential confounders in occupational contact dermatitis studies.^{17, 18}

Additionally, the workers were asked about some of their domestic activities, such as cleaning and dishwashing without gloves, car repair, house construction or redecoration, gardening or farming and other relevant hobbies.

Clinical examination of skin and transepidermal water loss

The skin status was assessed by clinical examination and by the measurement of the transepidermal water loss (TEWL). Hands and forearms of workers were examined visually for lesions by a trained physician. The lesions considered included erythema, scaling and other pathological findings. The grading of erythema and skin scaling was performed immediately during clinical examination in accordance with recently published studies with reference to the Organisation for Economic Co-operation and Development guideline: grade 0, no pathological skin findings; grade I, very slight erythema or discrete scaling; grade II, well-defined erythema or fine lamellar scaling; grade III, moderate erythema or rough lamellar scaling; and grade IV,

¹The authors are aware that a scientifically based characterisation of skin barrier and skincare creams is not available. The workers were asked to declare the use of the creams before and during work as skin barrier creams, and the use of the creams after work as skincare creams. In practice, it could be possible that not all workers applied the skin creams according to the recommendations of the manufacturers.

severe erythema or extensive scaling.^{9, 19–21} The physician was blinded to the exposure data while examining the skin.

Measurements of TEWL were carried out in the local medical care rooms of the plants. TEWL was measured in workers after completion of the questionnaires and acclimatisation to room conditions for about 20–30 min. TEWL was determined automatically by the Skin Monitoring Centre TC350 equipment (Courage+Khazaka Electronic, Cologne, Germany) and calculated as the mean of 10 single measurements within 30 s. To minimise the influence of ambient conditions, we kept those as similar as possible for all workers. Room temperatures measured during the examination were in a range of 20.6–22.8°C (median: 21.8°C). The skin-surface temperature was measured on the back of the dominant hand and of the volar forearm using a digital precision thermometer GTH 1160 (Greisinger Electronic, Regenstauf, Germany). The skin-surface temperature ranged from 26.1°C to 34.1°C (median: 31.2°C).

Statistics

The relationship between skin lesions in terms of erythema and Hb adducts for aniline and o-toluidine is represented as box-and-whisker plots.

Statistical analyses were performed with SPSS V 12.0 computer software. Correlation was quantified with the two-tailed Pearson's coefficient in cases of categorical variables or two-tailed Spearman's rank coefficient when only continuous variables were chosen. Non-parametric Mann-Whitney U test (two-tailed) was applied to calculate the statistical significance. The level of significance was $p < 0.05$.

To explore the influence of factors of occupational skin exposure on internal exposure, multiple linear regression analyses were carried out with the RIE index as dependent variable. The regression model included, simultaneously, the continuous variables—age of workers, daily wearing time of gloves, hand washing frequency at the workplace, application frequency of skin barrier and skincare creams. The categorical variables—wearing of breathing masks and wearing of gloves—were included as independent explanatory variables.

RESULTS

Ambient air and biological monitoring

Table 1 presents the results of ambient air and biological monitoring separated for non-smokers and smokers. The concentration of AA in the air was, with one exception, within the German occupational threshold limit values. In five urine samples, the concentrations of o-toluidine were below the analytical detection limit of 0.05 µg/l. The other results of biological monitoring were found to be above the detection limit. The correlations of o-toluidine concentrations in air and in urine, as well as for Hb adducts, were significant (Spearman's rank coefficient: 0.84 vs 0.78, $p < 0.001$). Also, the correlation between urinary AA values and Hb adducts was significant (Spearman's rank coefficient: 0.73, $p < 0.001$). No significant correlations were found for aniline, probably owing to the only slight elevated occupational exposure compared with the non-occupational background exposure from other sources—for example, diet.

In our study, non-smoking workers showed higher internal exposure for aniline and o-toluidine than smokers, but the difference was not significant ($p > 0.05$). Also, the airborne exposure at the workplace was not significantly different for both groups.

