

Adverse Reactions after Tattooing: Review of the Literature and Comparison to Results of a Survey

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Key Words

Tattoos · Adverse skin reactions · Hazardous substances

Abstract

The number of tattooed people has substantially increased in the past years. Surveys in different countries reveal this to be up to 24% of the population. The number of reported adverse reactions after tattooing has also increased including infections, granulomatous and allergic reactions and tumors. However, the case reports do not reflect the frequency of adverse reactions. This review compares the medically documented adverse reactions published in 1991–2011 with the findings of a nation-wide survey that recently revealed the features and health problems associated with tattoos. To compare the data with the survey, the sex of patients was reported and the location and color of tattoos were evaluated. The results show clearly that colored tattoo inks are mainly responsible for adverse skin reactions and that tattoos on the extremities are involved most.

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Introduction

Tattooing is an ancient technique and human tattoos have been identified from ancient times, dating back even to the Stone Age [1]. In some cultures, e.g. Polynesian tribes, tattooing was always an im-

portant tool for their religion and hierarchy. The meaning of tattoos in the Western world during the past centuries was ambiguous and was consistently associated with low social status.

Nowadays, tattooing has become very popular in many individuals world-wide. The tattoos are black or multicolored and can be found all over the body, even as so-called permanent make-up [2]. There are many tattooed role models like football, pop or movie stars which has led to a broader cultural acceptance of tattoos. Medical complications after tattooing are often seen by physicians, but are generally unknown to the public. Tattooed individuals or people who consider getting a tattoo are often unaware of the possible effects on their health.

Colored tattoo inks often contain azo pigments that are primarily manufactured for other purposes (e.g. the staining of consumer products) with no established history of safe use in humans. In addition, such pigments can be decomposed during light exposure into hazardous aromatic amines and can be disseminated throughout the human body [3]. Many pigments and, consequently, the decomposition products have been found in the lymph nodes [4–10]. Thus, the tattoo inks, impurities and decomposition products get in close contact with the immune system. Although the first regulations regarding tattoo inks have appeared in some countries, hazardous substances can still be detected

[11–13]. Even if there is a declaration of ingredients, contamination by metal particles which may act as possible antigens cannot be excluded (e.g. nickel) [14, 15].

Black tattoo inks are frequently neither analyzed nor controlled prior to use. Their manufacturing process is based on soot, and so they contain toxic, mutagenic or carcinogenic compounds such as carbon black and polycyclic aromatic hydrocarbons (PAHs) or phenol [13]. Furthermore, PAHs can absorb UV radiation and generate cytotoxic singlet oxygen, which might affect skin integrity [13, 16].

A survey conducted by Huxley and Grogan in 2005 [17] showed that there 'were no significant relationships between healthy behaviors, health value and numbers of tattoos. A significant proportion of tattooed participants had not considered possible health risks, others were often unaware of potentially serious health problems'. People usually assume that there are governmental regulations for tattoo inks as exist for other products, for example, cosmetics. Unfortunately, this is not true. Over time, various adverse reactions occurring in connection with tattoos have been reported in the medical literature, mostly as case reports or small-case series.

These case reports describe the adverse reaction based on medical examination of the respective patients. However, these single reports cannot provide an overview on the frequency of such adverse reactions.

We recently conducted a nation-wide survey to ascertain the frequency of health problems that are associated with tattoos [18]. In this survey, tattooed people were asked to report on their health problems. The results, however, are based on pre-defined questions, which were answered by medical laypersons.

We aimed to compare the findings of medical reports and the results of the survey. When reviewing the medical literature on tattoo-associated health problems, we considered the reports that appeared in PubMed between 1991 and 2011, using the key words 'tattoos', 'tattooing', 'side effects', 'adverse effects', 'adverse events', 'tattoo reaction', 'health problems' and the various diagnoses in combination with 'tattoo'.

Results and Discussion

For many years, tattooists used inorganic pigments that contained heavy metals such as mercury, chromium or cadmium. Nowadays, the colored tattoo inks mainly consist of azo or polycyclic pigments [19]. These pigments comprise two perfect features for tattooing: they exhibit brilliant colors and are insoluble in aqueous tissue (fig. 1a). The chemistry of black inks, which predominantly contain carbon black, has not changed considerably. Carbon black is a powder that mainly comprises amorphous particles of carbon with diameters of a few tenths of a nanometer (fig. 1b).

Although they are injected into the human body, tattoo inks usually fulfil no pharmaceutical requirements and contain a long list of admixtures and impurities [13]; a first list of detected substances is shown in table 1. At present, this list is still incomplete and further chemical analysis of the tattoo inks on the market is required. It is already known that the chemistry of colored and black tattoo inks differs; hence these inks may contain different admixtures and impurities [13, 19]. Colored pigments (azo dyes and polycyclic compounds) show a complex chemical synthesis containing many byproducts, whereas black inks are produced by imperfect combustion of hydrocarbons yielding soot mainly containing PAH. Consequently, the skin might react differently to colored or black ink suspensions.

In our recently published survey, participants reported adverse reactions immediately after tattooing and 4 weeks afterwards. About 6% of the 3,411 participants

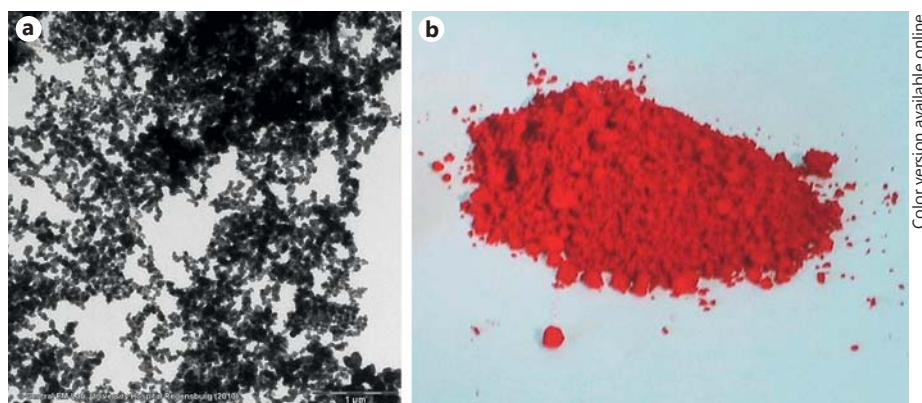


Fig. 1. Electron microscopy shows that tattoo inks (e.g. black inks, **a**) are usually small particles with diameters in the range of 30–100 nm. To produce a tattoo of about 100 cm², great amounts of tattoo inks are punctured into skin (carbon black, **b**).

reported persistent skin problems associated with their tattoos, which were frequently described as itching, intermittent or permanent edema or skin papules. Permanent edema could simply represent the formation of scars or granulomas. These side effects were significantly more frequent in female patients than in males and with colored rather than black tattoos [18].

In this review, we included 122 publications (280 patients) which deal with adverse reactions to decorative tattoos (table 2). We assigned the published cases to the following categories: granulomatous, lichenoid or hypersensitivity allergic reactions (category 1), infections (category 2) and tumors (category 3, see table 1). Some cases that did not fit into these categories are discussed separately. To compare the data with the survey, the sex of patients and location and the color of tattoos, reported in the reviewed case reports were depicted and evaluated in table 3.

Category 1: Granulomatous, Lichenoid or Hypersensitivity Allergic Reactions

The majority of papers (n = 62) describe allergic (often eczematous) and granulomatous reactions inside the tattooed skin area. As mentioned above, tattoo inks may contain various substances which have the potential to induce skin reactions. Once acute inflammatory changes have resolved, delayed reactions can also occur which may vary in time of occurrence from days to several years after tattoo application. Numerous clinical reports on these delayed reactions can be found (table 2).

A clear classification of the delayed tattoo reactions according to the clinical appearance and pathological patterns in the reviewed articles proved to be challenging, because the clinical manifestations were often not specific and the histological patterns overlapped. There are several reports of allergic tattoo reactions due to hypersensitivity to a tattoo pigment leading to contact or photoallergic dermatitis.