Influence of exposure conditions

Table 2 presents the data from the questionnaire investigation. The data were evaluated with regard to the variables, which could influence skin status and TEWL and also act as

Table 1 Results for ambient air and biological monitoring of two studies in the rubber industry

		Aniline		o-Toluidine	
Exposure variables	Unit	Non-smoker	Smoker	Non-smoker	Smoker
Our study		Range (median, mean) 95th centile		Range (median, mean) 95th centile	
Air concentration*†‡	µg/m³	1.0–37.4 (2.5, 6.6) 37.4	0.3–48.3 (3.3, 6.7) 33.5	0.1–524.0 (26.3, 61.4) 524.0	<DL–93.9 (0.4, 11.0) 72.5
Urinary concentration§	µg/l	3.2–37.6 (12.2, 12.7) 37.6	2.2–37.0 (10.2, 11.8) 36.4	<DL–292.4 (6.0, 38.6) 292.4	<DL–242.9 (0.6, 14.5) 100.0
Urinary concentration in the general German population¶	µg/l	<DL–35.5 (1.3, –)	<DL–34.6 (2.3, –)	<DL–11.9 (0.4, –)	
Hb adducts in exposed workers**	ng/l	6.6 367–2662 (1112, 1213) 2662	7.8 351–2584 (933, 1042) 2578	2.6 10–1986 (372, 432) 1986	11–1729 (43, 287) 1581
US study		Mean (SD)		Mean (SD)	
Hb adducts in non-exposed workers in the rubber industry††	ng/l	499 (242)	518 (145)	563 (893)	562 (1130)
Hb adducts in exposed workers in the rubber industry††	ng/l	2572 (1188)	3164 (1720)	6564 (6029)	6479 (3539)

DL, analytical detection limit.

*DL: 0.2 µg/m³ for aniline, 0.05 µg/m³ for o-toluidine.†The German maximum concentration in the workplace air for aniline is 8000 µg/m³.‡The German technical exposure limit in the workplace air for o-toluidine is 500 µg/m³.

§DL for both AA: 0.05 µg/l, for the relative internal exposure index half of the DL was used for five samples for o-toluidine.

¶Values are obtained from Weiss *et al.*²⁴ where o-toluidine values were not differentiated regarding the smoking status. Mean values were not calculated.

**DL: 0.5 ng/l.

††Hb adducts in the rubber workers in USA obtained from Ward *et al.*²⁹

confounding factors from the perspective of occupational exposure. None of the workers reported a history of atopic dermatitis. The exposure frequency of the domestic factors in our study group was low (table 2). There was no significant association between these domestic factors and the occurrence of skin lesions, as well as with the internal exposure to AA.

Skin lesions and transepidermal water loss

Table 3 presents the results of clinical examination of the skin. Visible skin lesions, especially in terms of erythema and/or scaling, have been observed almost symmetrically on both hands and/or forearms in 42 (82%) of 51 workers. The skin lesions can be classified as early stages of irritant contact dermatitis.

TEWL on the back of the hands in workers was in the range of 9.9–55.1 (median: 21.1) and on volar forearms of 5.4–28.0 (median: 11.4) g/m²h. There was no significant correlation between TEWL and the degree of erythema (Pearson's

correlation coefficient: 0.09, *p* = 0.55). Room and skin-surface temperatures did not significantly influence TEWL on hands (Spearman's rank coefficients: 0.19 and –0.20, *p* = 0.19 and *p* = 0.17).

Internal exposure and impaired skin

Figure 1 presents the relationship between cumulative internal exposure in workers and skin erythema on hands. Higher levels of Hb adducts were found in workers with an impaired epidermal barrier (skin erythema) compared with workers with healthy skin (mean values: for aniline 1150.4 vs 951.7 ng/l, *p* = 0.035; for o-toluidine 417.9 vs 118.3 ng/l, *p* = 0.039). Scaling of the skin, however, did not show an association with internal exposure. The skin-surface temperature was not a confounding factor regarding the dermal exposure, because no significant correlation with RIE indices (Spearman's rank coefficients: 0.19 and –0.20 (*p* = 0.23 and *p* = 0.22) for aniline and o-toluidine, respectively) was observed. Also, the use of

Table 2 Occupational and domestic factors with possible influence on internal exposure

	Range (median, mean)
Factors	
Age (years)	20–61 (37.0, 36.8)
Duration of occupation in the rubber plant (years)	0.8–40 (6.1, 10.2)
Influencing factors: workplace	
Workers using breathing masks	n = 3 (6%)
Hand washing frequency at workplace (times per day)	1–20 (4, 7.2)
Workers wearing gloves	n = 40 (78%)
Daily wearing time of gloves (min)	10–480 (240, 267)
Workers applying skin creams	n = 30 of 50 (60%)
Application of skin barrier cream (times per day)	1–8 (1.5, 2.3)
Application of skincare cream (times per day)	1–3 (1, 1.3)
Influencing factors: domestic	
Workers applying skincare creams	n = 28 of 50 (56%)
Daily cleaning/dishwashing without gloves	n = 14 (27%)
Daily house construction or redecoration	n = 3 (6%)
Daily gardening or farming	n = 2 (4%)
Workers identified as smokers by urinary cotinine concentration*	n = 36 (71%)

*The concentration of urinary cotinine ranged from 3 to 4471 µg/l, workers having >100 µg/l were considered as smokers.