Various patterns of tattoo reactions were histopathologically described, including granulomatous, lichenoid [20, 21], lymphohistiocytic and pseudolymphomatous [22, 23]. Our classification of the reviewed articles is in line with the diagnoses given in the publications. Medical examination of patients was frequently restricted to a histopathology examination without further test procedures (e.g. allergic testing). Some authors state that of the colored inks, red most frequently caused delayed tattoo reactions [24]. This is usually confirmed by the fact that the emerging tattoo reaction is confined to the red in the tattoo [25]. In the past, red colorants often contained mercury or mercuric sulfide (cinnabar), which obviously acted as antigens.

Histopathological examination of tattoo reactions often showed only nonspecific granulomatous reactions. What the reviewed articles have in common is that granulomatous reactions after tattooing could be subdivided into 2 main categories: sarcoidal granulomas (fig. 2a) and other granulomatous reactions, e.g. foreign body granulomas. It was striking that the majority of cases, which can be assigned to ec-



Fig. 2. Examples of adverse tattoo reactions. **a** A male patient developed sarcoidal granulomas in a tattoo on the upper arm. **b** A female patient suffered from allergic contact dermatitis with a bacterial superinfection.

zematous, lichenoid or granulomatous reactions were observed in colored tattoos. As mentioned above, this fact might be due to the chemistry of the colored inks used. In view of the various substances in tattoo inks, it remains very difficult to find the trigger for skin reactions after tattooing. Unfortunately, the listing of ingredients is usually not available due to a frequent lack of regulations.

Sarcoidal Granulomas. Sarcoidal granulomas can occur either as an isolated reaction in tattooed skin or they can represent the first 'visible' signs of systemic sarcoidosis. A granulomatous tattoo reaction

Table 1. Substances detected in tattoo inks

Compounds	References	Comments
Monoazopigment Disazodiarylide Naphthol-AS-pigment Quinacridone Dioxazine Cu-phthalocyanine Cu/Al-phthalocyanine-Br _x Cl _y	[11, 19]	pigment in color inks
Mercury Cadmium Cobalt Chrome	[62]	colored compounds in inks
Carbon black Iron	[13, 63, 64]	'color' of black, brown inks
Titanium dioxide Aluminium	[19, 63]	used for whitening of inks
Naphthol-AS 2-Methyl-5-nitroaniline 2-5-Dichloraniline 4-Nitro-toluene	[65]	synthesis educts and decomposition products of azo pigments
PAHs Phenol	[13]	residue of pyrolysis present in black inks
Dibutyl-phthalate Hexachloro-1,3-butadiene Metheneamine Dibenzofuran Benzophenone 9-Fluorenone 3,6-Dimethyl-1 heptyn-3-ol 1,6-Hexandiole, oleamide 7-Hexyl-2-oxepanone 1,1'Oxybis-2-propanol Carbitol cellosolve 1,2,3,4-Tetrahydro-1-phenyl-naphthalene	[12]	impurities in black inks

should thus always lead to further clinical investigation for underlying sarcoidosis [26]. In the articles reviewed, most of the patients with sarcoidal granulomas in their tattoos displayed systemic sarcoidosis (n = 16), only two case-series comprising 8 patients reported sarcoidal granuloma in tattooed patients without systemic sarcoidosis [27, 28]. In some cases of sarcoidal granuloma, which appeared in multicolored tattoos, the skin reaction was confined to a single tattoo pigment i.e. red, black or blue [27, 29–34].

Other Granulomatous Reactions. The introduction of foreign substances into the

skin can promote a toxic or an immunological response and reactions to various tattoo pigments have been described [21, 35, 36]. The timing of these delayed-type hypersensitivity reactions may vary from shortly after the tattoo application up to several years later [37, 38], and may be triggered by retattooing.