Table 3 Overview of skin lesions, depending on localisation and intensity

Skin lesions and grade	Workers with skin lesions, n (%)					
	Hands			Forearms		
	Erythema	Scaling	Both	Erythema	Scaling	Both
None	15 (29)	24 (47)	8 (16)*	29 (57)	38 (74)	23 (45)*
Lesioned skin	36 (71)	27 (53)	20 (39)†	22 (43)	13 (26)	7 (14)†
I grade	29 (57)	19 (37)		19 (37)	10 (20)	
II grade	6 (12)	4 (8)		3 (6)	3 (6)	
III grade	1 (2)	4 (8)		0	0	

*Number (%) workers not affected by any skin lesions.

†Number (%) of workers affected by erythema as well as scaling.

skin creams was not a confounding factor for the skin status, because workers with erythema did not apply skin barrier or skincare creams more frequently than workers without erythema.

The influence of personal protective equipment on internal exposure

A multiple linear regression analysis was performed to determine the efficacy of the occupational personal protective equipment to reduce the internal exposure. Table 4 gives the results. Wearing breathing masks significantly reduced the internal exposure. Considering the daily wearing time of gloves we assume that this protective measure was also efficient in terms of reduced dermal uptake of AA. Frequent washing of hands correlated with a higher incidence of erythema (Pearson's correlation coefficient: 0.33, $p = 0.018$) and resulted in an increased internal exposure against aniline and o-toluidine. The results of internal exposure demonstrated that hand washing seems to better eliminate o-toluidine from the skin than aniline (Spearman's rank coefficients: 0.55 and 0.22 respectively, $p < 0.001$ and $p = 0.11$). The use of skincare creams at the workplace was associated with a reduced internal exposure ($p < 0.03$), probably owing to regenerative effects on the skin. Regarding the results of the clinical examination, skin barrier creams obviously do not improve the skin status, but with increasing application enhance the percutaneous absorption of aniline and o-toluidine ($p < 0.03$).

DISCUSSION

There are only a few studies investigating the efficacy of occupational personal protective equipment to reduce the internal exposure of hazardous substances in workers. To monitor the workplace exposure occupational hygienists predominantly assess the concentration of chemicals in the air. Although in our study the German occupational threshold limit values for aniline and o-toluidine were not exceeded (table 1), the concentration of o-toluidine in the workplace air

was high, as indicated by a factor of at least 25 compared with values found in indoor and outdoor air.^{22–23} The occupational exposure to aniline was only slightly elevated (range: <analytical detection limit–35.8, median: 1.51, 95th centile: 7.4) compared with the background exposure from other sources—for example, diet.²⁴ In our study, the concentrations of aniline at the workplace air were higher than in discotheques (by a factor of up to 25), which might be considered as an environmental worst-case scenario.²³ Comparing our results of aniline and o-toluidine in urine with data from the literature, we proceed from the assumption that the internal exposure in the workers resulted primarily from occupational exposure.^{22–24}

In our study, non-smoking workers tend to have higher internal exposure for aniline and o-toluidine than smokers. These differences can be explained by the higher external exposure of non-smokers, especially for o-toluidine, compared to smokers. There is no additional intake of AA through smoking. The intake is mainly influenced by the workplace exposure. Therefore, and owing to the limited number of variables acceptable for our model, smoking was not included in the multiple linear regression analysis.

The ambient air concentrations of hazardous substances give insufficient information on the individual exposure of workers, and this can be determined only by biological monitoring.²⁵ The urinary concentrations of AA for the German general population compared with our study group were about 6.8-fold lower for aniline and 2.8-fold lower for o-toluidine (median values) up to a maximum difference by a factor of 24 for o-toluidine (table 1). Although the correlation of o-toluidine concentration in air and in urine, as well as for Hb-adducts was significant, this could not be observed for the aniline exposure. The significantly higher external exposure of the workers to o-toluidine compared to aniline can probably explain this result.