Comparison to Survey. The results of the survey confirm the case reports, which clearly show more frequent skin reactions (category 1) to colored tattoos (83.3%) than to black tattoos (12.5%). The chemistry of color pigments like azo or polycyclic compounds is quite complex and comprises

Table 2. Adverse reactions to tattoos

	References	Number of papers and patients	Age (years)	Comments
<i>Category 1: Allergic, lichenoid or granulomatous reactions</i>				
Sarcoidal granuloma	[27, 34, 66–76]	19, 25	23–54	patients with systemic sarcoidosis: n = 16, patients without systemic sarcoidosis: n = 8 and an allergic cause assumed: n = 1 [27]
Other granuloma	[77–84]	8, 8	17–44	granulomatous reaction resolved after biopsy [80], granuloma annulare-like tattoo reaction [83], perforating granulomatous dermatitis reaction [84]
Allergic hypersensitivity reactions (eczematous and lichenoid reactions)	[14, 15, 21, 25, 37, 85–98]	19, 39	19–61	lichenoid tattoo reaction [15, 21, 85, 86, 91–93, 96], contact dermatitis, positive scratch test [88], contact dermatitis to red color, positive patch test [89, 90, 92], reaction confined to red tattoo ink [25] and contact dermatitis to India ink [95]
Pseudolymphoma	[20, 22, 23, 99–105]	10, 18	32–59	pseudolymphomatous tattoo reaction with lichenoid aspect [20]
Other	[50, 106–112]	6, 6	21–47	hypersensitivity vasculitis [106, 107, 110–112], reaction to red tattoo ink [106] association with red tattoo ink is assumed, no microbiological examination of the tattoo ink [107], lichen sclerosus et atrophicus [108], scleroderma-like reaction restricted to red parts of tattoo [109], tattoo-induced lymphadenopathy in a patient with multiple tattoos [50]
<i>Category 2: Infections</i>				
Viral warts	[43, 113–116]	5, 5	17–37	
<i>Molluscum contagiosum</i>	[117–119]	3, 3	20–24	
HSV (<i>Herpes compuncctorum</i>)	[120]	1, 1	30	
Hepatitis C	[121–124]	4, 6	25–40	and epidemiologic articles [125, 126]
Inoculation tuberculosis (<i>M. tuberculosis</i> complex)	[127–129]	3, 4	33–40	
Inoculation leprosy (<i>M. leprae</i>)	[130–132]	3, 33	21–40	
Nontuberculous mycobacteria	[44, 133–141]	10, 47	20–51	often gray color due to dilution with tap water [138], 7 female patients treated by the same cosmetician [141]
CA-MRSA with skin and soft tissue infections	[142, 143]	2, 44	15–42	44 recipients of tattoos from 13 unlicensed tattooists in 3 states (Ohio, Kentucky, and Vermont, USA)
Other bacterial infections	[144–149]	5, 6	18–44	toxic shock syndrome [144], ‘necrotizing cutaneous reaction’ [145], epidural abscess [146], endocarditis [147, 148] and polymicrobial septicemia [149]
Tinea	[45]	1, 1	unknown	
Leishmaniasis	[150]	1, 1	30	visceral leishmaniasis with cutaneous lesions in tattoo of an HIV-positive patient
<i>Category 3: Tumors</i>				
MM	[151–158]	8, 8	26–56	several case reports of tattoo pigment in sentinel lymph node mimicking MM
BCC	[54, 159–162]	5, 6	35–72	2 older ladies from Iran: head tattoo
SCC	[163, 164]	2, 3	30–47	
KA	[165–168]	4, 11	36–66	in 82% of cases association with red tattoo color [168]
Other	[47, 169–172]	4, 5	20–41	dermatofibrosarcoma protuberans [169, 172], cutaneous leiomyosarcoma [170] and ‘autograft nevus’ [171]

Table 3. Review of the medical reports listing: sex of patients and tattoo location and color

	Patients number	Sex			Location				Color of tattoo ink		
		male	female	un- known	extremities	trunk	head	un- known	black	colored	un- known
<i>Category 1</i>											
Allergic reactions	39	25	11	3	14	2	4	19	2	37	0
Sarcoidal granuloma	25	12	12	1	16	2	3	4	9	12	4
Pseudolymphoma	18	11	7	0	11	3	0	4	0	18	0
Nonsarcoidal granuloma	8	4	4	0	4	1	2	1	0	8	0
Other	6	4	2	0	3	2	0	1	1	5	0
Subtotal	96	58.3%	37.5%	4.2%	50.0%	10.4%	9.4%	30.2%	12.5%	83.3%	4.2%
<i>Category 2</i>											
Lupus vulgaris	4	1	3	0	4	0	0	0	3	0	1
Leprosy	33	0	33	0	30	1	2	0	0	33	0
Nontuberculous mycobacteria	47	36	11	0	13	1	7	26	13	9	25
CA-MRSA	44	32	12	0	0	0	0	44	0	0	44
Viral warts	5	4	1	0	2	3	0	0	0	3	2
<i>Molluscum contagiosum</i>	3	2	1	0	2	1	0	0	2	1	0
Hepatitis C	6	3	3	0	0	0	3	3	0	0	6
HSV (<i>Herpes compuncctorum</i>)	1	1	0	0	0	0	0	1	0	0	1
Tinea	1	0	0	1	0	0	0	1	0	0	1
Leishmaniasis	1	1	0	0	0	0	0	1	0	0	1
Other bacterial infections	6	4	2	0	2	3	0	1	3	1	2
Subtotal	151	55.6%	43.7%	0.7%	35.1%	6.0%	7.9%	51.0%	13.9%	31.1%	55.0%
<i>Category 3</i>											
KA	11	8	3	0	10	1	0	0	0	11	0
MM	8	7	1	0	4	3	0	1	4	3	1
BCC	6	3	3	0	1	3	2	0	3	2	1
SCC	3	1	2	0	1	0	1	1	1	1	1
Other	5	5	0	0	5	0	0	0	2	1	2
Subtotal	33	72.7%	27.3%	0%	63.6%	21.2%	9.1%	6.1%	30.3%	54.5%	15.2%
Total	280	58.6%	39.6%	1.8%	43.6%	9.3%	8.6%	38.6%	15.4%	51.8%	32.9%

many hazardous substances that have the potential to provoke adverse skin reactions. The high frequency of adverse reactions to colored inks is of particular importance, because colored tattoos comprise about 40% of tattoos, less frequent than black tattoos (about 60%). The case reports show more frequent problems in males (58.3%) than in females (37.5%). This is contrary to the survey, in which males reported less adverse reactions associated with tattoos than females. On the one hand, this might be due to attitudes, with males underplaying problems with tattoos. On the other hand, the number of patients in the case reports of category 1 (n = 96) is clearly smaller than in the survey (n = 3,411) [18]. The survey showed that 45.2% of people have tattoos on the trunk, 50.8% on the extremities and 2.7% on the head and neck. When review-

ing the medical reports (table 3), a much higher incidence of adverse reactions is reported for the extremities (50.0%) than for the trunk (10.4%). In addition, the head as a tattoo location is mentioned an above-average number of times, possibly due to the reported cases of reaction to permanent make-up. As 30.2% of the adverse reactions were not assigned to a specific location, it remains difficult to assess these contradictory results. Some of the substances (table 1) in tattoo inks (e.g. PAHs and phthalocyanines) are excellent photosensitizers that can generate reactive oxygen species [13] in tattooed skin exposed to light. We could tentatively speculate that tattoos on the head and extremities are more frequently exposed to solar radiation, which might be what causes a higher rate of adverse reactions.

Category 2: Infections

Tattooing entails physical injury of relatively large skin areas that may promote the transdermal transmission of viral and bacterial infections, depending on the conditions of hygiene during tattooing [39]. In most of the published case reports, insufficient or a complete lack of sterilization procedures in the tattoo parlors was regarded as responsible for the transmission of infectious diseases. There are 3 potential origins of infections after tattooing. Firstly, the tattoo ink itself can be contaminated, especially by bacterial pathogens. Secondly, in the case of an inadequate disinfection of the skin area to be tattooed, residential bacteria can enter the skin during the tattooing process. Thirdly, during the healing process of the injured tissue after tattooing, patients often notice pruritus and

burning [18], with the risk of superinfecting the tattooed skin area due to scratching and therefore inoculating microorganisms (fig. 2b).