Hb adducts are a long-term parameter reflecting the cumulative internal exposure of about the last 4 months in accordance with the lifetime of the erythrocytes. For some AA,

Figure 1 Relationship between internal exposure expressed by the Hb adducts and erythema on hands. The large difference for the o-toluidine values between the workers with and without erythema made it necessary for a better data presentation to interrupt the y axis in the range 650–1150 ng/l. The bottom line of the box is the 25th centile, the top line is the 75th centile, the horizontal line in the box represents the median value and the filled square in the box represents the mean value. The upper whisker (vertical line) represents the highest values of Hb adducts without outliers. Extreme values are designated by an asterisk.

Table 4 Multiple linear regression analysis on the influence of occupational personal protective measures on the relative internal exposure

Variable	RIE of aniline		RIE of o-toluidine	
	β^* (95% CI)	p Value	β^* (95% CI)	p Value
Regression constant†	14.44 (9.53 to 19.36)	0.017	52.12 (40.91 to 63.34)	0.011
Age (years)	0.34 (0.27 to 0.40)	0.010	-0.19 (-0.34 to -0.05)	0.038
Wearing of breathing masks (yes/no)	-9.63 (-14.94 to -4.32)	0.028	-39.87 (-52.00 to -27.74)	0.015
Wearing of gloves (always, often, sometimes, never)	-2.69 (-3.28 to -2.09)	0.011	5.15 (3.80 to 6.50)	0.013
Daily wearing time of gloves (min)	-0.07 (-0.09 to -0.05)	0.014	-0.20 (-0.24 to -0.15)	0.012
Hand washing frequency at workplace (times/day)	0.35 (0.26 to 0.43)	0.012	-0.68 (-0.88 to -0.49)	0.014
Application of skin barrier cream (times/day)	3.54 (1.77 to 5.32)	0.025	16.45 (12.39 to 20.50)	0.012
Application of skincare cream (times/day)	-2.43 (-3.55 to -1.30)	0.023	-8.26 (-10.82 to -5.70)	0.016

RIE, relative internal exposure.

* β = regression coefficient with 95% CI.† R^2 (corrected) = 1.00.

significantly shorter cumulative exposure periods are expected from the determination of Hb adducts. However, the Hb adducts of AA still give information about the exposure situation several weeks earlier.²⁶ There are no literature data on aniline and o-toluidine Hb adducts for the German general population so far. Comparing the Hb adducts of our study group with values for the general population in other studies, the mean values in this study are higher by a factor of 1.4–7.0 for aniline and a factor of up to 18 for o-toluidine.^{27, 28} The workers in our study showed Hb adduct concentrations (mean values) for aniline of almost 2-fold lower and for o-toluidine of 20-fold lower than those of exposed workers with a high rate of bladder cancer in a US rubber industry plant.²⁹ Nevertheless, in this study a relevant internal occupational exposure was observed (table 1), which is a prerequisite to assess reliably the efficacy of occupational personal protective measures.

The point prevalence of skin lesions of the hands of workers in this study (82%) was higher than in our previous studies in dispatch department workers (73%) or in printers (75%).^{9, 10} These skin lesions were relatively slight. The apparently high percentage rate of workers showing impaired skin can be explained as minor skin lesions are generally accepted as a normal hazard of life.³⁰

Our study results do not allow us to identify a single agent for the development of skin lesions in workers. Irritant contact dermatitis in a work environment has mostly multifactorial causes. Of the workers, 62% regularly wore gloves, and 56% of the gloves used were made of rough cloth material. These gloves primarily prevent skin burns on the hands arising from contact with hot (about 180°C) rubber products during vulcanisation. Probably the rough material of the gloves is able to irritate the skin by mechanical friction. These gloves are also permeable to liquid chemicals. The exact breakthrough time of the cloth glove material is unknown, but it can be estimated to be in the range of few minutes. Skin occlusion from the cloth gloves is unlikely, but certain maceration in a wet environment can be expected from a long wearing time. Healthy skin with an intact stratum corneum forms a relatively effective biological barrier against external agents. In this study, workers with impaired epidermal barrier (erythema) showed a significantly higher internal exposure to AA than workers with healthy skin, when Hb adducts as a long-term indicator were taken into consideration (fig 1). Experimentally, both in vitro and in animals, impaired skin leads to an increase of percutaneous absorption of chemicals.^{31, 32} However, there are only few studies about the relationship of skin lesions and the percutaneous uptake of hazardous substances in exposed workers.^{9, 15} These studies showed a higher internal exposure to a glycol ether and carbon disulphide in workers with skin lesions compared with workers with healthy skin. This study shows, for the first time,

statistically significant differences for workers with slightly impaired skin.