Viral Diseases. According to epidemiological studies and case reports, there is strong evidence for the transmission of hepatitis B and C virus infections from tattooing (table 2). Tattooing could also, theoretically, transmit the human immunodeficiency virus (HIV) [40–42], although we found no cases of HIV infection in the literature directly related to tattooing. Cutaneous infections caused by human papillomavirus (HPV) include common, planar and juvenile warts. Cases of HPV infection have been observed due to transmission of the virus during the process of tattooing or the presence of HPV in the tattoo dye. In one case, a 32-year-old man experienced development of multiple warts restricted to the tattooed area after sunburn damage. The tattoo had been performed 2.5 years previously, so in this case, HPV persisted asymptotically for a long period before activation by local UV-induced immunosuppression resulting in multiple warts [43]. There are also reports on the appearance of *Molluscum contagiosum* caused by *Poxviridae* and of Herpes simplex virus (HSV) infection in tattooed areas, also via transmission during the tattooing process (see category 2, table 2).

Bacterial Infections. Reported cases on bacterial infections related to tattooing comprise – among others – *Streptococcus pyogenes* leading to impetigo, erysipelas and even septicemia, *Staphylococcus aureus* causing the rare toxic shock syndrome, skin and soft tissue infections caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), infections with atypical mycobacteria and even *Mycobacterium leprae* which causes leprosy. These bacterial infectious complications are caused by insufficient personal hygiene or lack of hygiene control measures in the tattooing process. Although hygiene in tattoo parlors has improved, official inspection is still rare. In recent years, several reports of infections with atypical mycobacteria after tattooing were published [44]. A few cases of leprosy after tattooing in India were caused by insufficiently hygienic conditions during the tattooing process, which had been performed by roadside tattooists. There was only one report on cutaneous fungal infections in the literature reviewed [45] and a ophthalmologic report of a 40-year-old asplenic man

with *Candida albicans* endophthalmitis of the right eye 1 week after tattooing [46].

Comparison to Survey. The detailed results of the survey showed that about 0.5% of tattooed participants suffered from infections manifesting as pus-filled skin areas [18]. As about 8 million people in Germany have tattoos, we estimate that about 40,000 people would have had bacterial infections in the tattooed skin area. These data fit with the high number of reported bacterial infections in the literature (table 3), in particular when extrapolating this number to other countries. The survey showed that the person's sex played no role for the risk of developing pyogenic bacterial infections. The case reports in the literature proposed a slightly higher number of male patients affected by bacterial infections than females. Again, tattoos performed on the extremities are more frequently involved in bacterial infections than those on the trunk. Unfortunately, in the literature, location was not provided in more than half of the cases. When asked about hepatitis, about 0.6% of the survey participants reported a positive test shortly after tattooing, but causality cannot be claimed here.

Category 3: Tumors

The occurrence of benign tumors like seborrheic keratosis, histiocytofibroma, epidermal cysts and milia after tattooing is well known; cases are only rarely published [47].

Several malignant lesions have occurred in tattoos including basal cell carcinoma (BCC), keratoacanthoma (KA), squamous cell carcinoma (SCC), malignant melanoma (MM) and dermatofibrosarcoma protuberans (table 2). MM has been reported to occur in tattoos, vaccination scars and tattoo sites used for radiotherapy field marking. To our knowledge, there are only 8 documented cases of MM after tattooing in the medical literature during the years reviewed (1991–2011), but there are several case reports on tattoo pigment in sentinel lymph node biopsies mimicking MM [4, 8, 48, 49]. In all these cases, the migration of tattoo pigments via lymphatic drainage was initially considered as evidence for metastatic tumors until proper histopathological examination. Meanwhile, the transportation of tattoo inks, admixtures and impurities from the skin to the lymph nodes is a well-known fact [3, 8, 50]. Tattooists often also tattoo into pre-existing nevi and pigmented lesions, thus impeding a correct clinical and dermatoscopic evaluation [51, 52].

BCC has been rarely found to appear after trauma, for example in surgical scars [53]. This is also the case with KA. Engel et al. [54] made quite an interesting observation. They reported an uncommon case of BCC of the thumb of a 58-year-old man due to an azo-pigment-containing colorant repeatedly used as a marker of fishing bait. The authors stated that azo pigment in the colorants can be cleaved to carcinogenic amines under light exposure, in particular after incorporation into the human body.