Bioengineering methods, especially measurements of TEWL, are used as sensitive methods in studies to assess impaired epidermal barrier function in occupationally exposed workers.^{9, 10, 19} We did not find a significant correlation of TEWL with erythema or scaling at the hands and forearms in rubber workers as already observed in our study of dispatch department workers from printing plants, whereas in printers, a positive statistical trend between TEWL and erythema was found on the forearms.^{9, 10} Thus, in this study, the clinical examinations of the skin were superior to the TEWL measurements in determining the damage to the epidermal barrier. Additionally, TEWL values did not show a relationship to the parameters of current and long-term internal exposure to AA. These findings are in agreement with the results of our previous study in printing workers exposed to a glycol ether.⁹

A multiple linear regression analysis was performed to determine the efficacy of personal protective equipment to reduce the internal and dermal exposure in rubber workers. The importance of percutaneous uptake on the total absorption can be deduced from the RIE index.¹⁵ The results in table 4 show that the wearing of breathing masks and increasing wearing time for gloves significantly reduces the internal exposure even for the workers wearing cloth gloves. A frequent washing of hands led to a higher incidence of erythema and consequently to an increased internal exposure. However, a better removal of o-toluidine from the skin by hand washing than aniline cannot be convincingly explained by the physicochemical properties of both AA (similar water solubility and logP of both compounds) or by the protonation of the amino groups in aqueous solutions (pK_a).

Skin barrier creams did not improve the skin status, but obviously significantly enhanced the percutaneous absorption of aniline and o-toluidine with increasing frequency of application (table 4). This phenomenon of skin barrier creams, known as “penetration enhancement”, is well established by experimental data in diffusion cell studies using various industrial chemicals.^{33–35} In the rubber industry, AA in the workplace air are primarily bound on particles.³⁶ The use of skin barrier creams with this type of exposure of hazardous substances at workplaces could promote the adherence of particles to the treated skin. Adams *et al* showed that for workers exposed to polycyclic aromatic hydrocarbons (PAH), the application of skin barrier cream on hands leads to an elevated percutaneous absorption for particle-bound PAH.³⁷

The increasing application frequency of skincare creams at the end of a work shift, however, was associated with a reduced internal exposure, although such effects were much less pronounced than the undesirable effects of enhanced penetration

Main messages

- This study demonstrates a consistent relationship between internal exposure to aromatic amines and the occurrence of impaired skin on the hands
- The internal exposure to aromatic amines increases with damage to the epidermal barrier
- Frequent use of skin barrier creams enhances the percutaneous uptake of aromatic amines, whereas skincare creams seem to be capable of supporting the regenerative effects of the skin, leading to a lower uptake

Policy implications

- Avoiding dermal contact with hazardous substances, especially when using skin creams, which could raise the total internal exposure
- Implementation of biological monitoring at workplaces, when sufficient exposure assessment to prevent dermal uptake is not practicable

in workers applying skin barrier creams. A scientifically based differentiation of skin barrier and skincare creams is not available. In Germany, skin barrier and skincare creams are distinguishable according to the recommendations of the manufacturers. Skin barrier creams should be applied before and during the work breaks, whereas skincare creams should be applied after the end of exposure. A classification of the creams based on the composition of ingredients does not exist.

In our study group, it appears that the more frequent use of skincare creams supports skin regeneration, owing to supposed regenerative effects on irritated skin.¹⁹ By contrast, the scientific evidence for the efficacy of skincare creams as an occupational protective measure is very weak.³⁸ In some workplaces skincare creams were usually applied after the end of exposure. Therefore, the effect of penetration enhancement did not appear. In view of the less investigated relationships between occupational protective measures and its influence on internal exposure, we included all variables simultaneously into multiple linear regression analyses. This model seems to be reliable, because it shows consistent associations for both AA and is supported by the evidence-based literature and the results of experimental studies.^{33–35 37 38}

AA are hazardous substances and exposure at the workplace should be minimised as far as possible. For a successful implementation of preventive measures one has to keep in mind that AA are easily absorbed through the skin.³⁹ Personal protection equipment, such as gloves and skin barrier creams, do not provide sufficiently safe protection to prevent percutaneous absorption. In contrast with common recommendations of manufacturers of skin creams, there is no evidence for the reduction of percutaneous absorption of hazardous substances by using skin barrier creams. Occupational hygienists recommending the use of skin barrier creams in workers handling hazardous substances should be aware that a percutaneous penetration enhancement could probably occur. The results of our study were gained with a relatively small group of workers and should be verified in larger studies in the future.

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