In view of the large number of people that have tattoos and the few cases of malignant lesions that have been reported so far, at present, the association might be coincidental. Numerous factors could be involved, including intradermal injection of potentially carcinogenic substances, exposure to UV radiation and genetic factors. Recently, high amounts of PAH such as benz(a)pyrene were detected in commercially available black tattoo inks [13]; these obviously enter the skin along with the black ink. At the same time, about 10% of the participants in our study reported having melanocytic nevi within tattooed skin areas. Whether the injection of such hazardous substances might affect melanocytic nevi is unclear so far and should be determined by means of epidemiological studies.

It is to be kept in mind that dark black tattoos cannot only impede a correct clinical and dermatoscopic evaluation, but can also mask the development of new melanocytic lesions or the change of existing nevi. Physicians should report all skin tumors which they observe in tattooed skin.

Comparison to Survey. Skin cancer associated with tattooed skin was rarely reported in the survey (0.1%, all male), which was equivalent to about 8,000 cases in Germany. The review of medical reports shows that 24 patients with tumors in tattooed skin were male (24/33). The affected tattoo was mainly colored (18/33), which again confirms that colored tattoos cause more adverse reactions than black tattoos (see also category 1, table 3). Again, the extremities and head (total: 72.9%) were more frequently involved as locations than the trunk. Exposure of tattoos to solar radiation might also play a role.

Miscellaneous Cutaneous

Complications after Tattooing

Several articles reported a flare of an isomorphic Koebner response after tattoo application in patients with active susceptible disease, e.g. psoriasis [55–57], lichen

planus and vitiligo. Punzi et al. [56] reported a 26-year-old male patient who developed psoriasis plaques in a tattoo 1 week after tattooing by an amateur. Subacute cutaneous and discoid lupus erythematosus following dermal injury during tattoo placement and pyoderma gangrenosum have also been described [58–61].

Although lichen planus lesions can theoretically develop in tattooed skin, they are difficult to differentiate from the lichenoid reactions described above and therefore we found no specific report on this diagnosis.

Conclusions

When comparing the results of the survey with the data of the reviewed case reports, there are some concurring and some contradictory results. However, the comparisons clearly show that colored tattoo pigments more frequently cause skin problems that are associated with granulomatous, lichenoid or hypersensitivity allergic reactions and even skin tumors.

It is also very interesting that the reported skin problems are clearly more frequent

for tattoos on the extremities than for those on the trunk, even though the frequency of tattooing is nearly the same for both locations. As photosensitizing agents were detected in tattoo inks, the more frequent exposure of the extremities to solar radiation might have been a contributing factor.

The review of published case reports show that the cause of the skin reactions was mainly investigated by histopathology. In the case of allergic or granulomatous reactions, in general, no further testing was applied to establish what triggered such reactions. However, diagnostic procedures to prove allergic reactions to tattoo colors remain challenging due to the numerous and usually unknown substances in the tattoo inks. So patch testing, as performed in several studies to confirm the diagnosis 'allergic reaction', might not be the appropriate approach. Subsequently, many authors limit their diagnosis to the histopathological pattern (e.g. 'granulomatous type IV-reaction') without a definite clinical diagnosis. This reflects the problematic interpretation of the observed 'patterns' and also hampers effective regulating of the use of tattoo inks by legislation. In the case of

infections, hygiene plays an important role, which includes the tattooing practice and the purity of the used tattoo inks.

The most important issue, the possible role of tattoo inks in the formation of tumors, is unclear so far. The review retrospectively considers the medical reports of the past 20 years (1991–2011). In view of the latency period for carcinogenesis, this time span should be correlated to the tattooing practice in the decades prior to this period. Tattooing has become increasingly popular in this period and the chemistry of tattoo inks has changed. The results may change within the next 20 years. It is obvious that well-known mutagenic or carcinogenic substances like PAHs and many amines should not be present in tattoo inks.

In the light of these results, in particular those regarding colored inks, we urgently recommend the regulation of tattoo inks that leads to application of inks that do not contain hazardous substances. A first step would be: the substances that are not allowed to be used in cosmetics on top of the skin should certainly not be allowed to enter the skin via the puncturing involved in tattoos.

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